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New direct oral anticoagulants and gastrointestinal bleeding

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Keywords: Oral Anticoagulants; Gastrointestinal Hemorrhage; Thrombosis; Bleeding**.**

Since their launch in 2008, the new direct oral anticoagulants (DOACs) have been increasingly prescribed in clinical practice, gradually replacing anti-vitamin K (warfarin) agents in the prevention of thromboembolic

events in non-valvular atrial fibrillation, and the treatment and prevention of deep thrombophlebitis. Their efficacy has been supported by several clinical trials [1].

These anticoagulants are factor Xa or anti-Xa inhibitors, inhibiting the main coagulation pathway. They have the advantage of a rapid and powerful action compared with warfarin therapy. They also do not require biological monitoring of anticoagulation levels.

A meta-analysis concluded that DOACs cause as much serious bleeding as warfarin therapy.

However, they are more associated than warfarin with gastrointestinal bleeding, particularly gastroduodenal bleeding [1]. This bleeding remains a frequent cause of admission to emergency departments.

The occurrence of gastrointestinal bleeding on anticoagulants should prompt discussion of temporary discontinuation of the anticoagulant and correction of the coagulopathy, depending on the severity of the bleeding and the patient's thrombotic risk. This management must be coordinated between the emergency physician, cardiologist, and gastroenterologist. It is important to note the time of the last DOACs dose, as DOACs generally lose their anticoagulant activity within 12 to 24 hours, given their relatively short half-life. Thus, most gastrointestinal bleeding can be managed by stopping the DOACs and waiting for the anticoagulant effects to wear off. Severe gastrointestinal bleeding may require plasma residual levels of DOACs, transfusion of hemostatic concentrates, and, in certain situations, administration of specific antidotes or even hemodialysis. It should be noted that the DOAC antagonist, used in cases of severe acute gastrointestinal bleeding, may increase the risk of thromboembolism. To date, little scientific data is available to assess this risk.

In all cases, the correction of coagulopathy should not delay digestive endoscopy or endoscopic or radiological hemostasis. Digestive endoscopy has made progress in the management of gastrointestinal bleeding. In the case of upper gastrointestinal bleeding, endoscopy enables lesion diagnosis, endoscopic hemostasis, and assessment of the risk of hemorrhagic recurrence. However, despite advances in medical and endoscopic management, morbidity and mortality remain high. This is particularly true of associated comorbidities and treatments, notably anticoagulants in the elderly [2].

Once gastrointestinal bleeding has been controlled, the timing of resumption of anticoagulant therapy with DOACs - within 7 days or sooner - depends largely on the patient's thromboembolic risk [3].

The difficulty in managing gastrointestinal bleeding associated with DOACs lies in assessing the risk of bleeding (or recurrence of bleeding) and thromboembolism. These are two life-threatening events on which the morbidity and mortality of gastrointestinal bleeding in these patients largely depend. The widespread use of these new anticoagulants is prompting clinicians to be vigilant in prescribing them, to avoid complications such as gastrointestinal bleeding. Studies focusing on managing gastrointestinal bleeding associated with DOACs are still to come, with the development of antidotes.

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ORIGINAL RESEARCH

B-lines Ultrasonography Assessment by Nurses for the Diagnosis of Heart Failure in the Emergency Department

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Abstract

Introduction: The use of lung ultrasonography (LUS) for B-lines quantification is pivotal in the rapid diagnosis of heart failure (HF). It has even been suggested that nurses can perform this test accurately.

Aims: Our study aimed to evaluate the accuracy and reproducibility of B-line quantification by emergency medicine (EM) nurses after 12-hour training in the diagnosis of HF in patients admitted to the emergency department (ED) with acute dyspnea.

Methods: This prospective cross-sectional study included 216 patients admitted to the ED with a chief complaint of acute dyspnea, conducted between January 2018 and 2019. LUS was performed by EM nurses and a trained emergency physician. The participating nurses completed a 12-hour structured LUS training course. The LUS score was calculated. The diagnosis of heart failure was the judgment of a blinded expert emergency physician unaware of the lung ultrasound findings. The agreement between physicians and nurses was assessed, and the diagnostic performance of the LUS score was evaluated by the area under the receiver operating characteristic (ROC) curve.

Results: In total, 216 patients with acute dyspnea were screened. There was good agreement between nurses and physicians regarding the diagnosis of HF (kappa value = 0.787). The discriminating power of the LUS score calculated by emergency physicians and nurses was good (area under the ROC curve of 0.8 and 0.73, respectively).

Conclusion: In our study, we have shown that following LUS short-course training, EM nurses could reliably diagnose HF in patients presenting to the ED with undifferentiated dyspnea.

Keywords: Lung ultrasonography, B-lines, heart failure, nurses, lung ultrasonography score

INTRODUCTION

Acute dyspnea is a frequent clinical emergency and one of the primary causes of in-hospital admissions.[1] Although clinicians are often faced with a broad differential diagnosis, heart failure (HF) remains one of the most common causes that need to be thoroughly investigated and can be challenging to distinguish from other etiologies. Although a prompt and accurate diagnosis is vital to ensure optimal treatment, the diagnostic modalities available for assessing dyspneic patients with suspected HF were characterized by a lack of specificity or sensitivity.[2,3] Echocardiography still remains the most commonly performed non-invasive cardiac imaging test, and has been shown to play a crucial role in the diagnostic workup of HF, but such a procedure requires high skills and is not always available in many emergency departments (EDs).[4,5] Recently, lung ultrasound (LUS) has rapidly emerged as a useful alternative tool that can be performed by novice sonographers.[6,7] LUS offers a myriad of advantages, the most important of which is that this non-invasive procedure is easily available at the bedside, can be performed quickly, and has a high accuracy rate, thus allowing a more timely detection and a more targeted treatment.[8,9] Consequently, LUS has become increasingly used in clinical practice, particularly in acute care settings.[10] It has even been suggested that nurses can perform this test accurately, but data reporting this important issue is limited.[11] Recent studies have shown that it is possible to achieve proficiency in quantifying B-lines on LUS after 2 hours of training.[12] Nonetheless, further studies are still needed to identify and validate the findings reported in these studies. The purpose of our study was to assess the accuracy and reproducibility of B-line testing performed by emergency nurses who received 12-hour training, in the diagnosis of HF in patients admitted to the emergency department with acute dyspnea.

PATIENTS AND METHODS

Research design: A prospective cross-sectional study was carried out in the EDs of Fattouma Bourguiba University Hospital of Monastir (Tunisia), Regional Hospital of Ksar Hellal (Monastir), Taher Sfar University Hospital of Mahdia (Tunisia), Sahloul University Hospital of Sousse (Tunisia) and Hached University Hospital of Sousse, from January 2018 to January 2019.

Participants and study setting: All patients admitted to the ED with a chief complaint of acute dyspnea were included. Patients aged less than 18 years, pregnant women, those in need of endotracheal intubation, and those considered too unstable to undergo sonography were excluded. Patients with post-traumatic dyspnea and those who expressed unwillingness to participate in this study were also excluded. All patients who met the inclusion criteria underwent a complete physical examination. Blood pressure, heart rate, and pulse oximetry were measured, and oxygen therapy was administered via face masks, as needed. Each patient underwent two LUS tests using a

SonoSite M-Turbo machine (Sonosite Inc., Bothell, WA, USA) and a broadband curved array probe (3.5-5 MHz). All tests were performed by a nurse and an emergency physician within the first six hours after ED admission. The order of testing of nurses and physicians was randomly determined according to electronic randomization. To avoid breaking the blind protocol, patients were asked not to disclose any information about their medical history to the LUS operators. All nurses participating in the study were allowed to perform this examination only after completing a 12-hour training session with at least 10 clinical tests supervised by a certified emergency physician who had completed a full mentoring program for "Ultra-Sound Life Support."

Data collection: The following data were collected: age, sex, medical history, ongoing treatment, and physical examination findings. We also collected the results of standard biological tests, blood gas, brain natriuretic peptide (BNP), chest X-ray, and electrocardiogram. All included patients underwent echocardiography to measure left ventricular ejection fraction and other relevant parameters.

Interventions: Depending on their respiratory tolerance, the patients were positioned in a semi-recumbent or supine position. For each side of the chest, 4 zones were assessed: 2 anterior and 2 laterals.[13] The LUS score, which was obtained by summing the B lines found in the 8 lung zones, was calculated.[11] B-line was defined as a vertical bright echogenic bundle with a narrow basis, spreading from the transducer to the deepest part of the screen[14]. The probability of HF was assessed according to the following ordinal scale: unlikely if the B-line score was < 15, likely if the B-line score was between 16 and 29, and very likely if the B-line score was ≥ 30. The final diagnosis of the origin of the dyspnea in each patient was evaluated by independent emergency physicians after examining the patient's medical files: clinical history, physical examination findings, diagnostic tests (chest X-ray, echocardiography, and brain natriuretic peptide), treatment, and outcome. In the event of disagreement, a third senior doctor was consulted and given the responsibility of making a conclusive assessment. The referring physician had no information regarding LUS results and the diagnosis. Informed consent was obtained from all the patients prior to the start of the study.

Statistical analyses: After normality distribution analysis, variables were expressed as the arithmetic mean and standard deviation (SD) or the median and 95% confidence interval (or interquartile range). Patients with HF (HF group) and those without HF (non-HF group) were compared using the Student's t-test for continuous variables and the Chi-2 test for categorical variables. Statistical significance was less than 0.05. The area under the receiver operating characteristic (ROC) curve was used to assess the discrimination power of the LUS scores calculated by the nurses and emergency physicians. An area under the curve (AUC)

value of 1 denotes a perfect test; an AUC of 0.5, denotes a worthless test and is not better than random prediction; and an ACU greater than 0.70 means that the accuracy of the diagnostic test is at least acceptable. The kappa agreement index for ordinal LUS scale classification was used to assess the agreement between the nurses' and experts' interpretations. The agreement was considered "low" when the kappa value was lower than 0.40 denoted a poor agreement, from 0.41 to 0.60 was considered "fair", from 0.61 to 0.80 "good" and from 0.81 to 1 "excellent". The Bland-Altman plot was used to assess the agreement for the LUS score as a continuous variable. The difference between the B-line score pairs around the average line and between the lines of − 2 and + 2 SD was considered a good match. The data obtained in this study were collected, recorded, and analyzed using SPSS software (version 18.0; Chicago, IL, USA).

RESULTS

A total of 216 patients (119 men and 107 women) with acute dyspnea were screened during the study period. Table I summarizes the characteristics of these patients. The patients were classified into two groups based on their final diagnoses. The HF group included 121 patients (56%) with an established diagnosis of heart failure. The non-HF group consisted of 95 patients with dyspnea attributed to exacerbation of chronic obstructive pulmonary disease (n = 40), pneumonia (n = 23), acute asthma (n = 6), and pneumothorax (n = 4).

Table I: *The characteristics of the 216 patients:*

	N=216
Age (years), mean(SD)	68 (13)
Sex ratio (male/female)	1.22
Past medical History, n (%)	
COPD	69(31.8)
Asthma	8(3.7)
hypertension	117(53.2)
Diabetes mellitus	93(42.3)
Chronic heart Failure	43(20)
Coronary artery disease	36(16.7)
Treatments, n (%)	
Angiotensin-converting	76(35)
enzyme (ACE) inhibitors	68(31.3)
Diuretics	45(20.7)
β 2 mimetics	151 (69.9)
Association	28(12.9)
No treatment	
Chest X-ray, n (%)	
Cardiomegaly	98(45.2)
Interstitial edema	152(70)
Vascular pulmonary redistribution	71(32.7)
Pleural effusion	59(27.2)
Atrial fibrillation	39(17.7)
LV ejection fraction n=186 (86.2%), n (%)	53(24.4)
EF <40%	37(17.1)
40=< EF<=49	96(44.7)
EF>=50%	828.7(455)
BNP (pg/ml), median (IQR)	

IQR interquartile range; *COPD* chronic obstructive pulmonary disease; *LV* left ventricle; *BNP* brain natriuretic peptide; cardiomegaly, cardiothoracic ratio > 0.5; HF heart failure

Based on the area under the curve, the discriminating power of the LUS score was found to be good. In fact, it was 0.8 and 0.73, for emergency physicians and nurses respectively. Using a cut-off of 15, the LUS score showed that sensitivity, specificity, negative predictive value, and positive predictive value were similar with trends to moderately higher sensitivity for the LUS score performed by seniors (83.3% vs. 80%) and higher specificity (81.2% vs. 66.7%). Table II summarizes the performance of LUS scores in the diagnosis of HF.

Table II: *Performance diagnosis of LUS score at a cut-off of 15 in the diagnosis of HF*

	Physicians	Nurses
Sensitivity (%)	83.3	80
Specificity (%)	81.2	66.7
Positive predictive value (%)	79.2	86.4
Negative predictive value (%)	76.4	60.3

The LUS score was suggestive of HF (B-line score ≥ 15) in 91 patients (42.1%). A good concordance was found between nurses' and physicians' interpretation as illustrated in the Bland-Altman plot (mean differences between LUS score = 0.16 ± 7.97, p: 0.53) (Fig. 1). Excellent agreement was observed between nurses and seniors regarding the determination of HF diagnosis (LUS ≥ 15) for both models, as shown by a kappa agreement index value of 0.78.

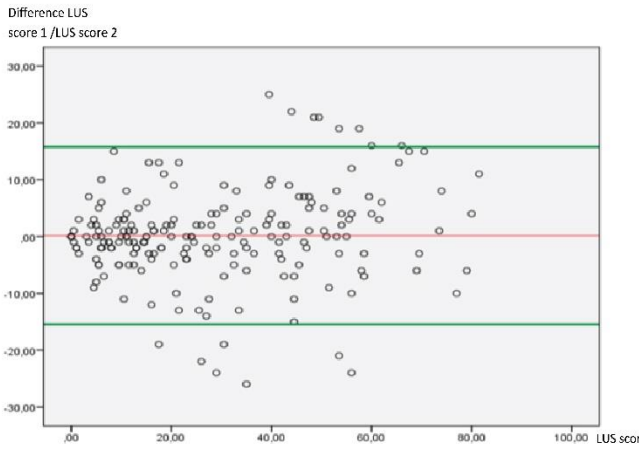

Fig 1: *The Bland-Altman plot for ultrasound lung comets scores. LUS score1 denotes the ultrasound lung comets score measured by the first operator; LUS score2 denotes the ultrasound lung comets score measured by the second operator of the same pair of sonographers; shaded area denotes agreement limits*

DISCUSSION

In our study, we showed that lung ultrasound B-line assessment is a reliable and reproducible tool that can enhance inexperienced nurses' ability to diagnose AHF in patients admitted to the ED for undifferentiated dyspnea. Improving paramedics' ability to perform a rapid evaluation and compare the initial findings with those of a subsequent scan is one of the main practical advantages of using LUS for the detection of HF. It can shorten the time between admission and diagnosis in EDs and in overcrowded medical facilities.

In 1989, Lichtenstein et al[15], has developed the concept of whole-body ultrasound and extended it to the lungs. Their work led to the development of the BLUE protocol published in 2008, which represented a standardized algorithm for triage and diagnosis of acute dyspnea in the ED.[13] Over the years, many studies have demonstrated the effectiveness of B-lines in the diagnostic evaluation of patients with HF with higher accuracy than clinical examination and chest X-ray.[9,16] The European Society of Cardiology stated that bedside LUS is a potentially useful way to assess pulmonary congestion and recommended it as a first intention test in the assessment of suspected AHF.[17] Prior studies have suggested that LUS for B-line assessment is one of the easiest ultrasound exam types to perform and interpret.[11] Many studies have demonstrated that after a short training session, novice learners with the ability to quantitatively assess LUS B-line presence using images that they have obtained on their own.[18]

A prospective study performed by Chiem et al[19] compared the performance of experienced and novice LUS sonographers in assessing the probability of AHF in 380 patients. Sixty-six emergency medicine residents who participated in this study were included. The AUCs for novice and expert sonographers were 0.77 (95% CI = 0.72 to 0.82) and 0.76 (95% CI = 0.71 to 0.82), respectively. The authors concluded that inexperienced sonographers can identify ultrasound B-lines with a sensitivity and specificity higher than 80% after brief training and that LUS has a positive predictive value for the diagnosis of AHF in the hands of both beginners and expert sonographers. In relation to this, we recently performed a similar study, in which we showed that lung ultrasound B-line assessment has good accuracy and excellent reproducibility in the diagnosis of AHF when performed by emergency medicine residents following a short training program.[14] Risler et al[20], in a prospective study assessing medical students' performed LUS in patients admitted to the hospital with a presumed diagnosis of decompensated AHF, found an almost perfect agreement between novice and expert practitioners. In an observational pilot study conducted on 63 paramedics, Schoeneck et al[21], showed good inter-rater agreement for the detection of any B-lines with expert sonographer interpretation. They concluded that larger funded trials will be needed to provide more definitive data. Ünlûer et al[22] conducted a prospective study to evaluate the accuracy of emergency nurse-performed LUS in patients admitted to the ED to establish whether their dyspnea had a cardiac or non-cardiac cause. The concordance between nurses' diagnosis and definitive diagnosis was excellent (kappa value, 0.917). Another study was carried out by Mumoli et al[11] assessing the diagnostic accuracy of pulmonary ultrasound performed by nurses in patients with acute dyspnea. They included 226 patients and showed a sensitivity of 95.3%, specificity of 88.2%, positive predictive value of 87.9%, and negative predictive value of 95.5%. The post-test probability of acute cardiogenic dyspnea increased to 88% with positive LUS and decreased to 4% when LUS was negative. The authors concluded that, overall, LUS performed by nurses with limited clinical and ultrasound experience provided good accuracy in the diagnosis of cardiogenic dyspnea. Although LUS is increasingly used as part of the primary assessment or follow-up of dyspneic patients, there is no international consensus on education, skills assessment, and certification. Based on current published studies, it is not possible to develop clear guidelines for future LUS training and certification. This systematic review showed that there is a lack of LUS learning studies. We must wait for other research studies, including validated tests, with better theoretical and practical modalities to obtain more informed conclusions.

Involving nurses in this work can only be beneficial because the learning method places them at the center of the training process. With adequate accompanying and guidance, they can benefit from active learning and improve the quality of patient care provided for patients with acute dyspnea.[23] In fact, our protocol has allowed us to obtain positive and promising

results for all nurses, showing that a tool like the LUS, if mastered, can be integrated into the emergency triage process effectively for dyspneic patients.

LIMITATIONS

This study has several limitations. First, the study was conducted in an academic department; therefore, if conducted in a different healthcare setting, it may yield different results. Second, given that only patients were included in this study, it might have been subject to selection bias, and the obtained results may not apply to patients with milder symptoms. Third, some of our patients were administered intravenous diuretics, nitrates, or CPAP before undergoing the LUS test, which could have eased their lung congestion, and the B-line number would have been reduced, which could have probably underestimated the sensitivity of B-line testing. Fourth, it is unclear whether the use of LUS in routine clinical practice will have an impact on medical decision-making and patient prognosis. The findings of this study do not allow us to draw definitive conclusions regarding this issue. However, the fact that LUS can be useful in rapidly identifying the diagnosis of HF makes physicians more confident when choosing the most appropriate and effective treatment.

Finally, nurses participating in this study were given a 12-hour training course, which might not be sufficient to make them comfortable using LUS. However, there is no international consensus on education and assessment of this issue. Based on the current evidence, it is not possible to develop clear guidelines for future LUS training and certification.[24]

CONCLUSION

The present study has shown that when used appropriately, point-of-care B-line studies can be a reliable and reproducible tool for non-expert nurses. It can enhance the ability to identify HF in patients with undifferentiated dyspnea. Our findings may have significant clinical implications if confirmed by larger, prospective, high-quality studies.

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Data availability statement: Non-digital data supporting this study are curated by our services.

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Prehospital Particularities of Covid-19 infection and factors associated with its severity during the omicron variant wave (East-center of Tunisia)

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Abstract

Background: The Omicron variant of SARS-CoV-2, characterized by high transmissibility and partial immune evasion, led to significant waves of COVID-19 globally. This study aimed to evaluate the epidemiological and clinical characteristics of COVID-19 cases during the Omicron wave in Tunisia, focusing on severity predictors.

