Procedural sedation in the emergency department: a randomized trial of ketamine versus etomidate

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Abstract

Introduction: Pain management, especially pain related to medical procedures, is a major concern for emergency physicians. While several drugs have proven effective, no single agent is considered ideal. This study aimed to compare the efficacy of Etomidate and Ketamine in preventing procedure-related pain in the emergency department (ED).

Methods: We conducted a prospective, randomized, single-center study over six months. The study included patients over 18 years old who required a painful medical procedure in the ED. Patients were randomly assigned to receive either a bolus of 0.1 mg/kg Etomidate or 0.5 mg/kg Ketamine. The primary outcome was a hybrid criterion: absence of awakening during the procedure and rapid recovery within 10 minutes.

Results: A total of 55 patients were enrolled, 25 in the Etomidate group and 30 in the Ketamine group. Four 15 patients experienced awakening during the procedure: three in the Etomidate group and one in the Ketamine group (p=0.3). The mean recovery time was 13.01 ± 3.7 minutes in both groups (p=0.26). Side effects occurred in 63.6% of patients (p=0.79). Complete recall of the painful procedure was reported in seven patients, six of whom were in the Etomidate group (p=0.03).

Conclusion: Ketamine does not appear to provide a significant advantage over Etomidate for procedural sedation in the ED. However, awakenings during the procedure were more frequent with Etomidate.

Key words: Pain, Sedation, Analgesia, Etomidate, Ketamine

INTRODUCTION

Pain management during medical procedures is a major concern for healthcare professionals, particularly in emergency settings. Procedural sedation is widely used by emergency physicians, achieving success rates of up to 98% (1). This approach involves administering sedative or dissociative agents, with or without analgesics (2). A thorough understanding of pharmacology is essential, as the selection of sedative and analgesic agents must be tailored to each clinical situation (3). Over the years, international guidelines for procedural sedation have been developed and updated. Commonly used medications include propofol, ketamine, fentanyl, midazolam, etomidate, and benzodiazepines (4,5). However, no single drug or combination fully meets all procedural requirements, explaining the lack of consensus on the optimal choice. Ideally, the perfect sedative agent would provide analgesic, hypnotic, anxiolytic, amnesic, and muscle-relaxant effects while being easily reversible, free of hemodynamic or respiratory complications, and offering both rapid onset and short duration of action (6). Since no such ideal drug exists, clinicians must carefully weigh the benefits and risks of each option based on the patient and the procedure (7,8). This study aimed to compare the efficacy and adverse event profiles of etomidate and ketamine in preventing procedure-induced pain in the ED.

METHODS

The study was conducted in the ED of a university hospital center in Tunis, receiving approximately 75,000 patients per year. This was a prospective, open-label, randomized, single-center, per-protocol clinical study conducted over a period of 6 months, from July 1st to December 31st, 2019. We included patients aged 18 years and over for whom a deemed painful, diagnostic, or therapeutic "medical act" was indicated by the attending emergency physician. We did not include pregnant or breastfeeding women, patients in shock or with a Glasgow coma score (GCS) <15, a respiratory rate <12 cycles/min, hepatic cirrhosis, a history of epilepsy, acute coronary syndrome, or allergy to morphine, ketamine, midazolam, or etomidate. We excluded patients for whom there was a protocol violation and those who were transferred to another department within 60 minutes after the start of the protocol.

Study procedure: For any patient presenting to the ED and meeting the inclusion criteria, the study interest was explained, and consent was documented. Once included, they were admitted to the Intensive Monitoring Unit, where vital signs monitoring was set up. Patients were randomized by random dice rolls to receive either a direct intravenous (DIV) bolus of 0.1mg/kg for the Etomidate group, or a single bolus of 0.5mg/kg based on weight for the Ketamine group. We administered a dose of 25 mg IVD for weights under 70 kg, 30 mg for weights between 70 and 90 kg, and 50 mg for weights of 100 kg or more. During ketamine administration, we encouraged pleasant dreams, and a bolus of 2 mg of midazolam was added when uncontrollable agitation was observed. Morphine hydrochloride, at a dose of 0.05 mg/kg, was used during sedation in both groups whenever the patient expressed verbal or facial pain during the procedure.