Methods: A prospective study was conducted from January 1st to February 28th, 2022, in the EMS03. Data were collected through patient records and follow-up interviews. COVID-19 severity was classified as mild, moderate, or severe per WHO guidelines. Predictors of severity were identified through univariate and multivariate analyses.

Results: Among 2,948 calls received, 420 confirmed COVID-19 cases were analyzed. The mean age was 48 years (±21.62), with 51% female. Comorbidities were present in 42.1% of cases, and 69.6% were vaccinated against COVID-19. The most reported symptoms were cough (67.5%), myalgia (61.2%), and fever (57.4%). Severe COVID-19 infection presentation was observed in 19.5% of cases, with 28.3% requiring hospitalization, 9.3% needing ICU care, and a mortality rate of 15.5%. Predictors of severity included advanced age, male sex, comorbidities, low education level, and lack of vaccination. Vaccinated individuals exhibited reduced severity, but severity was not significantly associated with the number of doses or type of vaccine.

Conclusion: The Omicron wave presented predominantly symptomatic cases with milder disease severity compared to earlier variants. However, age, comorbidities, and vaccination status significantly influenced outcomes. Enhanced vaccination coverage remains critical in mitigating severe COVID-19.

Keywords: Omicron variant, COVID-19 severity, predictors, Tunisia, vaccination, epidemiology

INTRODUCTION

In December 2019, an unexplained pneumonia outbreak was reported in Wuhan, Hubei Province, China[1]. A new coronavirus, "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) was identified, and the World Health Organization (WHO) named this infection coronavirus disease 2019 (COVID-19)[1].

Given the rapid spread of SARS-CoV2 worldwide, the WHO declared a Public Health Emergency of International Concern on 30 January 2020 and named the outbreak a pandemic on 11 March 2020[2].

In these late years, serial mutants of SARS-CoV-2 have triggered several waves of COVID-19 epidemics. To date, the WHO has identified five mutants characterized as specific Variants of Interest (VOIs) and Variants of Concern (VOCs), including alpha, beta, gamma, delta, and omicron [3,4].

In November 2021, South Africa experienced a rapid spread of SARS-CoV-2 fueling the fourth wave of COVID-19. The B.1.1.529 variant (Omicron) was first detected in samples collected in Botswana on November 11th and in South Africa on November 14th, and the WHO declared a VOC shortly thereafter[5]. Since then, Omicron has spread rapidly worldwide and was detected in Tunisia on 3 December 2021. It was brought from Istanbul by a 23-year-old Congolese tourist [6].

It was demonstrated that the Omicron has significantly higher rates of mutations, compared to previous SARS-CoV-2 variants (particularly in the S-gene, encoding the spike protein) [7,8]. These changes affected the virus's properties leading him to a higher potential of transmissibility [7].

Although full vaccination leads to a series of antibody productions, partial immune evasion has also been noticed with Omicron[9]. However, a marked reduction in hospitalization and mortality rates was reported in various studies [7,8].

In this context, we conducted our study with the aim of identifying the epidemiological and clinical characteristics of COVID-19 during the Omicron wave in the territory of the emergency medical service of the east center of Tunisia (EMS 03), and to study the severity of this variant and its associated factors.

METHODS

Study design and setting: A prospective study was conducted in the territory of EMS03 during the Omicron wave, dating from January 1st to February 28th, 2022.

The EMS03 manages pre-hospital medical emergencies occurring in its territory; in four governorates (Sousse, Kairouan, Monastir, and Mahdia). The EMS includes: (1) A medical regulation unit that ensures the appropriate medical response to any urgent call for care. During COVID-19, a sub-unit was created to receive calls for polymerase chain Reaction

(PCR) testing. PCR tests were carried out the day after to drivers or passengers in the EMS parking lot through the window of their car (Driving test). (2) A mobile resuscitation unit controlled by the regulation. It provides urgent medical interventions.

Study population: All subjects contacting the EMS 03 during the study period were included. Then, patients with a negative PCR and/or chest CT scan were excluded from the study analysis.

Study process and data collection:

-In the first step, we collected the patients' files during the study period.

-In a second step, we selected patients suspected of being infected by SARS-Cov-2; having contact with an infected subject, or presenting symptoms suggestive of a COVID-19 infection, and excluded subjects with no suspected COVID-19 infection.

-In the third step, we excluded subjects confirmed as not COVID-19-infected.

Data were collected via admission records for hospitalized subjects and by phone calls for subjects who did a Driving Test or those left at home after a medical intervention.

- First, we collected information concerning the patient's history and the clinical presentation from the intervention sheets and the digital regulation platform (SI-SAMU software).

Then, we followed up with the patients and collected information about the outcomes.

Measures: Sociodemographic features, medical history**,** and clinical presentation were assessed using a validated questionnaire (Supplementary material). The collected information included age, sex, area of residence, governorate, education level, healthcare profession, smoking, height, weight, comorbidities, vaccination status**,** and symptoms. A clinical examination and chest CT scan were performed to assess the severity. The COVID-19 infection was confirmed by Rapid antigen testing a PCR test**,** or a Chest CT scan.

The severity of COVID-19 infection was classified as mild, moderate, or severe; according to the WHO classification[10,11].

Statistical analysis: We used the Kolmogrov-Smirnov (KS) test to check the normality of the quantitative variables. Continuous variables with a normal distribution were expressed as mean and standard deviation (SD). Variables with asymmetric distribution were presented as the median and the interquartile range (IQR). Categorial variables were expressed as frequency rates and percentages. To assess the severity predictors of COVID-19 infection severity we, used the chi-square test or Fisher's exact test for qualitative variables and Student's test or Mann-Whitney's U test for quantitative variables. The variables were included at the 20% threshold in the multivariate analysis, to identify the determinants of severity. A multivariate analysis using the binary logistic regression models was performed to determine the independent factors related to COVID-19 severity. A p-value less than 0.05 was considered statistically significant.

RESULTS

We enrolled 2,948 calls, of which 1,448 were suspected of being COVID-19-infected. Only 420 patients were confirmed to have a COVID-19 infection (Figure 1). The mean age was 48±21.62 years with extremes ranging between 8 and 103 years. More than half (51%) were female. Almost half of the patients had a higher education level (49.6%) (Table 1). Only 3.8% were healthcare professionals. The proportion of patients with comorbidities was 42.1%. A history of COVID-19 infection was reported in 9.8% of cases. More than two-thirds of patients (69.6%) were vaccinated against COVID-19.

Most of the patients were symptomatic (99.3%). The major symptoms were cough (67.5%), myalgia (61.2%), fever/chills (57.4%), and fatigue (54%). No patient reported ageusia and only 1.9% presented anosmia (Table 2).

Infection was classified as severe in 19.5% of cases. Among the 420 patients, 28.3% required hospitalization (in an intensive care unit (ICU) in 9.3% of cases). Only 33.1% of the subjects needed oxygen. 3.3 % of subjects were intubated. The mortality rate was at 15.5%.

The COVID-19 infection severity predictors were as the age ($p \leq 10^{-3}$) (patients aged over 60 presented more severe forms); male sex (25.9% vs 13.6%; p=0.002); low education level ($p \leq 10^{-3}$); comorbidities (44.4% vs 13.6%, $p \leq 10^{-3}$). Patients vaccinated against COVID-19 developed a less severe presentation than unvaccinated ones (14.7% vs 31.9%; (p≤10-3).

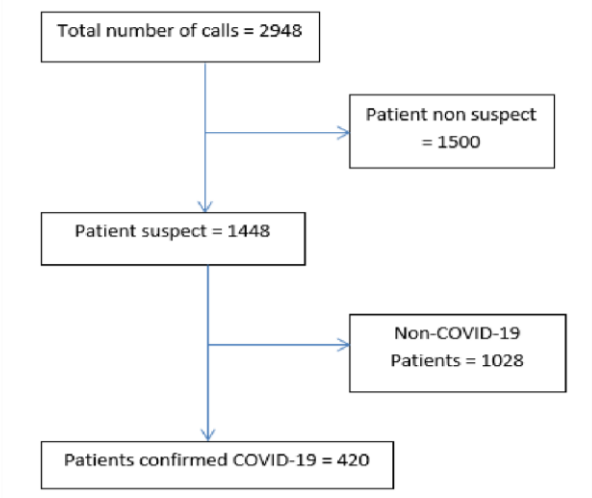

Figure 1. Flow chart of study population

On the other hand, we did not find an association between the severity and the number of doses (p=0.128), nor with the type of vaccine (p=0.054). Thus, influenza vaccination has no association with the presentation severity (p=0.351).

Clinical symptoms that were associated with a severe COVID-19 infection were cough (p=0.026), dyspnea($p \leq 10^{-3}$), sore throat($p \leq 10^{-3}$), and chest pain(p=0.042).

We did not find an association between severity and the healthcare profession (p=0.297)

The independent predictors of a severe presentation of the COVID-19 infection were the history of coronary artery disease, cancer, or auto-immune disease, and the presence of cough as an initial symptom. The presence of sore throat and vaccination were associated with a significant decrease in the severe presentation of COVID-19 infection.

Table 1: Participants' characteristics at baseline

Socio-demographiccharacteristics		n(%)
Age groups	< 19 years	34(8.4)
	20 - 59 yearsold	242(57.6)
	>60 yearsold	143(34)
Type	male	206(49)
	female	214(51)
Governorate of origin	Sousse	307(73.1)
	Monastir	57(13.6)
	Mahdia	51(12,1)
	Kairouan	5(1.2)
residence	Urban	328(81.4)
	Rural	75(18.6)
Level of study	Illiterate	60(14.9)
	Primary	42(10.4)
	Secondary	101(25.1)
	Superior	200(49.6)
Healthprofessional	no	381(96.2)
	yes	15(3.8)
smoking	no	316 (76.7)
	yes	96(23.3)
obesity	no	316 (89.3)
	yes	38 (10.7)
Flu vaccine	no	376 (98.4)
	yes	6 (1.6)
COVID vaccine	no	116 (30.4)
	yes	266 (69.6)
Number of doses	1	47 (17,8)
	2	178 (67.4)
	3	38 (14.4)
	4	1 (0.4)
type of vaccine	Inactivated (sinopharm-sinovac)	41(16.2)
	viral vector(sputnink-astrazenika-janssen)	53 (20.9)
	RNA (moderna-pfizer)	159 (62.8)
Comorbidities		177(42.1)
CVD		84 (20.0)
Diabetes		81(19.3)
HTN		68(16.2)
Coronaryarterydisease		14(3.3)
CRI /asthma		39(9.3)
Renalinsufficiency		13(3.1)
Systemicdiseases		7(1.7)
Neoplasia		9(2.3)
atopy		7(1.9)
PreviousCOVID-19		35 (9.8)

DISCUSSION

In our study, most of the patients were symptomatic (99.3%). This is consistent with results found in a study conducted in Norway reporting a rate of symptomatic subjects of 98.7% (91% having at least 3 symptoms) [12]. In another study conducted in Japan, the rate of symptomatic subjects was 91.1%[13]. It was similar in France with a rate of 89% [14]. However, in Korea, the rate of asymptomatic subjects reached almost half of cases with a rate of 47.5% [15].

Our patients mainly reported respiratory and general symptoms. Cough was the most common symptom (67.5%) followed by myalgia (61.2%), fever (57.4%), and fatigue (54%). These results are consistent with the literature. However, regarding upper respiratory symptoms, 26.7 % of patients had rhinorrhea and 23% had a sore throat which is not congruent with the literature showing a high prevalence of these symptoms among patients with Omicron.

A study conducted in the United States of America (USA) including 43 subjects infected with Omicron showed that cough and fatigue were the most reported signs (89% and 65% respectively). However, fever was present in 14% of cases [16]. A Norwegian study found that cough (83%), followed by rhinorrhea or nasal obstruction (78%), fatigue/asthenia (74%), sore throat (72%), headache (68%), and fever (54%) were the most common reported signs by patients with Omicron [12]. A Canadian study on 1,063 cases of Omicron found that rhinorrhea (73%), cough (65%), and headache (54%) were the most common symptoms [17]. A study in India on 1175 cases of Omicron reported that patients complained mostly of fever (43%), followed by soreness (23%), rhinorrhea (22%), and cough (21%) [18]. A study conducted in the United Kingdom (UK), including only vaccinated individuals who were infected with Omicron, found that rhinorrhea (77%), headache

Table 2: symptoms of covid-19 reported by the study population in Tunisia during Omicron wave from January 01 to February 28, 2022

Symptoms	n(%)
Cough	283 (67.5)
Arthromyalgia	257 (61.2)
Fever /chills	241 (57.4)
Fatigue	227 (54.0)
Headache	162 (38.6)
Dyspnea	162 (38.6)
Rhinorrhea	112 (26.7)
Sore throat	96 (23.0)
Vomiting/Nausea	22 (5.2)
Chest pain	21 (5.0)
Palpitation	16 (3.8)
Abdominal pain	13 (3.1)
Diarrhea	16 (3.8)
Anosmia	8 (1.9)
Agueusia	0 (0.0)
By system	
General signs	371 (89.0)
Respiratorysigns	320 (76.7)
ENT signs	170 (40.7)
Cardiovascularsigns	33 (8.1)
Digestive signs	42 (10.0)
severity	
hospitalization	
no	301(71.7)
yes	119(28.3)
Hospitalizationdepartment	
Medical Service	79(66.4)
Intensive care unit	40(33.6)
Oxygenation/ventilation	
no	281(66.9)
yes	139(33.1)
Oxygenation / Ventilation means	
LN	30(21.6)
MHC	42(30.2)
optiflow	9(6.5)
CPAP	13(9.3)
NIV	31(22.3)
Intubation	14(10.1)
Evolution	
survivors	337(84.5)
Deaths	62(15.5)

(75%), sore throat (71%) and sneezing (63%) were the most common symptoms [19].

Several studies compared the symptoms of Omicron and different variants and found a significant rise in upper respiratory symptoms, especially sore throats. For instance, one of these studies conducted in the US found significantly higher rates of sore throats during the Omicron wave than during the pre-delta period (29.6%, $P < 0.001$) and Delta (29.1%, $P < 0.001$) [20]. This is consistent with another study conducted in the UK [21]. However, sore throat was also common in symptomatic cases with negative PCR, suggesting that sore throats may not be a specific predictor of Omicron. Besides, symptoms reported during COVID-19 are like signs found in any infection by other respiratory viruses such as (influenza A and B, respiratory syncytial virus, adenovirus, parainfluenza, rhinovirus, and human metapneumovirus. As we did not perform sequencing to determine the variant, we can't conclude that the symptoms reported in our study are caused exclusively by Omicron alone. The non-predominance of upper respiratory signs can be explained by the coexistence of other variants of SARS-CoV-2 such as Delta during the study period.

None of our patients reported agueusia and only 1.9% reported anosmia. This is consistent with the literature which indicates a significant decrease in these signs among Omicron patients compared to other SARS-cov-2 variants [22][23]. This finding suggests that the site of the virus tropism may have changed between variants. This is further reinforced by the fact that the number of Omicron pneumonia is reduced compared to other variants [24,25]. Further reinforcing this hypothesis is that the incidence of sore throat has increased with Omicron, and it can be deduced that the viral replication site could be moved to the upper respiratory tract [19].

In our study, the prevalence of severe disease was 19.5%. Only 28.3% of patients required hospitalization. The hospitalization rate in a resuscitation unit was low (9.3%) and the death rate was 15.5%. Several studies found a significant decrease in severity and mortality with the new Omicron variant. Several cohort studies were conducted comparing the severity presentation of Omicron with other variants (namely the delta variant) and have demonstrated this result. In a study in South Africa, analyzing data from 11,000 patients with COVID-19, the authors found that the hospitalization rate of Omicron-infected patients was significantly lower than other variants. They also reported that the prevalence of severe forms was lower than delta-infected patients (OR 0.3, 0.2–0.5) [26]. A cohort study in Canada 11 622 Omicron cases paired with Delta cases noted that the hospitalization rate among Omicron cases was only 0.51% and the mortality rate was 0.03%, compared to 1.56% and 0.12% respectively for Delta cases. The risk of hospitalization or death among Omicron-infected subjects was 65% lower (relative risk,

RH = 0.35, 95% CI: 0.26, 0.46) than in the Delta-infected patients group. The risk of admission to an ICU or death was 83% lower (RH = 0.17, 95% CI: 0.08, 0.37) [27]. Another study in the UK showed that Omicron cases had a 59% lower risk of hospitalization than Delta and a 69% lower risk of death than Delta [28]. Another cohort study in Belgium found that the estimated risk of severe forms and admission to ICU was significantly lower in Omicron patients compared to Delta (RR = 0.63; 95% CI (0.30; 0.97) and RR = 0.56; 95% CI (0.14; 0.99), respectively), while no significant difference was found for mortality (RR = 0.78, 95% CI (0.28–1.29)[29].

Some studies tried to find an explanation for this decrease in mortality and severity with Omicron. They believe that cell-mediated immunity due to a previous natural COVID-19 infection or vaccination played an important role in decreasing the acuteness observed during the Omicron wave.

Studies showed that natural infection induces a diverse polyepitopical cell-mediated immune response that targets the spike protein (nucleocapsid protein and membrane protein) [30]. Therefore, cell-mediated immunity is likely more durable than humeral immunity, especially in small mutations affecting the spike protein [31], such as those seen in the Omicron variant. In addition, natural infection induces an immune response to memory T cells, including long-lived cytotoxic T cells (CD8+), which have a half-life of 125 to 255 days, ensuring longer-lasting immunity [32].

Although vaccination status appears to be well documented, in many cases, likely, previous infection by COVID-19 has not been documented and the rate of re-infection remains underestimated. If reinfections are less severe than primary infections, this fact could, in part, explain the reduced severity of the disease observed in patients infected with Omicron [33].

Although several studies suggest that Omicron is much less virulent than other variants, other studies taking into account the pre-existing immunity to COVID-19 (vaccination status and previous infection) assume the highest virulence of Omicron compared to other variants. Furthermore, Omicron has the ability to infect people with pre-existing immunity[9], thus protecting them from severe forms.

We found two studies comparing the intrinsic virulence of Omicron with the Delta, taking into account the immunizing effect of undocumented prior infections. Although these studies were conducted in regions where the prevalence of infected cases was different, after correction, each study showed that Omicron was approximately 75% as likely as Delta to cause hospitalization in subjects who were not immunized by either vaccination or previous SARS-CoV-2 infection [34,35]. This suggests that Omicron has similar intrinsic virulence with previous variants. With the available data, it is difficult to determine whether the low rate of

severe forms is related to the effect of pre-existing immunity to COVID-19 or the decrease in intrinsic virulence of Omicron. More comparative studies controlling pre-existing immunity, detection bias, care system capacity, and other factors are needed to conclude between these different assumptions.

Concerning associated factors for the severity of COVID-19 during the Omicron wave, we found in the univariate analysis a significant association between age and severity ($p<0.001$), however in multivariate analysis, this association has disappeared. A study on 25207 Chinese Omicron patients found that older subjects had a higher rate of severe forms than other age groups [[36]. Several other studies confirmed this association[37–40]. This can be explained by immune aging, which is responsible for developing weak immune responses to COVID-19 and inadequate immune responses to vaccination [41]. There is also a reduction in immunological memory associated with antibody loss, making elders more vulnerable to infection[41]. It is important to give more attention to older subjects with COVID-19 and to treat them earlier to prevent further deterioration.

In our study, males had a higher prevalence of severe forms. Several studies have shown an association between male sex and severity of infection by different SARS-CoV-2 variants such as Alpha, Gamma, and Delta [42–44]. Male patients may have a greater expression of the ACE2 enzyme, which is controlled by androgenic sex hormones, making this group of people more susceptible to infections and severe forms of SARS-CoV-2, knowing that this virus has great affinity to ACE2 receptors[42,45].

Our data showed a correlation between the risk of developing a severe form was associated with having at least one comorbidity (CVD, diabetes, HTN, coronary artery disease, system disease, COPD/asthma, and cancer). These pathologies were not independent predictors of severe presentation, this coincided with literature findings [36,44,46,47]. Diabetic patients have impaired phagocytic cells, making the treatment of infections ineffective [48]. Obesity, which is also among the severity predictors of influenza A (H1N1) infection [49], is associated with a decrease in functional capacity, expiratory reserve volume, and respiratory system compliance [50]. CVD and endocrine diseases may be responsible for changes in the expression of angiotensin-2 converting enzyme, which is the receptor where the spike protein of SARS-CoV-2 binds. This condition makes these subjects more susceptible to contracting COVID-19 and developing severe forms [45,51,52].

Regarding vaccination, we found in the univariate analysis that severity was significantly lower in vaccinated patients against COVID-19. However, no association was found after binary regression. Many studies have demonstrated the effectiveness of vaccination

against COVID-19. In fact, multiple doses provide additional protection against Omicron, inducing more effective immune responses against symptomatic infection and reducing the risk of hospitalization[53,54]. Considering the overall performance of the vaccination, some studies have reported that the efficacy of the vaccine is lower against Omicron compared to the other variants [55,56]. Additionally, Andrews et al. [57]analyzing South African, German, and British studies found a reduced neutralizing activity of vaccines against Omicron compared to that against Delta [57].

Strengths and limitations of the study

For logistical reasons, participants did not have a genotyping test to confirm infection with the Omicron variant. To genetically determine whether all cases were actually infected with the B.1.1.529 variant, additional laboratory testing is needed.

Our study only assessed clinical symptoms at the onset of the infection and did not track symptoms. Symptoms may superimpose after the swab test. To gain insight into the clinical presentation of this variant throughout the course of infection, more detailed data regarding clinical symptoms in the initial and later stages of infection are needed.

CONCLUSIONS

In 2021, the SARS-CoV-2 Delta variant was replaced by Omicron, which was classified as a VOC by the WHO [4]. Omicron appears to be different from previous variants; it is associated with an important ability of transmission, an ability to escape immune response, and it has a different clinical presentation, and a lower degree of severity [28].

Recognizing the factors associated with severity helps health actors to adopt strategies to deal with this variant. Staying alert to COVID-19 continuing vaccination efforts and adherence to prevention measures are needed to reduce the spread and impact of different variants. The public health system, and local, regional, and national authorities, must maintain the alert to detect, react, and adapt rapidly to the emergence of new variants.

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Prognosis in COVID-19: Impact of Pre-hospital Emergency Care

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Abstract

Background: Since the beginning of COVID-19 disease, each country has planned a consensus for patient management according to its health system. In Tunisia, Pre-hospital emergency care (PEC) worked in regulating and transporting COVID-19 patients. On the other hand, some patients have chosen to consult the Emergency Department (ED) themselves. Does the way to get to medical care have an impact on the prognosis?

Methods: This is a retrospective descriptive study carried out in the Intensive Care Unit (ICU) of Abderrahmane Mami's hospital for nine months (from March to November 2020). Patients included were those who were hospitalized for SARS-COV2 infection by PEC (Group1 (G1)) and those admitted via the hospital's ED (Group2 (G2)). The primary endpoint was mortality.

Results: We included 60 patients: 30 for each group. The average age was 62 years for G1 and 63 years for G2 (p=0.18) with a male predominance in both groups (p=0.4). The most common histories were hypertension (14 cases in G1 and G2, p=1), diabetes (10 cases in G1 and 8 cases in G2, p=0.75), and obesity (14 cases in G1 and 12 cases in G2, p=0.55). Patients in G2 consulted the emergency department later with a mean time from symptom onset to hospitalization of 9.6 days (vs. 6.5 days for G1, p=0.02). On admission, they were more asthenic (p=0.024), with a mean spo2 of 89% (vs. 95% in G1, p=0.008). Patients of PEC had less requirementforo mechanical ventilation (11 cases vs. 21 in G2, p=0.01). Mortality was significantly higher in G2 patients (21 cases vs. 10 in G1, p=0.04). By multivariate study, the way to get to the ICU (group 1 or 2) was not significantly associatewithto mortality and only the requirement of mechanical ventilation was (p<0,001; OR = 16,286 and 95% CI [18,406-3801,272]).

Conclusion: COVID-19 patients admitted to the ICU via PEC had earlier management compared with patients admitted via the ED; they had less serious symptoms with less mortality.

Keywords: COVID-19; Emergency Department; Intensive care unit; Mortality; Pre-hospital Emergency Care.

INTRODUCTION

In 2020, the exponential transmission of COVID-19 disease to an unprotected population threatened the stability of many health systems in the world, which were regularly described as being on the verge of collapse. In this regard, there was no standardized international approach to preserve health structures (1). Each country had planned a consensus for the care of its patients according to its health system, striking the right balance between health protection and the prevention of economic and social disorders**.**

In Tunisia, Pre-hospital Emergency Care (PEC) was the cornerstone of management of the first affected cases of COVID-19. After contacting 190 for a suspected or confirmed COVID-19 infection, An Emergency Mobile Unit (EMU) with protective equipment was moved the patient's home for examination, gravity evaluation, and then to direct him toward most appropriate hospital structure. Other patients did not call 190 and had chosen to go into the emergency department (ED) for various symptoms related to COVID-19 disease. The question was: Was it necessary to stay at home and call 190 for COVID-19 patients? Was it better to go immediately to the ED? The aim of our study was to evaluate the contribution of PEC intervention on the prognosis of COVID-19 patients hospitalized in the Intensive Care Unit (ICU) by comparing that to patients admitted through the ED.

METHODS

It was a retrospective observational study conducted in the ICU of Mami's hospital during a period of nine months (from March 2020 to November 2020). We included patients hospitalized in the ICU for a suspected COVID-19 disease through the ED of the same hospital and those who were transferred from their homes by the EMU. We did not include patients admitted from other structures or hospitals.

Were excluded patients in whom the diagnosis of COVID-19 was infirmed and those with missing data. The primary outcome was in-hospital mortality the and secondary outcome was the requirement of invasive ventilation. We defined two groups: Group 1: Group "PEC": Patients admitted to the ICU through EMU after contacting the PEC and Group 2: Group "ED": Patients admitted to the ICU after coming to the ED frinome with their own ways.

We applied the same therapeutic protocol for both groups according to international recommendations available. Data collection was carried out on a pre-established sheet.

For the statistical analyses, a comparison of two means was performed using the Student's t-test for independent series and by Pearson's chi-square test in case of invalidity of this test. The anonymity and security of the patients' personal data were respected. No data relating to ethnic origin, sexual life or morals were collected. We declare that there was no conflict of interest.

RESULTS

From March 2020 to November 2020, 132 patients were admitted to the ICU with CIVID-19 infection, 70 were not included because they were transferred from another hospital or from another department other than ED. Two patients

were excluded because of missing data and 60 were included in the study.

1. Descriptive study

The two groups were similar on epidemiological characteristics as represented in table 1. The median age was 63 years [57-72]; 62 [54-73] for group 1 and 64 [58-72] for group 2 (p = 0.7). Our population was divided into 41 men (68%) and 19 women (23%), with a clear male predominance, getting a gender ratio of 2.16 (p = 0.4). Twenty-one of the patients (35%) had no known pathological medical history. Hypertension was the most common history found: 46.7% of patients; 14 (47%) of group 1 and the same for group 2 (p=1). Ten patients had pulse oximeter at home (16.7%), without difference in the two groups (p=1). The most reported functional sign was headache, found in 55(91.7%) patients, 29 (97%) from group 1 and 26 (87%) from group 2, i.e. p = 0.1. Fever was reported by 40 patients, i.e. 80% of the population; 23 (77%) from group 1 and 25 (83%) from group 2, i.e. p = 0.4. The two groups were comparable on the symptomatology described, except for dyspnea and asthenia; these two signs were more described in the "ED" group. In fact, 29 patients (97%) in the “ED” group had dyspnea versus 12 (40%) in the “PEC” group; p<0.01. Twenty-eight patients (83%) of the “ED” group were asthenic versus 17 (57%) of the “PEC” group; p=0.02. The average duration between the date of onset of symptoms and hospitalization in the ICU was 8 ± 5 days. This period was shorter in the “PEC” group; 7 days ± 6 in comparison with the “ED” group; 10 days ± 4 i.e. p=0.02. The average duration between the date of onset of symptoms and the date of performance of the COVID-19 PCR on nasopharyngeal swab was 7 ± 5 days. This duration was shorter in the “PEC” group; 6 days ± 6 versus 9 days ± 4 in the “ED” group, i.e. p=0.05. The average time spent in the emergency room before being admitted to intensive care was calculated at 23 ± 16 hours. The latter was statistically longer than the extended time between the PEC call and the patient's arrival in the department, which was 3 hours ± 3 or p < 0.01. Patients in the “ED” group had more serious initial clinical features; the mean initial SpO2 was 83% for the “PEC” group versus 66% for the “ED” group, i.e. p < 0.01. All the patients in the “ED” group had ARDS on admission, versus 18 (60%) in the “PEC” group, i.e. p < 0.01. Table 2 details clinical features, therapeutic characteristics and evolution in the ICU of the two groups. Twenty-one patients (70%) in the “ED” group were intubated in the ICU department versus 11 (37%) for the “PEC” group, i.e. p=0.01. Acute renal failure appeared in 53% of cases (n=32) and it was significantly higher in the "ED" group compared to the "PEC" group (67 vs. 40%, p=0.04). Multiple organ dysfunction syndrome was in 25 patients, more marked in hospitalized emergency patients (60 vs. 23%, p=0.04). The evolution was favorable for 29 patients but fatal for 31 (52%). Mortality was significantly higher in the “ED” group compared to the “PEC” group (70 vs. 33%, p=0.04).

Table 1 *Descriptive study and differences between the two groups before ICU.*

		General population (n = 60)	Group 1 Group "PEC" (n = 30)	Group 2 Group "ED" (n = 30)	P
Demographic characteristics	**Gender-ratio**	2,16	1,73	2,75	0,4
	Median age (years)	63[57,72]	62[54,73]	64[58,72]	0,7
	BMI > 30 n (%)	26 (43)	14 (47)	12 (40)	0,5
	Diabetes n (%)	18 (30)	9 (30)	8 (27)	0,7
	HBP n (%)	28 (47)	14 (47)	14 (47)	1
	Self-monitoring by pulse-oximeter n (%)	10 (17)	5 (16)	5 (16)	1
Clinical characteristics before ICU	**Fever n (%)**	48 (80)	23 (77)	25 (83)	0,4
	Cough n (%)	41(68)	21 (70)	20 (67)	0,7
	Dyspnea n (%)	**41 (68)**	**12 (40)**	**29 (97)**	**< 0,01**
	Asthenia n (%)	**42 (70)**	**17 (57)**	**25 (83)**	**0,02**
	Diarrhea n (%)	6 (10)	5 (17)	1 (3) 0,09	0,09
Therapeutic characteristics before ICU	**Nasal oxygen cannula n (%)**	16 (27)	11 (37)	5 (17)	0,08
	High concentration oxygen mask n (%)	**37 (62**	**12 (40)**	**25 (83)**	**< 0,01**
	Non-invasive ventilation n (%)	**6 (10)**	**0**	**6 (20)**	**0,01**
	Invasive ventilation n (%)	1 (2)	1 (3)	0	0,31
Access to medical care delays	**Time from onset of signs to ICU admission (days) Mean ± SD**	**8 ± 5**	**7 ± 6**	**10 ± 4**	**0,02**
	Time from onset of signs to PCR (days) Mean ± SD	**7 ± 5**	**6 ± 6**	**9 ± 4**	**0,05**

BMI *Body mass index*, HBP High blood pressure, ICU Intensive Care Unit, PCR Polymerase Chain Reaction, PEC Pre-hospital Emergency Care, SD Standard Deviation.

Table 2 *Descriptive study and differences between the two groups in the ICU.*

		General population (n = 60)	**Groupe 1 Group "PEC" (n = 30)**	**Groupe 2 Group "ED" (n = 30)**	**p**
Initial clinical features in ICU	**ARDS n (%)**	**48 (80)**	**18 (60)**	**30 (100)**	**< 0,01**
	Severe ARDS n (%)	27 (45)	10 (30)	17 (57)	0,07
	HR bpm Mean ± SD	91 ± 16	90 ± 14	91 ± 18	0,7
	MBP mmHg Mean ± SD	94 ± 15	94 ± 16	94 ± 14	0,9
	SpO2 (%) Mean ± SD	**74 ± 22**	**83 ± 19**	**66 ± 22**	**< 0,01**
Therapeutic characteris-tics in ICU	**HFNC therapy n (%)**	14 (23)	5 (17)	9 (30)	0,2
	Non-invasive ventilation n (%)	**32 (53)**	**8 (27)**	**24 (80)**	**<0,001**
	Ventral Decubitus n (%)	**36 (60)**	**9 (30)**	**27 (90)**	**<0,001**
	Invasive ventilation n (%)	**32 (53)**	**11 (37)**	**21 (70)**	**0,01**
	Therapeutic-dose Anticoagulation n (%)	60 (100)	30 (100)	30 (100)	1
	Antibiotic therapy n (%)	58 (97)	28 (93)	30 (100)	0,1
	Vitamins therapy n (%)	60 (100)	30 (100)	30 (100)	1
	Corticosteroids n (%)	**54 (90)**	**24 (80)**	**30 (100)**	**0,01**
Evolution in ICU	**Acute renal dysfunction n (%)**	32 (53)	12 (40)	20 (67)	**0,04**
	Severe sepsis n (%)	32 (53)	12 (40)	20 (67)	**0,04**
	Multiple organ failure n (%)	25 (42)	7 (23)	18 (60)	**0,04**
	Mortality n (%)	31 (52)	10 (33)	21 (70)	**0,04**

ARDS Acute respiratory distress syndrome, HFNC High Flow Nasal Cannula, HR Heart rate, ICU Intensive Care Unit, MBP Mean Blood Pressure, PEC Pre-hospital Emergency Care, SD Standard Deviation.

2. Analytic study:

Mortality factors in univariate analysis:

Intra-hospital mortality was about 52 %. In univariate analysis, 8 factors leading to mortality were identified (p; OR; 95% CI): Age (0,006; 3,221; [2,729-15,622]), Delay in access to medical care (<0,001; 4,381; [2,087-9,197]), First SpO2 (0,001; 4,377; [20,873-38,395]), Group "ED" (0,004; 2,222; [1,217-4,059]), ARDS (0,001; 1,706; [1,256-2,316]), Acute kidney injury (<0,001; 5,906; [2,355-14,812]), Invasive ventilation (<0,001; 26,250; [3,823-180,258]) and Multiple organ failure (<0,001; 5,833; [2,816-12,085]).

Multivariate analysis showed that only invasive ventilation was directly related to mortality with p<0,001; OR = 16,286 and 95% CI [18,406-3801,272].

DISCUSSION

Our study showed that patients of group 2 "ED" had later management compared to "Pthe EC" group with a greater delay between the onset of symptoms and ICU admission (OR = 0.31, CI [0.370.77], p= 0.02). And this delay was on average **8 ± 5** days. Armstrong noted, in a meta-analysis of 24 observational studies including 10150 patients admitted to intensive care, that the median time from onset of illness to dyspnea was 5 to 8 days, and the median time from onset of illness to admission to intensive care was 4 to 8 days. The median time from onset of illness to admission to intensive care was 10 to 12 days (2); this was true for all types of transport for patients admitted to the ICU.

Dyspnea was more described in the "ED" group (p<0.01). It was the only symptom significantly associated with both severe COVID-19 (OR 3.70, 95% CI 1.83-7.46) and ICU admission (OR 6.55, 95% CI 4.28 to 10.0) according to a meta-analysis investigating the predictive factors of severe COVID-19 and ICU admission (3).

According to a study done at Tongji Hospital in China in January 2020, which included 344 COVID-19 patients admitted to the ICU, dyspnea was more frequent in non-survivors (p<0.001), accompanied by a higher respiratory rate and a lower SpO2/FIO2 (S/F) ratio (p<0.001)(4). In our study, 80% of patients were in ARDS. The patients who came from the ED (group 2) were all in ARDS however only 60 % of group 1 patients were in ARDS (p<0,01). These results are consistent with the Chinese experience in Wuhan where 81% of patients admitted to the ICU had ARDS (5). A review of the literature comparing ARDS due to COVID-19 with conventional ARDS found that ARDS due to COVID-19 appears to have a poorer prognosis than conventional ARDS, where ICU mortality was 35.3% (95% CI, 33.3% to 37.2%) (6), whereas it ranged from 26% to 61.5% for ARDS secondary to COVID-19, and could be as high as 94% if mechanical ventilation was used (7).

This fact could explain why the requirement of mechanical ventilation (OR = 0.33, CI [0.09-0.58], p= 0.01), as well as mortality (OR = 0.37, CI [0.12-0.61], p= 0.04) were statistically higher in group 2 patients (ED). Group 2 patients were carried out later so they were consulting ED with more developed symptoms and severe hypoxemia. That may be explained by the fact that these people were denying their disease during that period of the pandemic COVID-19 illness. However, group 1 patients were more attentive to their health, so they were in contact with the PEC from the first symptom. PEC was available to go to patients' homes in order to evaluate patients, confirm the diagnosis, and to insist on preventive measurements. So PEC patients were carried out earlier with a better prognosis.

Diagnosis by PCR was made later in the ED group (OR = 0.19, CI [0.02-0.06], p= 0.05). Initial intervention time was longer in the ED group (p< 0.01).

Moreover, the time spent by the SMUR teams with the patient before bringing him back to the department was significantly shorter than the time spent in the emergency department before hospitalization in the intensive care unit (3 vs. 7 hours, p<0.001).

Impact of Pre-hospital Emergency Care on COVID-19 prognosis

Pre-hospital care and management of COVID-19 patients is an important step in the first assessment, triage, and packaging of patients, besides the contribution to the control of the virus spread. Our study showed that medical transport of COVID-19 patients admitted to the ICU with ARDS reduced mortality when patients are hospitalized early with few symptoms and less ARDS compared with patients admitted via the ED. Few studies evaluating the impact of pre-hospital COVID-19 patients' care on their prognosis are available. Feedbacks on pre-hospital emergency transport and care of COVID-19 Patients were described (8,9). In France, An intervention of a task force took action from March 26th to May 7th, 2020. The task force included nurses and specialists of the county general hospital. There were a total of 770 residents distributed in eight facilities with capacity varying from 53 to 145 residents. The number of deaths peaked at 139 in week 2 and the trough at 0 occurred in weeks 6−7. Comparison between periods (before vs after intervention) showed a significant decrease in the number of new deaths (83/770; 11% vs 35/687; 5%, p = 0.0001) and new COVID-19 cases (348/770; 45% vs 123/422; 29%, p < 0.001)(10). The SAMU 94 and the Faculty of Health of the University of Créteil, France, have jointly implemented an online unit dedicated to nursing homes. Feedback has shown that this geriatric unit is a valuable concept that has been able to improve the management of stress and anxiety in elderly subjects, their families, and staff (11).

We decline any conflict of interest in the establishment of this study.

CONCLUSION

In conclusion, Pre-hospital Emergency Care reduced mortality when patients were treated early with regular control and continued contact with the health system. On the other side, patients consulting later Emergency Departments with developed symptoms of hypoxemia and ARDS had the worst prognosis, required more invasive ventilation, and had higher mortality with multiple organ failure. The development, enforcement, and improvement of pre-hospital care teams are important to achieve better control of COVID-19 disease.

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Traditional Medicine with Cade Oil in Pediatric Emergency Care

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Abstract:

Despite the advancements in modern medicine, traditional medicine remains relevant in our country. This is exemplified by the practice of traditional therapy using cade oil, commonly referred to as "camel soap," "tar," or "القطران," which is increasingly observed in Tunisia. It is not uncommon to admit patients to the hospital who are victims of these practices.

We conducted a prospective study over a 6-year period from January 2018 to December 2023. We included newborns, infants, and children under 14 years of age who had undergone traditional therapy with cade oil. We excluded all other forms of traditional therapy.

The aim of our study was to raise awareness of the increasing frequency of cade oil traditional therapy in our region, the potential damages that can result, and the importance of taking appropriate medical and legislative measures to address this phenomenon.

Twenty cases were recorded in our department for this reason. All children had a low socioeconomic status. Thirteen were from rural areas and seven were from urban areas. The reasons for resorting to these practices included a lack of resources in one case, and in all other cases, parental beliefs in the effectiveness of these methods compared to modern treatments. The average interval between the application of cade oil and consultation at the hospital was 14 hours. The average age was 18 months, with a minimum age of 10 days and a maximum of 4 years. The primary reason for consultation was gastrointestinal symptoms, including diarrhea and vomiting, often in a febrile context.

Medical therapeutic management included symptomatic measures in all cases, with specific treatment provided in 2 cases. Legislative measures involved all living patients, represented by notification to the child protection delegate. The outcome was favorable for 14 cases, unfavorable with death in four cases, and neuro-sensory sequelae in two other cases.

Prevention plays a crucial role in addressing this phenomenon by raising awareness among both parents about the side effects of irrational use of this product and healthcare personnel about the need to consider cade oil poisoning in children presenting with unexplained multi-organ involvement to ensure early and appropriate management.

Keywords: Cade oil, Tar, Child, Poisoning, Traditional therapy

INTRODUCTION

Traditional therapy with cade oil, used for addressing physical, mental, or social health issues, is becoming increasingly embedded in Tunisian culture. The danger lies in exposing children to the harmful effects of cade oil through these popular practices.

Cade oil is distilled from the branches of *Juniperus oxycedrus*, which, despite its known toxicity due to its phenol content, continues to be used in traditional medicine.

Poisoning from this product manifests through cardiovascular disturbances (hypotension, tachycardia), neurological disorders (headaches, hypotonia, seizures, or even coma), respiratory issues (acute pulmonary edema and respiratory distress), and gastrointestinal symptoms (diarrhea, vomiting).

Diagnosis is based on a combination of anamnesis, clinical findings, laboratory results, and radiological examinations.

Management is multidisciplinary, focusing primarily on symptomatic measures.

METHODS

This is a retrospective study covering a 6-year period from December 2017 to December 31st, 2023, involving children hospitalized with a reported history of cade oil use.

The study was conducted at the Pediatric Intensive Care Unit of Hédi Chaker University Hospital in Sfax. We included all infants, children, and adolescents under 14 years of age who had undergone an application of tar. We excluded children who were poisoned by substances other than cade oil. During this study, we documented the epidemiological, clinical, and outcomes.

RESULTS

We compiled data on twenty cases with an average age of 18 months (ranging from 10 days to 4 years). There were 2 boys and 8 girls. Seven children were from urban areas, while the remaining 13 were from rural areas. Three modes of poisoning were observed: inhalation (1 case), cutaneous application (6 cases), and transcutaneous application via scarification (9 cases). The combination of cutaneous and respiratory routes was seen in 4 patients.

Neurological manifestations were present initially in 16 patients, including:

- Consciousness disturbances ranging from apathy and drowsiness to coma in 5 patients.
- Behavioral disturbances in 6 patients, including moaning in 3 patients and plaintive behavior in 3 patients.
- Axial and peripheral hypotonia in 4 patients.
- Seizures in 5 patients.

Thirteen of our patients showed signs of dehydration upon admission. Eight of these had severe dehydration (stage III), and seven patients have also presented associated hemodynamic disturbances. Respiratory manifestations were described in 12 patients: tachypnea (n=12), signs of respiratory distress (n=6), and abnormal pulmonary auscultation (n=5 patients).

Cade oil application was made in multiple locations on the same patient. Parents applied

the oil to the ear lobules, around the nostrils, on the forehead, chest, and extremities. Scarification lesions on the forehead, trunk, and all four limbs were noted in 12 patients (Figures 1 and 2).

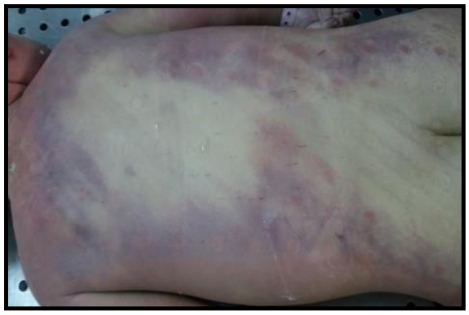

Figure 1: *Image showing scarification lesions on the back*

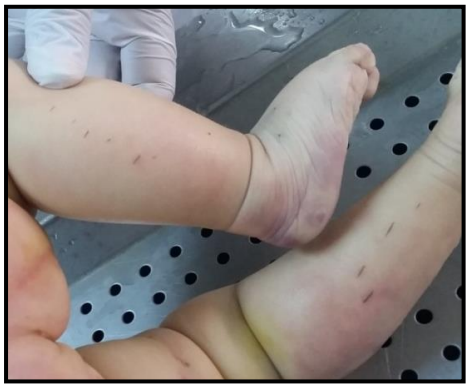

Figure 2: *Image showing scarification lesions on the feet*

The biological tests performed for all patients showed: leukocytosis (n=9), transient neutropenia (1 patient), thrombocytopenia (3 patients), thrombocytosis (3 patients), normochromic normocytic anemia (n=6), hyponatremia (n=11), hypokalemia (n=8), metabolic acidosis (n=12), hepatic cytolysis (n=7), and functional renal failure (n=3).

Toxicological screening blood and urine tests were performed in 4 patients; they were positive for organophosphates in 2 patients. Cholinesterase activity testing was performed for 2 patients, showing normal serum activity and low globular activity.

Chest X-rays were performed for all patients, with normal results in 16 patients and only 4 showing pulmonary radiological abnormalities.

Brain CT scans were performed in 8 patients, revealing toxic origin anomalies in 2 patients, old anterior abnormalities in 1 patient, and normal results in 5 cases.

Brain MRIs were performed for 3 patients, showing in one case a hyperintense signal in the thalamus, probably of toxic origin, and in the other two cases, bilateral and symmetrical signal abnormalities in the cortical-subcortical regions, basal ganglia, and corpus callosum, suggestive of toxic encephalopathy (Figure 2).

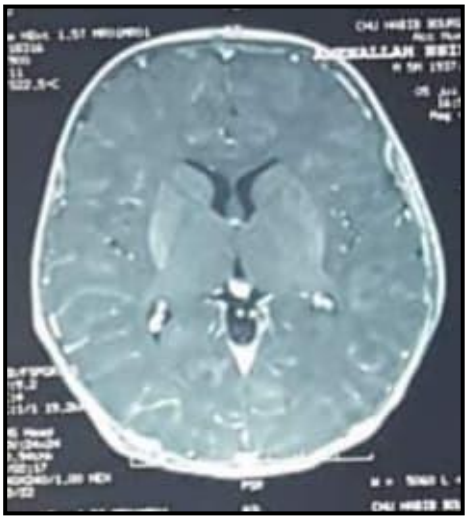

Figure 2: *Brain MRIs showing in one case a hyperintense signal in the cortical-subcortical regions, basal ganglia, and corpus callosum*

The electroencephalogram (EEG), performed for eight patients, was abnormal in 7 cases. It showed severe global anoxic-ischemic brain damage (see Figure 4) in three patients, slow and

polyspike waves in the temporal and bilateral temporal occipital regions with diffuse rapid rhythms in three patients, and poorly organized with the presence of multifocal anomalies in the remaining two cases.

Symptomatic treatment was based on rehydration in all cases. Antibiotics were administered to 18 patients. Anticonvulsant treatment was given to 8 patients. No specific treatment or antidote for tar was administered. However, Pralidoxime and Atropine were given to two patients whose enzymatic assays and toxicological evaluations showed low globular cholinesterase activity with the presence of organophosphates in the urine.

The outcome was favorable for 15 patients. Two cases resulted in severe neuro-sensory sequelae, and the remaining 5 cases had a fatal outcome.

DISCUSSION

Cade oil is a tar obtained by pyrolysis of the wood of the cade tree (*Juniperus oxycedrus*), a Mediterranean shrub commonly known as juniper (1-8). It is a viscous, thick, and homogeneous liquid that is black or dark brown color, with a distinctive unpleasant empyreumatic odor and a consistency similar to tar, with a bitter and caustic taste (1-8). It is produced from the carbonization of the trunks and large branches of old juniper trees.

Juniperus oxycedrus (Figure 4) is a plant widely distributed in countries with a Mediterranean climate (around the Black Sea and the Middle East) (9). It is one of the species in the juniper genus, belonging to the Cupressaceae family, and is highly valued for its essential oil and secondary metabolites, which are extensively used in traditional medicine (10). All parts of the plant contain highly aromatic essential oils (11).

Figure 4: *Branch of* Juniperus oxycedrus *(5)*

1. Pharmacological Properties of Cade Oil

A variety of pharmacological properties are documented in the literature, some scientifically proven and others still requiring further investigation. This product exhibits antipruritic activity (12), mainly due to the presence of phenols such as cresols (1,2,5,13), as well as keratolytic action (1,2,5,13), anti-inflammatory effects, antiseptic properties (9,14-17), healing activity (9,14,17), toning and energizing effects (18-20), and antimicrobial and antifungal action (9,10). Cade oil also has parasiticidal properties (1,2,5,13). Additionally, it demonstrates analgesic, antispasmodic, and calming effects (9,17-19,20,21), an impact on blood pressure with hypotensive effects independent of the adrenergic system, likely due to the vasorelaxant effect of methanol (13,17,23), antidiabetic activity through anti-amylase effects (9,24,25), diuretic action (9,24), anticholinergic effects, and anti-Alzheimer effects stimulating memory (15,17,26).

2. Toxicity of Cade Oil

When used for therapeutic purposes, cade oil can cause a significant number of toxic reactions, which can even be fatal. According to data from the global poison center CAPM, this toxicity has a mortality rate of approximately 10.5% (28). In our study, five cases were fatal.

Toxicity often results from iatrogenic causes, primarily due to ingestion of a large amount or, particularly in infants and newborns, from prolonged and extensive cutaneous application. The surface-to-weight ratio, combined with the immaturity of metabolic and elimination processes in infants, explains the severity of the toxicity when the product is applied topically (5).

In our series, no cases of ingestion were noted; one case involved inhalation, six cases were through cutaneous exposure, nine cases involved transcutaneous absorption via scarification, and four cases had both cutaneous and respiratory exposure.

Cade oil contains phenol, which has life-threatening effects (corrosive, cardiac, hemolytic, pulmonary, and renal) (3). It is the most toxic component. Its absorption is rapid, and its metabolism is primarily hepatic. Systemic toxicity is multi-organ and is explained by the formation of cytotoxic metabolites (semi-quinone radicals) when the absorbed amount exceeds hepatic conjugation capacity (3,5,6,8). The severity of intoxication ranges from benign symptoms to life-threatening conditions.

2.1. Neurotoxicity

Alterations in the central and peripheral nervous systems have been reported following cade oil intoxication, including involuntary movements, headaches, hypotonia, mental confusion, and even myoclonic or convulsive coma (4) due to increased acetylcholine release at the neuromuscular junction, leading to heightened central nervous system activity (28). In our study, consciousness disturbances were reported in 16 patients.

2.2. Cardiovascular Toxicity

Cardiovascular disorders (such as sinus bradycardia, myocardial excitability disturbances, hypotension, and even cardiovascular collapse) have been documented in the literature (3,13,15,32). Toxic doses of phenol cause initial hypertension followed by a marked drop in blood pressure (4). In our study, seven patients exhibited hemodynamic disturbances. However, no electrical anomalies were observed.

2.3. Respiratory Toxicity

Pulmonary involvement can range from pneumonia to acute pulmonary edema (OAP) (3,33). In our study, respiratory symptoms were illustrated in 12 cases, with four having evident radiological findings.

2.4. Nephrotoxicity

Renal damage can be reversible or permanent, affecting the glomeruli, tubules, and interstitium. Hematuria and/or albuminuria (34,35), functional renal insufficiency (3,4,7,36), and organic renal failure (37) can be

observed. In our study, three cases of acute functional renal failure were noted.

2.5. Hepatic Toxicity

Liver damage ranges from hepatic cytolysis to hepatic cellular failure (4). In our study, seven cases of hepatic cytolysis were recorded.

2.6. Digestive Toxicity

Phenol's corrosive effect leads to diarrhea and vomiting of varying severity, sometimes resulting in severe dehydration (13). Digestive symptoms were predominant in our study, affecting all of our patients.

2.7. Hematological Toxicity

Methemoglobinemia, deep vein thrombosis, and hemolytic anemia (38) have been reported after exposure to cade oil, with effects attributed to phenol (13,26). Neutropenia, thrombocytopenia, and consumption coagulopathy are also observed (13).

2.8. Adverse Effects on Skin and Mucous Membranes

Short-term, this substance has an irritant effect (8). Long-term, cade oil contains polycyclic aromatic hydrocarbons such as benzopyrene, which is known to be carcinogenic (8,39).

3. Management of a Child with Cade Oil Poisoning

A thorough interview with parents, their surroundings, or witnesses often allows for the precise determination of the cause of poisoning, the circumstances, the time of exposure, initial symptoms, and any complications, thus avoiding costly and sometimes unnecessary tests, especially toxicological analyses.

Apart from cyanosis associated with methemoglobinemia, the presence or absence of a blackish discoloration due to the toxic product can easily guide the diagnosis. A brown-black discoloration may be due to the presence of hemoglobin or myoglobin, but the blackish color of cade oil itself can also cause this coloration. The distinctive odor of cade oil is another important diagnostic clue.

Symptoms are very varied and can involve all organs, including central neurological disturbances, cardiovascular issues, respiratory, and digestive disorders. Certain biological abnormalities have significant diagnostic value and can even suggest the toxin (41). It is recommended to perform blood glucose testing to check for hypoglycemia (9,24,25), an electrolyte panel to detect ionic disturbances, a gas analysis to assess metabolic acidosis, and a coagulation profile to identify hemorrhagic syndromes secondary to hepatic failure or disseminated intravascular coagulopathy within the context of multi-organ failure.

Measuring transaminases helps assess the extent of cytolysis and toxic aggression (3). Radiological exams have non-specific indications for determining the presence of lesions or complications (e.g., chest X-ray for pulmonary edema, atelectasis, pneumonia). EEG remains valuable in cases of convulsive or myoclonic states and in monitoring post-anoxic comas (40). Digestive endoscopy is indicated in case of significant cade oil ingestion since some of its constituents are considered corrosive (42).

Toxicological analysis is certainly diagnostically useful. However, if the diagnosis is evident (history, symptomatology), its main relevance becomes medico-legal (41). Methemoglobinemia should be investigated in the presence of slate-gray cyanosis, unexplained by hypoxemia, and unresponsive to oxygen, when arterial blood shows a chocolate-brown hue unaltered by exposure to air or oxygen bubbling.

Regarding cholinesterase levels, a decrease in plasma and especially erythrocyte cholinesterase activity is usually a direct indicator of the severity of organophosphate and carbamate insecticide poisonings.

4. Severity Diagnosis

This is a fundamental step as it determines the therapeutic strategy and monitoring. The progression of poisoning is a dynamic process dependent on the kinetics and toxicodynamics of cade oil.

5. Therapeutic Management

Therapeutic management should begin as early as possible to prevent systemic effects. For systemic intoxication, therapeutic management is primarily symptomatic, based on resuscitation measures (ventilatory and hemodynamic support if indicated, anticonvulsants for seizures, correction of ionic and acid-base disturbances if biological anomalies are present, and administration of methylene blue in cases of methemoglobinemia (43)) to maintain vital signs and simultaneously decontamination to prevent systemic effects. Depending on the route of exposure, cutaneous and ocular decontamination or digestive decontamination is implemented.

No specific antidote for cade oil is currently available due to limited knowledge of the product. Emergency antidotes include Atropine for cholinergic syndrome and pralidoxime when toxicological tests are positive for organophosphates (41). Administration of N-acetylcysteine (Fluimucil®) may be considered to attempt to neutralize reactive metabolites from hepatic biotransformation.

Medico-legal management with a report to child protection is mandatory.

CONCLUSION

In Tunisia, cade oil is available to consumers without prescription or market authorization. Its irrational use leads to severe, sometimes fatal adverse events. Public awareness is essential. Likewise, informing healthcare professionals about these side effects is crucial to ensure early and effective management in a resuscitation unit in cases of poisoning.

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Jejunal Diverticulosis: Review

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Abstract

Jejunal diverticulosis is a rare pathology (less than 5% of the general population). It often has a non-specific symptomatology making its diagnosis usually difficult. It may be complicated by diverticulitis, perforation, acute intestinal obstruction, gastrointestinal bleeding, or intestinal malabsorption. Conservative treatment of symptomatic jejunal diverticulosis may be performed with however poor outcomes. Surgery is then unavoidable. Short and limited intestinal resection should always be preferred to prevent short bowel syndrome. The main poor prognostic factors are diagnosis and surgery delays.

KEYWORDS : Jejunum; Diverticulum; Complications; Diagnosis; Treatment; Mortality.

INTRODUCTION

Diverticulosis of the small intestine was reported for the first time by Sommering and Baillie in 1794 in their autopsy studies [1]. In 1881, W. Osler [2] published the first clinical observation on this issue. Jejunal diverticulosis (JD) is a rare entity (1 to 4.6% of the general population) [3] whose evolution is often asymptomatic. Its diagnosis is difficult and often neglected or delayed because of the location of the disease and its nonspecific clinical presentation.

There is no international consensus for the management of JD today. The objective of this narrative review is to work out the appropriate modalities for the diagnosis and treatment of JD taking into consideration recent medical improvements.

EPIDEMIOLOGY

JD is very rare in children [4]. It is usually reported in patients aged between 50 and 70 years [5]. Men seem to be more affected (58%) than women [6].

JD can be associated with colonic diverticula (70-20%), duodenal diverticula (10 to 40%), and oesophageal or gastric diverticula (2%) [7, 8]. These associations suggest a common etiology.

ANATOMOPATHOLOGY

The jejunal diverticulum corresponds to a herniation of the intestinal mucosa and submucosa with no muscular layer in the diverticular wall. It is a "pseudo-diverticula", whereas Meckel congenital diverticulum is a true one as its wall has a muscular layer [9]. There are two kinds of acquired diverticula: the narrow collar type and the wide collar type [10].

JDs thrive at the weak points of the small intestine wall which are the intestinal micro vessels' entries (vasa recta). Therefore, the JD is strictly localized at the level of the mesenteric side of the small intestine [11]. The jejunal diverticulum of the anti-mesenteric side is a very rare model (only one case was reported) [12]. Its forming mechanism would be different.

The proximal jejunum is the preferred site of small bowel diverticula (75%) [13]. This would be attributed to the larger diameter of the vasa recta and their larger sites of penetration into the bowel wall [9].

The size of jejunal diverticula varies from a few millimeters up to 3 centimeters, but sometimes it exceeds 10 cm [14]. Generally, the jejunal diverticula are large and numerous in the proximal jejunum while they are few and small in the distal jejunum [13].

PHYSIOPATHOLOGY

Although its etiology is still uncertain, it is believed that the jejunal diverticulum develops because of intestinal peristalsis anomalies (intestinal dyskinesia) and high intra-luminal pressure [7]. These conditions can be promoted by an internal hernia or by some surgical procedures such as Roux-en-Y reconstruction or Omega loop [15, 16].

Intestinal dyskinesia is probably related to abnormal smooth muscle or to abnormal neuro-myenteric plexus, which are of 3 types: progressive systemic sclerosis, visceral myopathy, and visceral neuropathy [17]. Some authors suggested a link between bowel diverticulosis and

Neuromuscular diseases that are Cronkhite-Canada syndrome, Fabry disease, neuro-gastrointestinal mitochondrial encephalopathy, Elhers-Danlos syndrome, progressive systemic sclerosis, myasthenia gravis, primary or secondary amyloidosis and jejuna lipomatosis [18–26]. In addition, the relative lack of fat in the mesentery may be another contributory factor as it would further weaken the intestinal wall at vasa recta entries. JD may be also a hereditary family disease (most probably autosomal dominant transmission) especially among families with autoimmune diseases (2 cases were published [27,28]), or be associated with mesenteric malrotation that may cause an intraluminal hyperpressure [29].

CLINICAL MANIFESTATIONS

The clinical suspicion of JD remains difficult, and its diagnosis is often overlooked or delayed as it is usually done when the disease becomes symptomatic or complicated. Indeed only 30% of patients with JD are symptomatic, and less than 10% would have severe complications [30]. Noncomplicated JD symptoms are non-specific such as chronic postprandial abdominal pain, vague abdominal pain, nausea, vomiting, alternating diarrhea constipation, steatorrhea, weight loss, fever, and anaemia [6, 31]. The only definitive way to attribute these symptoms to JD is to get their resolution after surgical resection of the jejunal diverticula.

Clinical presentation of acute or chronic complications of JD is also not specific and variable: it is sometimes discreet but often misleading and may simulate colonic diverticulitis, appendicitis, or acute cholecystitis. Acute complications include massive bleeding, diverticulitis, perforation, and acute intestinal obstruction. Chronic complications are mainly malabsorption but also include intestinal dyskinesia and chronic intestinal hemorrhage [32]. It seems that the risk of complications is higher in patients with multiple jejunal diverticula.

COMPLICATIONS OF JEJUNAL DIVERTICULOSIS

Jejunal diverticulitis

Diverticulitis is much less common in JD than in colonic diverticula. It is probably due to the diverticulum's larger size, better intra-luminal flow, and relatively sterile jejunal content [33]. Perforation may happen (7%) and cause a local abscess or generalized peritonitis [34].

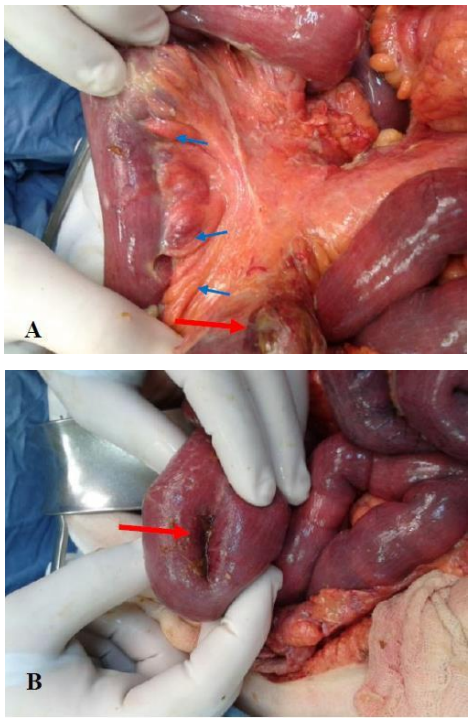

Figure 1: *Diffuse jejunal diverticulosis (A) (blue arrows) with abscessed and perforated diverticulum (red arrows) (A and B): this is a mesenteric abscess related to jejunal diverticulitis.*

The incidence of diverticulitis ranges from 2 to 6% [35]. Its mortality rate was high (24%) in the past then it declined sharply thanks to medical improvements [36]. Jejunal diverticulitis is rarely diagnosed preoperatively because of its nonspecific clinical presentation as acute abdominal pain with infectious syndrome and sometimes gastrointestinal bleeding. In addition, it is sometimes very difficult to distinguish, on a CT scan, between a perforated diverticulum and other differential diagnoses that have a similar image as an inflammatory process next to an intestinal loop. These differential diagnoses are

mainly intestinal neoplasms then Crohn's disease [37] and more rarely intestinal perforation by a foreign body, traumatic hematoma of the intestinal wall, and drug-induced intestinal ulceration [38, 39]. However, it is worth noting that the inflammation of Crohn's disease affects the whole intestinal wall circumference, unlike jejunal diverticulitis which causes asymmetric intestinal wall inflammation [40].

Perforation of jejunal diverticulum

The perforation of JD is rare (2.1 to 7% of diverticulitis) [41] probably because of intestinal intraluminal low pressures. Diverticulum perforation leads to generalized [42] or localized peritonitis. The latter usually ties in with a mesenteric abscess which is the most common presentation of this perforation (figure 1) [43]. As a rule, this wouldn't cause immediate peritoneal contamination. Therefore, diagnosis of such complications is delayed and would lead to a possible disastrous clinical evolution, particularly in debilitated and/or elderly patients. The other complications of diverticulum are digestive fistula, intra-peritoneal abscesses, and liver abscesses [36, 44].

From a pathophysiological standpoint, possible causes of diverticulum perforation are necrotizing inflammatory reaction (82%), progressive ulceration in diverticulitis, blunt trauma (12%), foreign body impaction (6%), and cocaine intoxication [31, 45].

Apart from any peritonitis, JD may cause chronic pneumoperitoneum by air diffusion through the semipermeable membrane of the diverticulum thin wall. This also may be due to diverticular micro perforation [42]. Jejunal diverticulum perforation may lead to high mortality rates ranging from 21 to 42% [46].

Acute intestinal obstruction

Intestinal obstruction remains the rarest complication of JD (2.3 - 4.6%) [14]. It may be due to intestinal dyskinesia (10-25%) resulting in what is called a "functional acute bowel obstruction" or a "pseudo-obstruction" [30]. Otherwise, it is usually due to a mechanical obstruction cause that may be as follows:

- A large diverticulum or an inflammatory pseudotumor relevant to jejunal diverticulitis leading to an extrinsic intestinal compression [47].

- Intestinal intussusception caused by an enterolith formed in the jejunal diverticulum [47].

- Adhesion band formed mainly due to repeated outbreaks of jejunal diverticulitis usually pauci-symptomatic. This band would cause a small bowel volvulus [14, 48, 49].

- An intestinal fibrous stenosis is generally due to multiple jejunal diverticulitis flare-ups [50].

- Stenotic jejunal tumor developing inside the diverticulum [51].

Enterolith formation within the jejunal diverticulum is rare: real enteroliths derive from Choleric acid (product of conjugation of

bile acids) and fake enteroliths form by impaction of food debris in the diverticulum. Small enteroliths are sometimes dislodged and transit through the colon uneventfully while large stones can cause obstruction: it is an "enterolithical ileus" like a gallstone ileus [52].

Diverticular bleeding

Hemorrhage complicates 2 to 8.1% of JD [53]. JD causes less than 5% of rectal bleeding [54]. The pathophysiology of diverticular bleeding is the same regardless of the location of the diverticulum on the digestive tract. Hemorrhage is usually due to arterial erosion by a diverticular ulcer, diverticulitis, an enterolith, or drug intake (NSAIDs). It can be occult bleeding with iron-deficiency anemia.

Vascular lesions such as arteriovenous malformations and venous ectasia, which are the most common causes of bleeding in the small intestine, can rarely coexist in the jejunal diverticulum (only 2 cases were reported in the literature) [55, 56]. Furthermore, there are other causes of bleeding from the jejunal diverticulum such as ischemic colitis, ectopic pancreas, and small bowel tumors (adenoma, adenocarcinoma, endocrine tumour) which may also exist in non- diverticular intestine.

Malabsorption

It is the most common complication of JD. It is due to intestinal stasis and bacterial overgrowth [57]. Malabsorption would result in Vitamin B12 deficiency (megaloblastic anemia) and/or in steatorrhea due to deconjugation of bile acids and disturbance of fat absorption. This triad (JD, megaloblastic anemia, and steatorrhea) was described for the first time in 1933 [58].

Malignancy in jejunal diverticulosis

Malignancies such as leiomyosarcoma, adenocarcinoma, endocrine tumors, and stromal tumors may rarely arise in the Jejunal diverticulum [51, 59]. The risk is higher in patients with multiple jejunal diverticula.

EXPLORATIONS

Abdominal x-ray

It can show distension of jejunal loops and air-fluid levels within large diverticula. JD may take on the appearance of an air-filled structure on the mesenteric border of the proximal small.

Intestine [60]. An opacity (calcification) is suggestive of a possible enterolith [52], but unfortunately, it also suggests biliary and urinary stones.

Small bowel follow-through (SBFT)

Before the advent of abdominal computed tomography (ACT), the SBFT was the gold standard for the diagnosis of JD [57]. However, it is prohibited if complicated JD is suspected. The diverticulum appears in SBFT as a gas clarity (bubble) or as a pediculate barite collection on the mesenteric border of the jejunum and in continuity with the intestinal lumen [57].

Echo-doppler (ED)

The ED would be very helpful in diverticular bleeding because of its good sensitivity (73.7%),

high specificity (97.1%), high positive predictive value (87.5%), and high negative predictive value (93.2%) [61].

Multi-slice computed tomography (MSCT)

Nowadays, the MSCT is the reference imaging tool for the diagnosis of JD as well as its possible complications [38] (figure 2). It may show jejunal diverticulum as:

- a sac on the mesenteric side of the small bowel, or
- a focal and asymmetric thickening of the intestinal wall or
- an inflammatory pseudo-tumor or
- an abscess next to a jejunal loop with infiltration of the surrounding mesenteric fat [62].

The MSCT also allows ruling out other abdominal inflammatory conditions such as colonic diverticulitis, Crohn's disease, and appendicitis.

A recent meta-analysis showed that abdominal angiostatin is effective and very precise in diagnosing or excluding active gastrointestinal bleeding with high sensitivity (79-100%) and specificity (85-100%) [63, 64].

Mesenteric angiography (MA)

The MA has a diagnostic profitability of 61-72% in patients with active bleeding [53]. However, it can only detect bleeding with an outflow of at least 0.5 ml/min. Angiographic pathognomonic sign of diverticular bleeding is the extravasation of contrast medium into the diverticulum. MA offers also the possibility of super-selective embolization (success rate of 58-100%) however with a risk of intestinal ischemia (0-7%) and rebleeding (15%) [64].

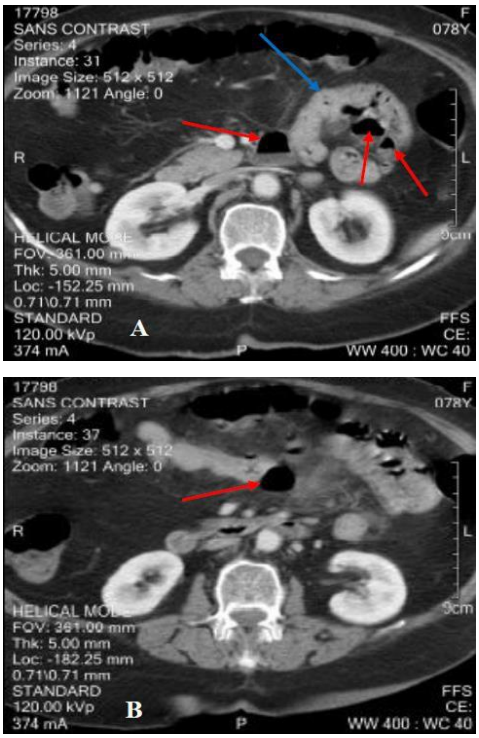

Figure 2**:** *Abdominal CT-scan showing multiple jejunal diverticula (A and B) (red arrows) with thickening of the first jejunal loops wall (A) (blue arrow) suggesting a jejunal diverticulitis.*

Red blood cell scintigraphy (RBS)

RBS can be used to detect and localize gastrointestinal bleeding even if they are of very low outflow (0.1ml/minute) with high sensitivity (93%) and specificity (95%) [64, 65]. However, it is still considered an accessory tool usually needed when the source of intestinal bleeding is still unknown after endoscopy and abdominal angiostatin [64, 66].

The combination of RBS (locates the bleeding) and MA (embolization) is highly efficient in diagnosing and treating hemorrhagic JD [33].

Endoscopic explorations

The enteroscopy is efficient in finding out the cause of gastrointestinal bleeding inherent to the small intestine, but it is useless in emergencies. The double-balloon enteroscopy (DBE) is significantly more effective than conventional enteroscopy in the diagnosis of small bowel lesions ($p < 0.0001$) [67]. It is also better than the video capsule endoscopy (VCE) which remains an excellent exploration method of obscure gastrointestinal bleeding particularly those of small bowel origin [68-70].

TREATMENT

Emergent surgery is required in 8-30% of patients with complicated JD [17]. The total laparoscopic approach is possible and it is safe and efficient even for complicated JD [43].

It is worth noting that diverticula may spring afresh after surgical resection of all jejunal diverticula [71].

Asymptomatic JD

Asymptomatic diverticula usually do not need any treatment. Nevertheless, surgery should be considered for large diverticula with dilated intestinal loops because of the high risk of complications [8].

Symptomatic uncomplicated JD

Medical treatment is usually sufficient otherwise; resection is indicated [5].

Jejunal diverticulitis

Management of uncomplicated diverticulitis with hemodynamic stability requires fasting and systemic antibiotherapy (oral antibiotics are debatable). Surgery has to be considered if medical treatment fails [38]. Considering the high-risk recurrence and other JD complications in this case, surgical resection is highly recommended [3, 7].

Perforated JD

A conservative treatment based on intravenous antibiotherapy should be considered first for mesenteric or peri-diverticular abscesses. Patients may also undergo whenever needed CT-guided percutaneous drainage. On the other hand, the surgical approach (taking away the perforated diverticulum) becomes mandatory in the following situations:

- A generalized peritonitis
- Failure of
- Infeasible percutaneous drainage

Immediate digestive anastomosis should be avoided in shocked or high-risk patients and jejunostomy must then be rationally performed [7, 57].

Two surgical techniques are currently prohibited as they are Unsafe and significantly increase (3 times) the risk of death. These techniques are simple diverticulectomy, the suture of the diverticulum perforation, and burying the perforated diverticulum [72]. Paradoxically, it seems.

reasonable to use one of these techniques if the perforated diverticulum is close to the duodéno-jejunal angle because an intestinal anastomosis at

this level would be difficult to manage.

Extensive intestinal resection is prohibited because of a short bowel syndrome risk. Thus, in case of extensive JD, intestinal resection limited to the perforated diverticulum is recommended.

Haemorrhagic JD

Double balloon enteroscopy and embolization are very seducing approaches for management of jejunal diverticula bleeding [73]. Endoscopic haemostasis is burdened with a high mortality rate because of high risk of bleeding recurrence. Contrariwise embolization has a success rate of 85% and seems to be the best alternative in debilitated and high anaesthetic risk patients [64, 74]. However, surgical resection of the involved intestinal loop with immediate anastomosis remains the reference treatment of haemorrhagic JD. Unfortunately, preoperative diagnosis of the precise source of bleeding is rarely done [3, 53]. Thus, for patients with diffuse JD, intraoperative endoscopy via enterotomy would be helpful to locate the source of bleeding with a success rate of 76% [75]. In case of obvious colonic diverticula bleeding, jejunal diverticula should be resected whenever possible. Preoperative abdominal angioscan may be useful in patients with colonic and jejunal diverticula so as to avoid unavailing colectomy [53]. Immediate and long-term cessation of bleeding after resection is the certainty criterion that the source of bleeding is the jejunal diverticulum.

JD with acute intestinal obstruction

JD with intestinal obstruction may be managed with gentle digestive aspiration but due to high failure rate surgical approach is oftenly performed [47, 76]. In case of enterolithical ileus, the surgeon must attempt to manually crush the enterolith and to push its fragments in the distal colon [47]. Otherwise, an enterotomy may be carried out close to upstream or downstream of the obstruction site. Laparoscopic handling of enterolith (crushing, mobilization and extraction) is not recommended because it is potentially traumatic for congestive intestine. Moreover, laparoscopic complete verification of all jejunal diverticula is illusive [45, 52].

In case of intestinal obstruction without enterolith, the rule is intestinal resection with immediate anastomosis. Any adhesive band should also be sectioned. Complications as perforation, necrosis or stenosis necessarily require intestinal resection [76].

JD and malabsorption

Megaloblastic anaemia is classically treated by parenteral administration of Vitamin B12. Broad-spectrum antibiotics covering enteric flora (Rifaximin, Metronidazole, Amoxicillin / Clavulanic acid, ciprofloxacin and tetracycline) reduce efficiently diarrhoea and abdominal distension [77]. These antibiotics are typically prescribed for two weeks. Their rotating use is necessary to prevent microbial resistance.

MORTALITY - PROGNOSIS

JD is a benign pathology with a good prognosis in general. The mortality rate of complicated JD ranged from 21 and 30% but thanks to medical improvements, recent publications reported much lower mortality rate (0-5%) [78, 79].

Elderly patients, comorbidities, severe complications, diagnosis delay and mainly late surgery for diverticular perforation are associated with poor outcomes [33].

RESEARCH PRIORITIES CONCERNING JEJUNAL DIVERTICULOSIS

Medical researchers should try answer to these questions:

1) Is there any genetic test to detect JD in high-risk patient with neuro-myenteric plexus pathology?

2) What is the optimal combination of medical imaging that is most effective for diagnosing symptomatic and complicated JD ?

3) Is there any indication for small bowel transplant in diffuse JD ?

CONCLUSION

Clinical data of JD are always nonspecific and thus unsubstantial for its diagnosis. Therefore, MSCT and less frequently DBE and VCE are clearly contributing. Conservative treatment of symptomatic JD may be performed with however poor outcomes. Surgery is then unavoidable. Short and limited intestinal resection should always be preferred to prevent short bowel syndrome. The main poor prognostic factors are diagnosis and surgery delays.

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Civil-Military Collaboration for health emergency preparedness

STMU 2024 congress conference

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The role of military assistance in responding to natural disasters including accidental or deliberate incidents related to biological and chemical has been long established. While the military has historically not been involved in as a potential partner in responding in natural outbreaks, the engagement of militaries in the response against the covid-19 pandemic at national and international levels illustrate clearly the advantages of the implementation of a civil-military health collaboration system against pandemics.

The comprehensive approach

The scale and the complexity of nowadays emergency situations such as biological threats, chemical deliberate or accidental incidents, hybrid attacks and natural disasters following climate change have shown the urgent need for building and strengthening partnership between the public health sector and non-traditional health stakeholders such as the military institution in a framework of an intersectoral and a multi-institutional approach and based on a comprehensive approach.

The comprehensive approach (CA) is a way to achieve a common understanding and approach among all (interested) actors at national level, it requires actors to work together with a shared sense of responsibility and openness, considering and respecting each other's strengths, mandates, roles, and decision-making autonomy [1]. In other words, the Comprehensive Approach is not hierarchical but rather a collaborative effort among equals.

From a pure military perspective, the North Atlantic Treaty Organization (NATO) is very different in this regard. It views civil-military cooperation as essentially about achieving military goals [2]. CIMIC activities, however, serve the military mission, follow military priorities, and focus on reaching political goals, thereby deviating from humanitarian principles of humanity, impartiality, neutrality, and independence. Over time, NATO has adopted the belief that military operations sometimes must be integrated with civilian and political elements to achieve lasting peace and stability in fragile regions. This comprehensive approach (CA) sees military operations as Joint and comprehensive enterprises. Still, the achievement of military interests remains key in this approach [3].

The Need for a Military- Civil partnership

The civil-military collaboration (CIMIC) must be established earlier before emergency situations occur through a joint capacity building in the framework of a national response plan against health emergencies and at each phase of it, joint vulnerability assessment and prevention, preparation plans, joint response action and a national resilience global approach.

But why is there a need for CIMIC? Several military strength points must be highlighted:

- Terrain deployment expertise and experience
- Medical logistics: Equipment and capabilities more available
- Nuclear, Radiological, biological and chemical (CBRN) expertise
- Well trained personnel on disaster and on situations of exception
- Rapidity of deployment and means to access hostile environment

Levels of Interaction

Levels of interaction between civil and military stakeholders can go from coexistence (the lower level of collaboration) with no interaction at all to integration (highest level of collaboration) defined as the process of operating together to achieve a unified end state. Integration represents the maximum level of interaction between two actors, which involves working to plan and execute mutual actions within a common engagement space [3]. For example, civil and military authorities form an integrated staff to plan and synchronize military and non-military activities to plan a military operation and mitigate the impact on civil society.

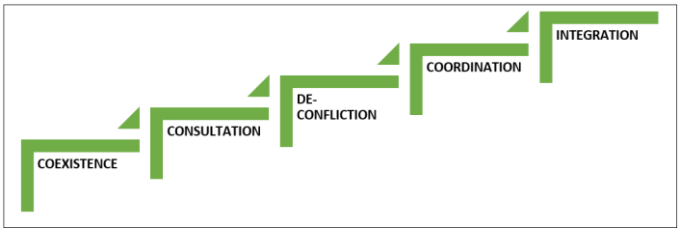

Figure 1: *Levels of Civil-military cooperation*

Areas of collaboration

The WHO National civil–military health collaboration framework for strengthening health emergency preparedness- 2021 outlines key aspects and linkages to related technical areas that countries need to take into consideration preceding civil–military health collaboration for capacity development at the national and subnational levels [3]. Six key aspects were identified:

1. Historical, political, social and legal context
2. Health emergency versus national state of emergency
3. National disaster management
4. Public health emergency operations centre (PHEOC)
5. Emergency medical teams (EMTs)
6. Chemical, biological, radiological and nuclear (CBRN) emergencies

Civil-Military cooperation in Tunisia: Level of collaboration

Analysis of two main features of civil military collaboration:

- Integrated trauma system
- Covid 19 pandemic collaboration

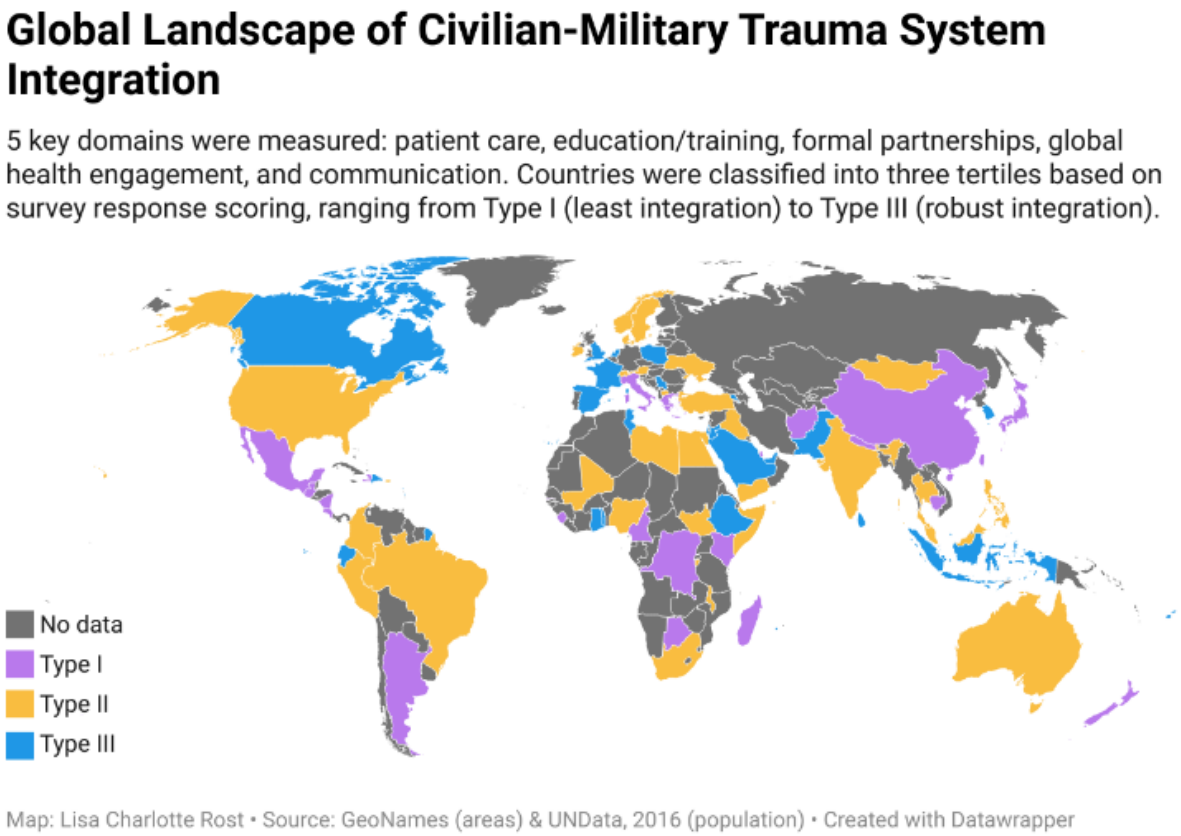

Figure 2: *Global landscape of civil-military Trauma system integration* [6]

Integrated trauma system related to terrorist attacks

Civil-military collaboration within the framework of the terrorist attacks in Tunisia was manifest through the integration of the civilian hospitals in the roles of medical care system. In several cases, military medical teams worked jointly with civilian colleagues within Regional public health hospitals, the equivalent of field hospital Role 2 (NATO terminology for combat surgical hospital). The integration of university military hospitals and prehospital emergency medical system (EMS) to the national public health system allowed military ambulances to participate and evacuate casualties to military hospitals during terrorist attacks inn town. The Integrated Military Partnerships and Civilian Trauma Systems (IMPACT) Study [6] aimed to understand the function and capabilities of military trauma systems, and the level of integration that may exist with civilian trauma systems. Tunisian civil military collaboration in Tunisia was categorized level 3 (robust integration). The study measured 5 key domains: patient care, education/training, formal partnerships, global health engagement, and communication. Countries were classified into three tertiles based on survey response scoring, ranging from Type I (least integration) to Type III (robust integration) Figure 2.

Civil military collaboration within the covid-19 pandemic

The efficiency of the Tunisian National response against the covid 19 pandemic was in a huge part possible thanks to the tight and strong

collaboration between civil and military medical sectors. This collaboration was made possible because of a long collaboration history between the two institutions.

CIMIC experiences and analysis included areas such as political framework, strategy, structure, nature of civil-military interaction and concrete mission reports [5]. Themes covered a broad spectrum of pandemic disaster management subjects such as capacity and surge capacity building, medical and pharmaceutical logistics, patient care under austere circumstances, SARS-CoV-2 testing support, intelligent and innovative information management, vaccination support, and disaster communication. In Tunisia, several cimic features are to be cited:

- The joint steering committees at strategic level
- Daily sharing of information, data and reports
- Effective communication channels
- Deployment of field military hospitals for civil patients
- Activation of the Tunisian taskforce against biothreats and decontamination teams to repatriate Tunisian to homeland during quarantine periods and global shat down
- Deployment of the mobile laboratory of microbiology for covid19 tracing tracking and testing
- Joint vaccination campaigns
- Logistics Management of equipment sets and capabilities, oxygen and personal protective equipment through join committees
- Joint training and workshops
- Joint participation for validation of national response plans against pandemics

CONCLUSIONS

Since 2018 the WHO has urged states and governments for a strong Civil-military collaboration to establish an integrated health system against emergencies. Tunisia has achieved huge step towards integration level of CIMC thanks to a long history of joint work and the establishment of CIMIC integration tools. Further studies are needed to assess vulnerabilities and shortfalls, and additional steps are needed to convince all stakeholders, decision and policy makers to prioritize the CIMIC integrated health system.

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Diagnostic Challenges and Treatment Strategies in Axillary Trauma: A Case Report

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Abstract

Introduction: Axillary trauma is a rare and complex injury that involves a high risk of vascular and nerve damage due to the concentration of critical structures in the axillary region. This case report highlights the diagnostic challenges and treatment strategies in managing a severe axillary injury.

Case Presentation: We present the case of a 70-year-old woman with no significant medical history, who sustained a penetrating axillary injury after a fall onto an iron bar. Upon arrival, the patient exhibited severe pain, absence of the left radial pulse, and neurological deficits in the left upper limb, suggesting significant vascular and nerve involvement. A CT angiogram confirmed injury to the brachial artery and axillary nerve. The patient underwent emergency surgery involving a multidisciplinary team approach, which included extraction of the foreign object, arterial repair, and decompression of the nerve. Postoperatively, she received prophylactic antibiotics and tetanus immunization. Her recovery was uneventful, with no major complications.

Conclusion: This case underscores the importance of early recognition, a coordinated surgical approach, and comprehensive postoperative care in managing axillary trauma. Long-term follow-up is essential to assess functional recovery and mitigate the risk of chronic sequelae.

Keywords: Axillary trauma; Emergency; Management; Surgery.

INTRODUCTION

Axillary trauma, though commonly underestimated compared to other types of injuries, plays a crucial role in frontline trauma care [1-4]. The significance of these injuries lies in their potential impact on patients' quality of life. If not properly diagnosed and treated, axillary injuries can lead to chronic pain, functional limitations, and long-term complications [5]. Diagnostic and treatment challenges may be compounded by the region's anatomical complexity, where vital structures are closely intertwined.

CASE PRESENTATION

This case involves a 70-year-old woman with no significant medical history. She sustained a fall from her height and, during the fall, came into contact with an iron bar that pierced her

axillary region. The iron bar penetrated deeply into her axilla, resulting in significant vascular and nerve injuries. The patient was urgently admitted to the emergency room (Figure 1). On admission, she was conscious and cooperative but in severe pain, with a blood pressure of 90/60 mmHg and a heart rate of 102 beats per minute.

The left radial pulse was absent, while all other pulses were present. The trauma team suspected a vascular trauma. Neurological examination found motor deficits in the left upper limb and thermo-analgesic anesthesia (loss of temperature and pain sensation) in the axillary nerve distribution, indicating nerve damage.

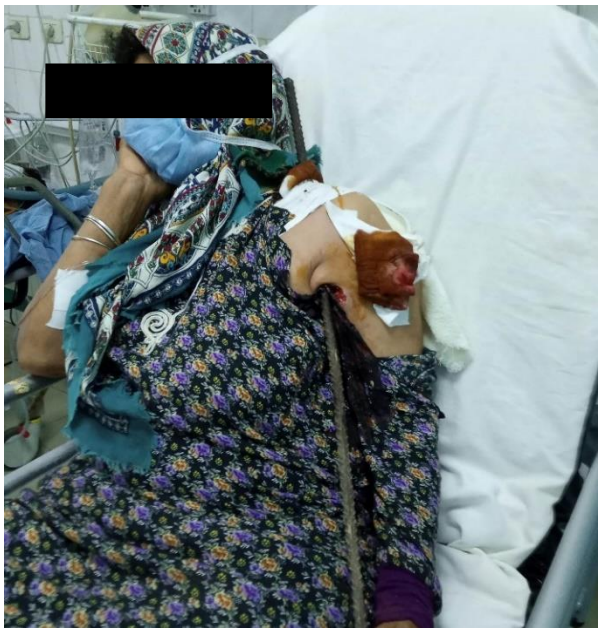

Figure 1: *On-admission presentation of the patient*

A CT angiogram of the left upper limb was urgently performed. It demonstrated damage to the brachial artery and elongation of the axillary nerve with injury to its motor and sensory branches.

An urgent dual team surgery was performed, including cardiovascular surgeons and orthopedists. The surgical steps were as follows: extraction of the iron bar, suturing of the damaged arterial wall, decompression of the axillary nerve, tissue continuity restoration with irrigation, hemostasis, and closure with a Redon drain. The postoperative outcome was uneventful, with no major reported complications.

DISCUSSION

Axillary trauma is a rare but significant injury due to the dense concentration of vital structures in this region, including major vessels, nerves, and muscles [1-4]. The complexity of the axillary anatomy makes, both, the diagnosis and management of such injuries challenging. In this case, the patient suffered extensive vascular and nerve damage, which underscores the severity of penetrating axillary trauma.

Vascular and Neurological Implications: The absence of the left radial pulse in this patient was a clear sign of vascular compromise, confirmed by the CT angiogram showing damage to the brachial artery. Vascular injuries in the axilla can lead to ischemia, delayed healing, or loss of function in the affected limb if not promptly addressed. The patient's neurological deficits, including motor loss and thermo-algesic anesthesia, point to axillary nerve damage, which can result in long-term disability. Early identification and repair of nerve injuries are crucial in minimizing permanent loss of function, though full recovery may not always be achievable.

Multidisciplinary Approach: The successful management of this case highlights the importance of a coordinated, multidisciplinary approach in treating complex axillary injuries. Collaboration between emergency physicians, radiologists, cardiovascular surgeons, and orthopedic teams allowed for simultaneous vascular repair and nerve decompression. This approach ensures that immediate life-threatening complications, such as arterial bleeding, and long-term risks, like functional deficits, are addressed promptly. Studies emphasize that delayed intervention in cases of combined vascular and nerve injuries can lead to poor outcomes, including chronic pain, muscle atrophy, and permanent loss of limb function [6-7].

Operative Challenges and Considerations:

The decision to perform simultaneous vascular and nerve repair is essential in preventing further complications. Removing the iron bar without causing additional damage required extreme precision. Besides, repairing the damaged structures posed significant challenges. The use of Redon drains in the postoperative period minimized the risk of fluid accumulation or infection, which are common complications in such extensive trauma cases.

Postoperative Management: Postoperative care, including prophylactic antibiotic administration and tetanus immunization, had a key role in preventing infections and promoting recovery. The uneventful outcome of the patient, here reported, emphasizes the importance of comprehensive perioperative and postoperative management, tailored to prevent both short-term and long-term complications [8-10].

This case is consistent with the literature on penetrating axillary injuries, which suggests that while these injuries are rare, they often involve complex surgical interventions. Studies report that while vascular injuries can be successfully managed in most cases, nerve damage commonly poses greater challenges in terms of long-term recovery, with many patients experiencing persistent sensory and motor deficits. Despite advances in microsurgical techniques, nerve repair outcomes can be unpredictable, with recovery times varying from months to years, and some patients experiencing permanent disability.

Limitations and Future Considerations:

Although the surgical outcome in this case was favorable, it is important to recognize that chronic pain and limited functionality are common in patients with similar injuries. Long-term follow-up is necessary to monitor for chronic sequelae, including nerve regeneration and functional recovery. Additionally, the need for early rehabilitation, including physical therapy, cannot be overstated, as it plays a critical role in maximizing functional outcomes and reducing chronic pain.

CONCLUSION

This case highlights the complex nature of axillary trauma and the need for a rapid, multidisciplinary approach to prevent life-threatening complications and optimize long-term outcomes.

Vascular and nerve injuries in the axilla require timely diagnosis and intervention to minimize the risk of chronic disability. Future studies should focus on refining surgical techniques for nerve repair and improving rehabilitation protocols to enhance functional recovery in these patients.

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Spontaneous Pneumomediastinum as Uncommon Complications of COVID-19 Pneumonia: 2 case reports and review of literature

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Abstract

Spontaneous pneumomediastinum is a rare clinical finding and is a significant concern for clinicians. These are two cases of fatal spontaneous pneumomediastinum among COVID-19 patients. The first patient was an 84-year-old woman who developed COVID-19 pneumonia. Her clinical course was complicated by pneumomediastinum, and, unfortunately, she died 12 days following the admission. The second patient was a 63-year-old man who developed a severe pneumomediastinum and extensive subcutaneous emphysema and died 10 days after hospitalization.

Thus, paying attention to these complications as a severity marker of COVID-19 pneumonia is necessary.

Keywords: Spontaneous, Pneumomediastinum, COVID-19, Complication

INTRODUCTION

As the COVID-19 pandemic progresses, clinicians should be aware of the uncommon presentations of the disease, such as the case of pneumomediastinum. Recent evidence suggested that these can occur in the context of COVID-19 pneumonia, even in the absence of mechanical ventilation–related barotrauma (1)

We report 2 cases of spontaneous pneumomediastinum among 2 COVID-19 patients with fatal evolution.

CASE REPORTS

Case 1: The first case was an 84-year-old woman with a past medical history of hypertension. She presented to the emergency department (ED) with 7 days of marked chest pain, and dry cough with progressive dyspnea. On admission, her vital signs showed tachypnea at 22 breaths per minute, high temperature at 38.2°C, increased heart rate at 110 beats per minute, and pulse oximetry at 85%. On physical examination, she had bilateral basal crackles and peripheral

cyanosis. Laboratory results showed an elevated C-reactive protein (CRP) of 181 mg/L (normal range 0–6 mg/L). The suspicion of COVID-19 was confirmed by real-time reverse transcription polymerase chain reaction (RT-PCR) analysis of nasopharyngeal swab samples. Non-contrast chest computed tomography (CT) showed some ground-glass opacities of peripheral subpleural location, associated with multiple areas of consolidation in posterior segments of both lower lobes, with a pneumomediastinum measuring 7mm. (Figure 1).

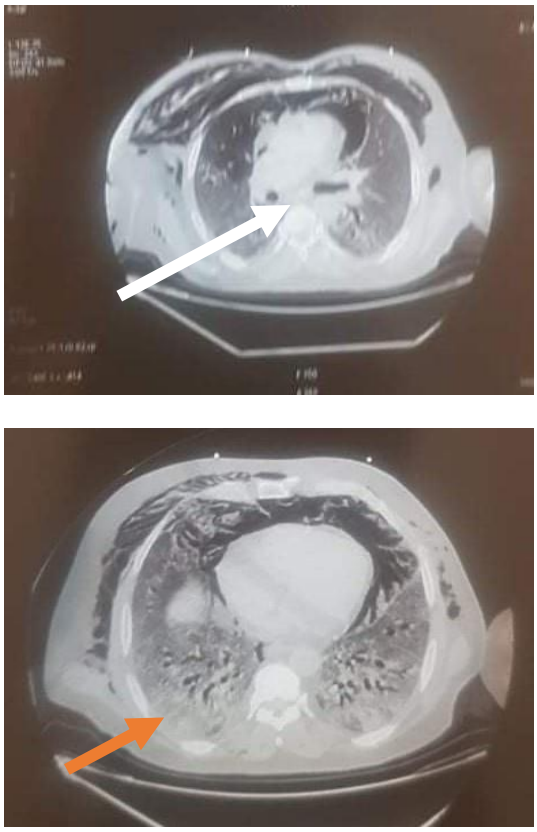

Figure 1: *Non-contrast chest computed tomography (CT) showing some ground-glass opacities of peripheral subpleural location, associated with multiple areas of consolidation in posterior segments of both lower lobes (red arrow), with a pneumomediastinum measuring 7mm (white arrow).*

The therapeutic protocol consisted of antibiotics, steroids, and oxygen supplementation with a reservoir mask. She did not receive non-invasive positive pressure ventilation.

After 10 days, she developed a septic choc and received nosocomial antibiotics with noradrenaline. However, despite the support measures, the patient died from respiratory failure 12 days after admission.

Case 2: The second case was a 63-year-old man who was admitted to the ED for fever, cough that lasted for 6 days, chest tightness, and shortness of breath that developed a day ago. He had no history of any specific diseases such as hypertension, diabetes, or heart disease nor had any traumatic injuries. The patient exhibited a clear consciousness, with a blood pressure of 130/62 mm Hg, and a pulse rate of 83 beats per minute. His oxygen saturation was only 80%, and 90% after applying an oxygen mask. His blood count showed leukocytosis at 12700 cells/µL. There were elevated blood levels for C-reactive protein at 188 mg/L. His RT-PCR was positive for SARSCoV-2 infection. Management included pharmacological treatment with azithromycin, ceftriaxone, levofloxacin, hydrocortisone, and oxygen supplementation.

During his hospitalization, he presented progressive deterioration of respiratory function with dyspnea despite oxygen therapy. A chest CT scan was performed and has shown bilateral ground-glass opacities (90%), severe pneumomediastinum measuring 40mm with

extensive subcutaneous emphysema mainly extending superiorly in the thorax and into the neck.

Unfortunately, his respiratory state worsened, and the patient was intubated and put on regular prone positioning. Despite prompt management, the patient died 10 days after hospitalization.

DISCUSSION

Pneumomediastinum in COVID-19 patients is most often caused by increased airway pressures, secondary to mechanical ventilation or airway obstruction (2). While not commonly seen in viral pneumonias, Spontaneous pneumomediastinum (SPM) has been described in patients with COVID-19 pneumonia, despite no history of mechanical ventilation. SPM is an uncommon presentation of COVID-19. Data on the incidence, pathogenesis, and outcomes of SPM during the recent SARS-CoV-2 pandemic are limited and are confined to a few isolated case reports (3–5). SPM is defined by the presence of air in the mediastinum without evident causes - traumatic, iatrogenic, organ perforation, or surgery (6). Although SPM is generally considered a benign and self-limiting condition, its appearance in viral pneumonia may be of clinical significance.

In the case of pulmonary infections due to SARS-COV-2, the virus causes a breakdown of the alveolar membrane integrity as it infects both type I and II pneumocytes (7). Therefore, the damage of the alveolar membrane in coronavirus infections can be one of the mechanisms leading to alveolar rupture thus the occurrence of SPM.

Most commonly patients present with shortness of breath, cough, and/or chest or neck pain. Our patients have almost the same symptoms. Physical signs can include tachycardia, tachypnoea, hypotension, and subcutaneous emphysema (8). Pneumomediastinum may be visible on a plain chest X-ray; however, it may only be detected on CT of the chest. In our cases, the CT scan led us to the diagnosis.

The treatment approach is based on rest, oxygen therapy, and analgesia (9). The association of pneumomediastinum with COVID-19 does not imply a specific treatment but should be feared as a potential aggravating factor specifically in case of extensive pulmonary lesions.

In fact, a recent case series described three cases of COVID-19 pneumonia complicated by SPM and pneumothorax, all of which were followed by a severe course of disease with fatal outcomes (10). The two patients we report had the same evolution after a few days. So the spontaneous pneumomediastinum may be considered a severity predictor in pulmonary infection by SARS-CoV-2 2.

CONCLUSION

SPM is a rare complication of COVID-19 pneumonia and was associated with a severe course of disease in our patient. Future studies are warranted to assess whether SPM severity predictor of COVID-19 pneumonia.

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A dramatic course of COVID-19-associated meningoencephalitis without respiratory involvement: a case report

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Abstract

Even though COVID-19 affects mainly the respiratory system, neurological complications have been widely reported. We report a case of a 27- 27-year-old female who was brought to the emergency department with severe confusion and abnormal behavior. The cerebrospinal fluid polymerase chain reaction (PCR) for SARS-CoV-2 was positive. Brain MRI findings were consistent with meningoencephalitis. The treatment was started accordingly, but the evolution was unfortunate, and the patient died two weeks later. Therefore, neurological
symptoms should be always kept in mind by physicians during the COVID-19 pandemic. Early diagnosis may prevent death.

Keywords: COVID-19, Meningoencephalitis, Neurological symptoms, SARS-COV2.

INTRODUCTION

On March 11th, 2020, the novel coronavirus disease 2019 (COVID-19) was announced as a global pandemic. It is caused by the SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2). While the first data suggested a purely respiratory infection, reports are emerging of neurological manifestations due to SARS-CoV-2, which range from milder presentations such as headache, dizziness, olfactory or taste dysfunction to severe complications such as seizures, stroke, Guillain-Barre syndrome, and meningoencephalitis. Although rare, these neurological manifestations are sometimes the sole initial presenting complaint of COVID-19. It is important to increase awareness of these rare presentations among physicians and healthcare workers and facilitate early diagnosis and management to prevent the horizontal spread of the disease.

Case report

This report is about the case of a 27-year-old female patient who did not suffer from any comorbidities and did not have any history of substance abuse or alcohol intake. She has also never been to a foreign country. She was confirmed positive for SARS-COV2 infection with mild symptoms in December 2020 for which she was self-isolated and received an out-patient symptomatic treatment with good response.

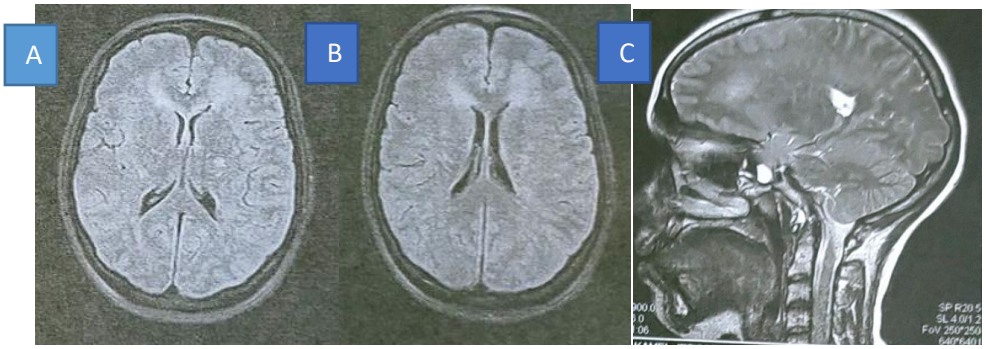

Figure 1. *Fluid-attenuated inversion recovery (FLAIR) axial images (A, B) and sagittal T2 images (C) show asymmetric bilateral hyperintensity in frontal and temporal regions, mostly involving the white matter.*

On late Mars 2021 (Day 1) the patient complained of headaches, generalized fatigue, vomiting, and fever of over 40 degrees Celsius (104 degrees Fahrenheit). She was treated with antipyretic agents and vitamins by her general practitioner but did not undergo any COVID-19 testing. The symptoms resolved under treatment. One week before her admission to the ED (Day 9), she became prostrate, and apathetic and developed muscular twitching. On April 2021 (day 14), the patient became disoriented, and she was brought to the ED by her parents.

Upon admission (Day 14), her vital signs were stable: RR=16cpm, oxygen saturation=100%, HR=85bpm, BP=130/70mmHg); clear bilateral lung sounds; normal cardiovascular examination; no obvious EKG abnormalities; normal blood sugar level and no fever. Neurological examination revealed acute confusion (GCS=13/15), neck stiffness, rigid limbs with exaggerated deep tendon reflexes, diffuse hyperesthesia, no focal neurological deficits, and normal cranial nerves.

Laboratory results were remarkable for a normal white blood cell count of 7400/ mm3, lymphocytes of 1550/ mm3, platelets of 221000/ mm3, and hemoglobin of 13.4 g/dl. The serum electrolytes panel, muscular enzymes (CPK, LDH), and CRP levels were within normal limits.

A brain computed tomography scan showed no acute abnormality.

A Brain MRI was performed. Diffusion-weighted images (DWI) showed hyperintensity in the frontal and temporal lobes bilaterally (Figure 1).

Shared decision-making was conducted with the patient's family and a lumbar puncture (LP) was performed due to concern for meningoencephalitis showing a clear and colorless cerebrospinal fluid and a normal opening pressure of 20 cm H2O (normal range 10–20 cm H2O).

The patient was started empirically on IV acyclovir, vancomycin, and ceftriaxone. She also received Sodium valproate and Clobazam for seizure prophylaxis.

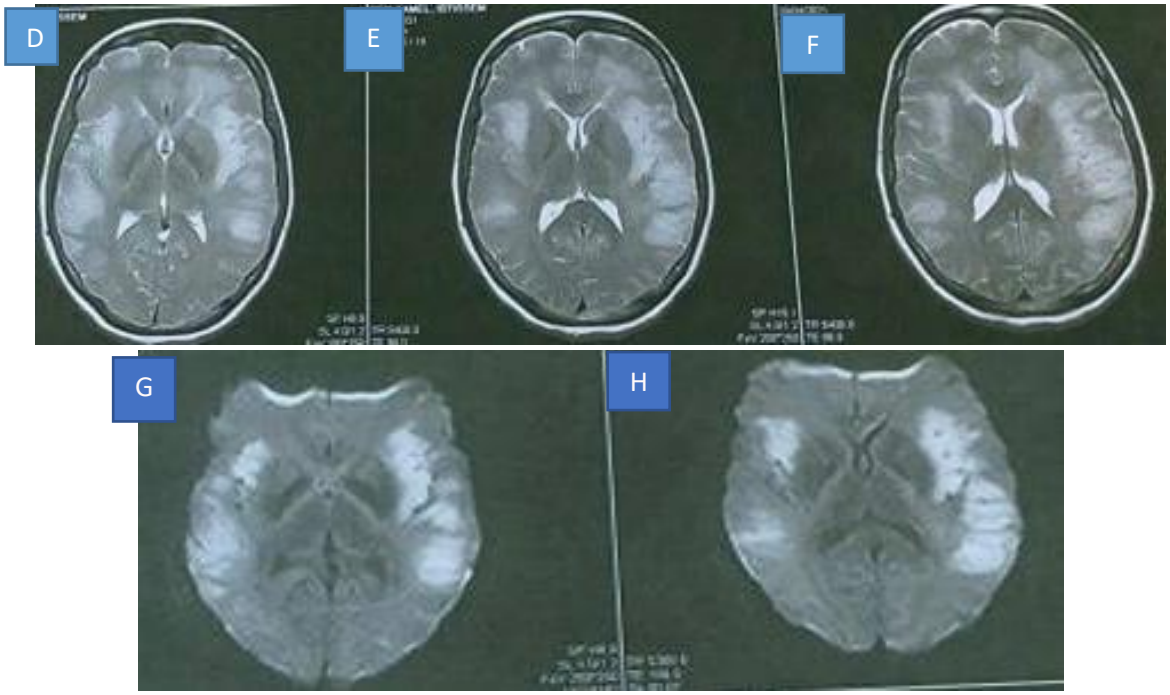

Figure 2. Axial fluid-attenuated inversion recovery FLAIR images (D, E, F) show hyperintensity in bilateral frontal-parietal-temporal and insular regions involving grey and white matter. Diffusion-weighted images (G, H) show hyperintensity with restricted diffusion.

The cerebrospinal fluid (CSF) laboratory analysis showed: a leukocyte count of 30 cells/mm³ (90% lymphocytes), 20 red cells/mm³, protein level of 2.4 g/L (normal value: 0.16 – 0.40 g/L), and glucose of 2.4 mmol/L (CSF glucose/blood glucose = 0.4). Gram's stain showed no bacteria.

A polymerase chain reaction (PCR) multiplex in CSF for several neurotropic viruses including cytomegalovirus, enterovirus, herpes simplex virus 1 and 2, human herpesvirus 6, and varicella-zoster virus showed negative results.

The determination of SARS-CoV-2 by reverse transcriptase polymerase chain reaction (RT-PCR) was performed using a nasopharyngeal swab and CSF because we assumed that SARS-CoV-2 was involved in the outbreak. Although the specific SARS-CoV-2 RNA was not detected in the nasopharyngeal swab, it was detected in CSF.

The chest x-ray as well as a chest CT were normal.

Treatment was carried out with IV human immunoglobulin (0.4g/kg daily for 5 days), and Methylprednisolone (1g daily for 3 days) with Enoxaparin (40 mg once a day) that was prescribed for deep venous thrombosis prophylaxis.

During the second day of ED hospitalization (Day 15), the patient presented with generalized convulsive status epileptics. She was intubated and started on Levetiracetam (1g two times per day), in addition to IV Sodium Valproate (1600mg per day). The patient was subsequently transferred to the intensive care unit where a second brain MRI was performed, one week

after her admission (Day 21), revealing extended lesions (Figure 2) and veinous thrombosis (Figure 3).

The evolution was unfortunate 13 days after her admission to the ED (day 27), the patient presented bilateral mydriasis and passed away 3 days later.

Figure 3. *Axial T2 weighted image (I) showing hypo intensity of the left anterior vein of pellucid septum related to thrombosis*

DISCUSSION

The literature review reveals that while the most common presenting symptoms of COVID-19 are fever fatigue and mild respiratory symptoms like dry cough and shortness of breath, there is a dramatic range of symptoms related to this disease such as headaches, anosmia, dysgeusia, meningitis, encephalitis, and acute cerebrovascular accidents (1)

This case indicates that neurological symptoms can be the sole manifestation of COVID-19, and highlights the neurotropic potential of SARS-CoV-2.

To date, the underlying pathophysiological mechanisms through which SARS-CoV-2 reaches the central nervous system (CNS) are not fully understood, however, the direct neuroinvasion and, mainly, the neurological sequelae due to the systemic innate-mediated hyper-inflammation are involved (2).

CONCLUSION

Neurological symptoms can be the first presentation of covid-19. This information should be kept in mind especially during the pandemic period to prevent delayed diagnosis or misdiagnosis and to avoid the adverse outcome of the disease.

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Low Back Pain Revealing Bilateral Proximal Pulmonary Embolism with COVID-19

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Abstract

Background: Pulmonary embolism (PE) is frequently encountered in emergency departments. It is a serious condition with significant morbidity and mortality. A high prevalence of thromboembolic events has been reported with COVID-19. The similarity in clinical presentation between the two diseases makes accurate diagnosis even more difficult. Atypical presentations can lead to delayed diagnosis and treatment, with a fatal outcome within hours. We report the case of a man who presented to the emergency department with bilateral low back pain as a presenting sign of bilateral proximal PE due to COVID-19.

Case Report: A 35-year-old man visited the emergency department for bilateral low back pain with a fever. His medical history included type 2 diabetes. Vital signs were as follows: blood pressure was 120/80 mmHg, heart rate was 110 bpm, respiratory rate was 21cpm, desaturation of 80% on room air and temperature was 37.8°C. An unprepared abdominal radiograph revealed significant aerosols. A thoracoabdominal-pelvic CT scan was performed revealing bilateral proximal pulmonary embolism with a floating thrombus of the main pulmonary artery associated with signs of severity and extensive COVID-19 pneumonia on the CT scan. Anticoagulation was initiated and the patient was transferred to the COVID-19 unit.

Conclusion: The diagnosis of PE should always be considered in the presence of any abdominal or lumbar pain of undetermined etiology. The presence of atypical pain in a patient with COVID-19 pneumonia could be a sign of a discrete evolving PE, which should be diagnosed as early as possible to ensure timely and appropriate management.

Keywords
Low back pain, pulmonary embolism, COVID-2019

Abbreviations list
PE: Pulmonary embolism, COVID-19: coronavirus disease 2019, LBP: low back pain, ED: emergency department, aPTT: activated partial thromboplastin time, CT: computed tomography, RV: right ventricular, LV: left ventricular

INTRODUCTION

Pulmonary embolism (PE) is frequently encountered in the emergency department. A higher prevalence of thromboembolic complication has been described recently in patients with coronavirus disease 2019 (COVID-19), increasing its morbidities [1].

Low back pain (LBP) and abdominal pain are common reasons for emergency department (ED) visits. Atypical presentation of PE is rare and makes accurate diagnosis even more difficult [2]. The polymorphism of clinical symptoms of PE and their low sensitivity could be the reason for the delayed

diagnosis of this condition, which could be life-threatening within hours. In some cases, patients with PE may present with unusual symptoms such as LBP and/or gastrointestinal signs that could refer to other diagnoses related to the affected organ [2]. Further medical evaluation should be considered if no convincing explanation has been found for the diagnosis of back and abdominal pain, given the potential severity of the underlying pathology.

CASE PRESENTATION

A 35-year-old male patient was admitted to our ED in July 2021 with persistent bilateral LBP. Initial symptoms have been evolving for 12 days and consist of Influenza-Like Illness including fever and asthenia. He attended a General Practitioner who performed a nasopharyngeal swab followed by the detection of the COVID-19 viral genome with a reverse transcriptase-polymerase chain reaction. The test was positive, and the patient was initiated on a symptomatic treatment. Regarding the worsening of his medical condition and the onset of progressive dyspnea associated with intense bilateral LBP spreading to the abdomen, the patient was referred to our emergency department. No drug, surgical, or smoking history was reported, but the patient did report a past medical history of type 2 diabetes mellitus.

On examination, the body temperature was 37.8°C. The heart rate was 110 beats per minute and the blood pressure was 120/80 mmHg. The patient's respiratory rate was 21 breaths per minute and the SpO2 was 97% on room air. Heart and pulmonary auscultation were normal. Glasgow Coma Scale score was 15 and the neurological examination was normal. The abdomen was tensely distended, painful, and tympanic. An electrocardiogram was performed and revealed a sinus tachycardia over 102 beats per minute. An abdominal X-ray was done and found a large bowel gaseous distension (Figure 1).

Figure Captions

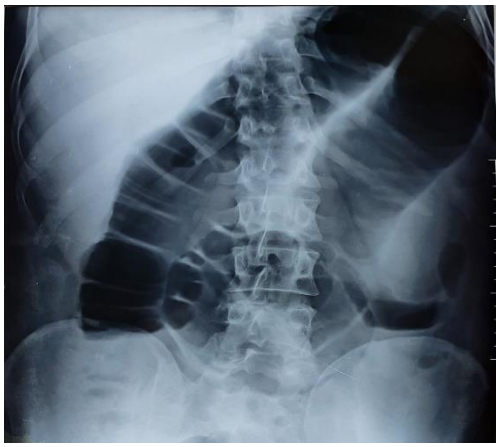

Figure 1: *Abdominal X-ray showing large bowel gaseous distension*

The blood test results showed Hyperleukocytosis of 17750/mm3 (normal range [4000-10000/mm3]) with a large amount of neutrophil containing of 14540/mm3 (normal range [2000-7500/mm3]), hemoglobin of 11.4 g/dl, thrombocytosis of 439000/mm3 (normal range [150000-400000/mm3]), increased C -reactive protein of 371.7 mg/l (normal range < 5 mg/l), blood urea of 9.5 mmol/l (normal range 8.3<mmol/l), creatinine of 85 µmol/l (normal range [62 – 106 µmol/l]), increased high-sensitivity cardiac troponin of 20.9 ng/l (normal range < 14 ng/l), activated partial thromboplastin time (aPTT) ratio of 1.01 and Prothrombin Time of 75% (normal range [70 – 100%]). Other investigations such as liver enzymes, D-Dimer, arterial blood gas, fibrinogen, procalcitonin, and N-terminal pro-brain Natriuretic Peptide were unavailable.

The evolution was characterized by the rapid drop in oxygen saturation below 80 % on room air. Chest, abdominal, and pelvic computed tomography (CT) scan with contrast revealed a

bilateral proximal PE with a floating clot in the pulmonary trunk associated (Figure 2) with heart right dilation (right ventricular (RV) / left ventricular (LV) volume ratio > 1). The interventricular septum was straight. It also showed bilateral lower lobe predominant ground-glass opacities associated with crazy paving patterns. The estimated degree of pulmonary impairment was between 25-50% (Figure 3). The abdominal and pelvic imaging were normal.

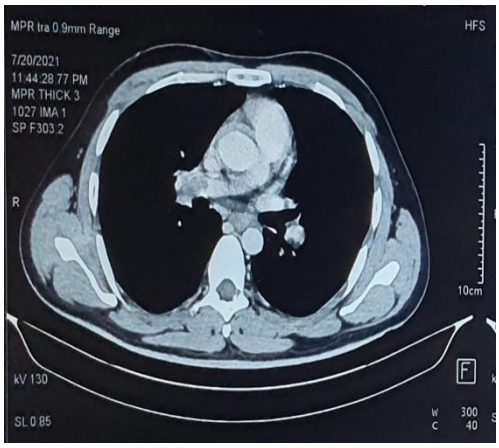

Figure 2: *Chest computed tomography scan with contrast showing bilateral proximal pulmonary embolism*

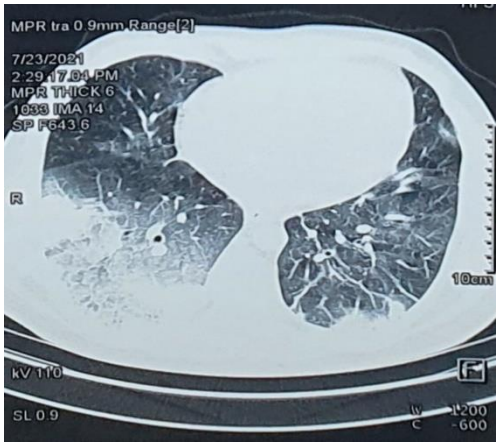

Figure 3: *Chest computed tomography scan showing bilateral ground-glass opacities associated with crazy paving pattern*

The patient was transferred to our COVID-19 unit. Thrombolytic therapy was initially discussed because of critical findings on the chest CT scan. Given the fact that our patient was hemodynamically stable and did not present signs of heart failure, he was initiated on unfractionated heparin.

The evolution was characterized by a clinically relevant improvement. Dyspnea and LBP have completely disappeared. We performed two other chest CT scans with contrast on the fourth and the eighth day of hospitalization which revealed a significant improvement in comparison with the first CT scan and a regression of the heart right dilation (RV/LV volume ratio < 1). The patient was discharged home on the fifteenth day of hospitalization, with instructions to continue the anticoagulant treatment (Rivaroxaban) and re-attend the clinic for pulmonary and cardiovascular assessment in 1 month.

Informed written consent was obtained from the patient for publication of the report and radiological findings, as well.

DISCUSSION

The diagnosis of PE is not always easy although there are multiple scores that can be used such as Well's criteria and Geneva score, leading us to classify probability as low, intermediate, and high. These scores guide us to choose the appropriate additional examinations to establish the diagnosis [3].

The similarity of respiratory signs in PE and other cardiorespiratory diseases could make it difficult to make an accurate diagnosis as well and clinical signs such as dyspnea, cough, tachycardia, and chest pain are not specific and could be found in other clinical conditions such as acute coronary syndrome, aortic dissection, pneumothorax, pericarditis [4] and COVID-19 infection. In the case of LBP, physicians usually think of renal or rheumatologic disease first. In this case, the patient was admitted initially for

LBP extending to his abdomen without symptoms suggestive of PE. He was initially misdiagnosed with a surgical emergency regarding the large bowel gaseous distension found on the abdominal X-ray. The appropriate diagnosis was suspected, and further investigations were performed following the appearance of desaturation during monitoring.

We looked for similar cases in the PubMed/MEDLINE database using the keywords “pulmonary embolism”, “back pain” and “low back pain”. We found two cases of PE with back pain and only one case of PE with LBP [1,5,6].

Rare cases of PE revealed by gastrointestinal signs have been reported in about 6.7-11% of patients with PE which is considered a significant rate [7].

The mechanisms of LBP in patients with PE are not well known. Some studies suggest that PE can be responsible for abdominal pain. This may be caused by gallbladder or liver capsule dilation induced by right heart failure secondary to PE [7]. Pulmonary hypertension may cause hepatobiliary portal infiltration and abdominal lymphedema. The elevation of right ventricle pressure could be responsible for the re-opening of the foramen ovale which may decrease blood supply to the abdominal organs [8]. Increased blood viscosity and low oxygen may induce small embolus that causes focal necrosis of abdominal organs [9]. Some studies suggest that neurological disorders such as pseudo-ileus can be caused by PE [10]. The last situation is similar to our case and explains the large bowel gas distension found on the abdominal X-ray. Other studies suggest that the abdominal pain may be caused either by lateral stimulation of the diaphragm or by the stimulation of the ending sensitive nerve of the abdominal wall and the back secondary to thrombus formation in the blood vessel wall [11].

Through this observation, we wanted to highlight the interest of an etiological research of an unexplained abdominal and LBP with appropriate additional examinations such as chest and abdominal CT-scan especially in patients with COVID-19 infection so the diagnosis of a possible PE could be performed earlier.

CONCLUSION

PE should always be kept in mind in front of atypical symptoms such as LBP and abdominal pain for which no accurate diagnosis, related to the affected organ, was found. These symptoms, especially in patients with COVID-19 infection, must draw attention to a possible PE so that we can establish the diagnosis earlier and treat it if this condition rapidly evolves in a negative way.

Conflict of Interest Statement

The authors declare no conflict of interest.

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Ischemic acute cholecystitis: a case report

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Abstract

Acute cholecystitis is the sudden inflammation of the gallbladder. Symptoms include right upper abdominal pain, nausea, vomiting, and occasionally fever. In most cases, it is caused by the blockage of the cystic duct by a gallstone which causes bile stasis in the gallbladder and results in secondary bacterial infection.

It occurs without evidence of gallstones or cystic duct obstruction in 2 to 15% of the cases [1]. This condition is called acalculous acute cholecystitis (AAC). The etiology of AAC is multifactorial and likely results from bile stasis or ischemia (or both) [1-3]. It is mostly diagnosed in critically ill patients, particularly those with cardiovascular diseases.

In this article, we report a case of ischemic acute cholecystitis.

KEYWORDS: Cholecystitis, Acalculous, Gallbladder Wall, Ischemia, Bile Stasis

INTRODUCTION

Acute cholecystitis (AC) is the sudden inflammation of the gallbladder (GB). It is a prevalent surgical condition and a frequent cause of abdominal pain.

In most cases, it is due to the obstruction of the cystic duct by a gallstone (GS), which exists for a long period before this condition occurs in asymptomatic patients or those having neglected biliary colic.

Symptoms include right upper abdominal pain in most cases. Fever, nausea, and vomiting are less frequent. Paralytic ileus was also described in some patients. Physical examination generally finds a Murphy's sign.

Abdominal ultrasound can confirm the diagnosis. However normal ultrasound findings don't exclude the diagnosis of AC. These symptoms are found in patients with no radiological or surgical evidence of gallstones or cystic duct obstruction in approximately 10% of the cases. This condition is called acalculous acute cholecystitis (AAC).

The etiology of AAC is multifactorial. Its pathophysiology includes bile stasis, ischemia, or both [1-3].

We report a case of an ischemic AAC diagnosed in our emergency department.

Case report

A 50-year-old male patient with a medical history of diabetes, hypertension, ischemic stroke, and kidney failure presented to our emergency department

suffering from right upper abdominal pain, asthenia, and vomiting starting 4 days before admission, without intestinal abdominal disorders. No chest pain was reported.

On initial physical examination, he was conscious, with a normal respiratory rate and a pulse oximetry of 100 %. He had a heart rate of 135 beats per minute and a normal blood pressure of 130/80 mmHg. No signs of circulatory impairment or right heart failure were found. The temperature was 36.9^{c} and the blood sugar level was > 5g/l. The abdominal examination found tenderness with guarding in the epigastric, the right hypochondriac, the right lumbar, and the right iliac region. An electrocardiogram showed a sinus tachycardia.

Blood panel showed: white blood cells elevation but normal CRP level (WBC=14610 el/mm3; CRP = 7.4 ng/l), normal liver enzymes (AST=26 u/l; ALT =40 u/l), elevated creatinine and urea levels (715 µmol /l; 15.6 mmol/l), normal lipase (33u/l) and normal ultra-sensible troponin level (12.2 ng/l). The lactate was 5.8 mmol/l.

The abdominal ultrasound showed a distended gallbladder with normal wall thickness associated with hyperechogenic, and heterogeneous content without GS.

DISCUSSION

AAC remains challenging because of its complex multifactorial pathogenesis and nonspecific presentation.

AAC risk factors include severe trauma requiring blood transfusions, heavy surgery, shock of any kind, large burn injuries (with an incidence between 0.4 and 3.5%), and critically ill patients requiring ICU care and sepsis [1, 4, 5].

Less frequently described risk factors are endoscopic retrograde cholangiopancreatography, cardiovascular risk factors (diabetes mellitus, hypertension, atherosclerotic, obesity), end-stage renal failure, vasculitis (Churg–Strauss, giant cell arteritis, Henoch–Schoenlein (purpura, polyarteritis nodosa, lupus, Takayasu's syndrome), Immunodeficiency conditions (AIDS, Transplant) [1,4,6].

Two other rare risk factors are worth mentioning:

-ACC after transarterial chemoembolization of hepatocellular cancer, which is reported with an incidence between 0.3% and 10% [7].

-ACC is associated with an aortic dissection which is rarely described in the literature. Only 5 cases of AAC associated with an aortic dissection have been reported previously [8-11].

Our patient had an AAC which is related to the superior mesenteric artery stenosis. To the best of our knowledge, no similar cases have been described before in the literature.

AAC pathophysiology is complex, but studies found that it involves two major phenomena: bile stasis and ischemia [1, 4].

Bile stasis can be caused by fasting, obstruction, postsurgical/procedural irritation, ileus (total parenteral nutrition), or opioid analgesia (spasm of the sphincter of Oddi causing elevated bile duct pressure). This stasis modifies the chemical composition of bile, resulting in gallbladder mucosal lesions [1, 4].

The decrease of the gallbladder perfusion pressure, resulting in ischemia, may be the result of many of the risk factors stated above and it results in heavy injuries directly to all layers of its wall [1, 4].

Bacterial invasion of the ischemic tissue is a secondary phenomenon. The immunity response to this invasion may produce or contribute to GB tissue damage [4].

These pathophysiological mechanisms are well described in the literature, such as the histopathological data provided by Laurila et al [12], through comparing histologic findings of the gallbladders with and without ACC. Histological abnormalities reported in this study were : (1) an increased leukocyte margination (suggesting involvement of ischemia and reperfusion-mediated injury) ; (2) capillary thrombosis and increased focal lymphatic dilation (ischemia related) and (3) increased and deeper bile infiltration in the GB mucosa (suggesting that bile stasis and increased epithelial permeability exist, leading to epithelial damage).

As for the clinical presentation, there are no symptoms nor signs that are specific to AAC. Fever may be the only sign present in critically ill patients, unable to communicate their symptoms. For this kind of patient, AAC is a diagnosis among many others to suspect facing sepsis or a septic shock. It is sufficiently common and should be discussed in every critically ill patient with a clinical presentation of sepsis or icterus and no other obvious cause [1, 4].

The clinical presentation may also include right upper abdominal pain, fever, nausea, and vomiting.

Physical findings show fever, and tenderness with or without guarding in the epigastric region and/or the right hypochondriac. Clinically, AAC is indistinguishable from acute calculous cholecystitis [1]. Laboratory evaluation is also unreliable. Leukocytosis and CRP elevation are common but not specific. Lactate elevation is common.

Normal inflammatory markers with elevated lactates may be an early sign of an ischemic disorder but it is not specific.

The confirmation of the diagnosis rests on imaging. Abdominal ultrasound and computerized tomography (CT) scans are usually sufficient with an excellent reported sensibility and specificity (for the US: 92 % sensitivity and 96 % specificity; For CT scan: 100 % sensitivity and specificity) [13].

Other exams such as HIDA (hepatobiliary iminodiacetic acid scan) are used but they are expensive and not immediately available.

Diagnostic criteria were defined for both US and abdominal CT scans in many radiologic studies [1, 4, 13-16]:

Criteria for abdominal US: 2 major or 1 major and 2 minor

Major: 3.5- to 4-mm (or more) thick wall

Striated gallbladder.

Intramural gas Pericholecystic fluid

Sloughed mucosal membrane

Minor: Gallbladder distention (>5 cm in transverse diameter)

Echogenic bile (sludge)

Criteria for abdominal CT: 2 major or 1 major and 1 minor

Major: Gallbladder wall thickening >3 to 4 mm

Subserosal halo sign

Pericholecystic infiltration of fat

Pericholecystic fluid

Mucosal sloughing

Intramural gas

Minor: Gall bladder distention (>5 cm in transverse diameter)

High-attenuation bile (sludge)

AAC complications are numerous. The prevalence of gallbladder gangrene in AAC exceeds 50% [4]. Gallbladder perforation, abscess formation, generalized peritonitis, or severe sepsis with multiple organ dysfunction syndrome are commonly reported.

CONCLUSION

Although ACC is mostly described in critically ill patients, it remains a possible diagnosis in patients with multiple cardiovascular risk factors.

Clinical presentation is not specific, the laboratory assessment, is as well.

Abdominal US and abdominal CT scan criteria are the key to the diagnosis with excellent sensitivity and specificity.

An early accurate assessment is essential for the management to avoid poor outcomes.

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A complicated pulmonary hydatid cyst mimicking pneumonia: A case report

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Abstract

Introduction

Hydatic cyst is an important helminthic zoonotic disease in humans that commonly affects the liver and lungs. It results in high morbidity rates, particularly in endemic regions. Hydatic cyst disease may cause atypical clinical and radiological features and complications that cause difficulties in diagnosis. Misdiagnoses may end up with a delay in treatment.

Case presentation

We report a case of a 56-year-old female, with no past medical history who presented to our Emergency Department (ED) for sudden dyspnea and fever. Her physical examination showed altered facies and fever. Examination of the respiratory system revealed decreased vesicular breath sounds and vocal resonance and an impaired percussion note in the right lower lung field. Complete blood count (CBC) came with a high white blood cell (WBC) (73% neutrophils). Chest X-ray (CXR) showed an atypical right basal triangular opacity with an outer vertex and an inner base and thoracic CT demonstrated a complicated hydatic cyst partially ruptured in the right lobe.

Conclusion

Due to their varied presentations, pulmonary hydatid cysts may imitate other chest diseases especially when complicated and the diagnosis imposes major challenges. The disease should be considered in endemic regions.

Keywords: Case Report, Hydatid Cyst, Complications, Misdiagnosis, Management.

INTRODUCTION

Hydatid cyst, or Echinococcosis, is an important helminthic zoonotic disease in humans that commonly affects the liver and lungs. This disease results in high morbidity rates, particularly in endemic regions. In Tunisia, this disease is endemic, and the surgical incidence is. 15/ 100000 habitants [1].

Hydatic cyst disease may cause atypical clinical and radiological features and complications that cause difficulties in diagnosis [2]. It can be asymptomatic or present with complications such as infection and perforation [3]. Hydatid cysts can be diagnosed by various imaging methods such as direct chest radiography and thoracic computed

tomography (CT) [4]. Uncomplicated hydatid cysts, seen as round opaque lesions on chest radiography, are easily diagnosed, whereas complicated cysts (infected or/ and perforated) may change the radiographic appearance of the hydatid cyst, causing an incorrect diagnosis and delayed treatment.[5]. Here, we are reporting a patient with a complicated hydatic cyst that resembled pneumonia.

CASE PRESENTATION

A 20-year-old female with no past medical history presented to our Emergency Department (ED) with complaints of sudden dyspnea and fever. Her general physical examination showed altered facies. She was febrile, and alert with a pulse rate of 96/min, respiratory rate of 28/min, and blood pressure of 110/76 mmHg. Examination of all other organs was essentially normal. Examination of the respiratory system revealed decreased vesicular breath sounds and vocal resonance and an impaired percussion note in the right lower lung field. Complete blood count (CBC) came with a high white blood cell (WBC) count of 13 600 cells/L with 73% being neutrophils. Chest X-ray (CXR) showed an atypical right basal triangular opacity with an outer vertex and an inner base with excavated density associated with an overlying focus of alveolar condensation (Figure 1). Initially, the patient was treated for pneumonia with antibiotics. CT scan demonstrated a complicated hydatic cyst partially ruptured in the right lobe (Figure 2). There was no other detectable lesion in the liver or any other organ.

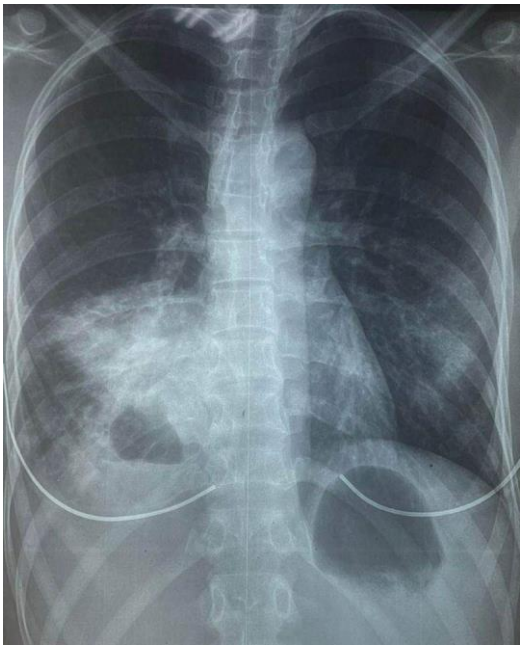

Figure 1: *Chest X-ray with a right basal excavated density associated with a focus of alveolar condensation.*

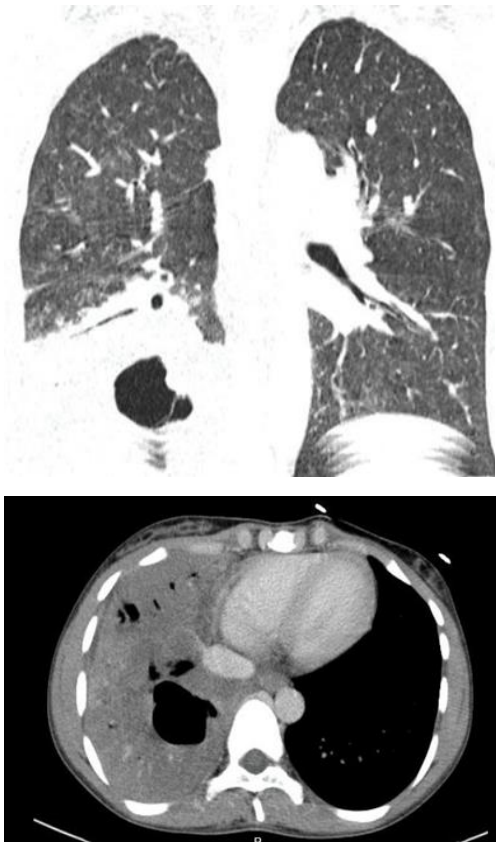

Figure2: *Thoracic CT showing a complicated hydatic cyst*

Further, there was no history of any pet dog. Based on clinical and radiological findings, she was diagnosed as having a complicated hydatid cyst. Surgery was indicated and the patient was admitted to "the thoracic surgery department".

DISCUSSION

Pulmonary hydatid disease is a serious problem in many countries, including several Mediterranean countries, New Zealand, Australia, North America, South America, Central America, and Asia [6]. Most hydatid cyst diseases are caused by the larval stage of Echinococcus granulosus affecting mostly the liver and lungs, respectively [7,8]. In 60% of the cases, it is in the right lung, and in 20% of the cases, the lesions are bilateral [9]. In our case, the lesion was unilateral and located in the right lung. The growth of hydatid cysts is slow and may remain undiagnosed for long periods [6]. Hydatid cysts have many presentations although the majority are asymptomatic and hence found incidentally [10]. However, they can rupture, which can cause symptoms of productive cough, coughing out cystic contents, hemoptysis, and chest pain. The diagnosis is usually easy by typical radiological findings, especially if they are accompanied by hepatic hydatid cysts [10]. Uncomplicated cysts, seen as round opaque lesions on chest radiography, are easily diagnosed. However, infected and or perforated cysts, known as "complicated" cysts, may change the radiographic appearance of the hydatid cyst, causing an incorrect diagnosis and delayed treatment [11]. Imaging modalities and serology establish the diagnosis in most cases. However, when they are complicated with infection, the diagnosis can be quite challenging as the clinical and radiological findings become atypical [11]. Routine hematological and biochemical tests are unsupportive in the diagnosis of hydatid disease [12]. In the diagnosis of hydatid cysts, tests such as indirect hemagglutination or indirect fluorescent antibody can be applied [13]. In our case, the serological test was not done. Since the clinical and laboratory findings are not specific in the diagnosis of hydatid cysts, radiological scans gain importance at the diagnosis stage. Cysts that are not complicated are seen as well-demarcated round or homogeneous masses in computer tomography and lung graphics. Larger cysts can result in atelectasis in the lungs, mediastinal shift, or pleural effusion depending on the level of pressure on the neighboring tissue. Lung graphics of the complicated cysts can show air-fluid level, water lily, or meniscus signs. Ruptured cysts can appear as masses or abscesses in computer tomography. In another study conducted on this issue, it was reported that hydatid cyst disease can easily be confused with thoracic empyema, mediastinal mass, tuberculosis pleurisy, and thoracic wall tumor [14].

It should be kept in mind that pulmonary hydatid cysts in endemic regions clinically and radiologically can mimic lung infection when complicated.

CONCLUSION

Due to their varied presentations, pulmonary hydatid cysts may imitate other chest diseases especially when complicated and the diagnosis imposes major challenges. The disease should be considered especially in endemic regions.

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