An antidote administration protocol (Naloxone and Flumazenil) was established. Patients were

kept under surveillance and monitoring with the collection of various vital parameters: respiratory rate, SpO2, heart rate, blood pressure, level of consciousness (according to the Alertness Scale) at 5, 10, 20 minutes, and until patient awakening at 60 minutes with recovery to a normal state of consciousness.

We defined Sedation Time (ST) as the time interval between the injection of the Etomidate or Ketamine bolus at T0 and the achievement of effective sedation, defined by an alertness scale score <2. Recovery Time (RT) was defined as the time interval between the initial Ketamine or Etomidate bolus injection at T0 and the recovery of a strictly normal state of consciousness (alertness scale score = 12). Effective Sedation Duration (RT – ST) was defined as the time interval between achieving effective sedation and recovering a strictly normal state of consciousness. The primary outcome criterion was the absence of awakening during the procedure (alertness scale less than 2 throughout the procedure) and a rapid recovery within 10 minutes of the end of the procedure to a good state of consciousness. The secondary outcome criteria were the occurrence of adverse effects, amnesia of the painful episode, defined by a vague or absent memory of the procedure, apprehension of potential future sedation, and the occurrence of dreams during the procedure.

Statistical tests and computer equipment: Data were entered and analyzed using SPSS version 22 software. Percentages were calculated for qualitative variables, and means with standard deviations for quantitative variables. Comparison of means was performed using the Student's T-test for independent series. To compare percentages on independent series, we used Pearson's chi-squared test, and in case of non-validity of this test, Fisher's exact bilateral test. In all statistical tests, the significance level was set at 0.05. At the end of the univariate study, we conducted a multivariate analysis using logistic regression to calculate an adjusted OR with a 95% confidence interval (CI) for each factor directly related to the event.

Ethical Considerations: We declare no conflict of interest. Written consent was obtained from each patient. The two molecules we used are internationally recommended for procedural sedation. Information was processed anonymously, and we respected medical confidentiality for all patients.

RESULTS

During the study period, we collected 55 patients (Figure 1). The mean age of the population was 39 ± 15 years in the etomidate group and 34 ± 16 years in the ketamine group (p = 0.3).

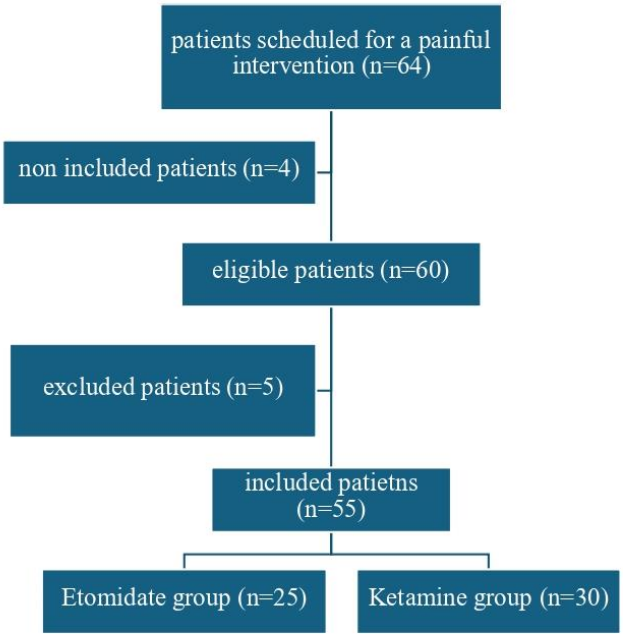

Figure 1: Flow chart of the study population

A male predominance was observed in both groups, with a sex ratio of 3.2 in the etomidate group and 2.3 in the ketamine group (p = 0.7).

Two patients (8%) in the etomidate group had received morphine within the six months preceding the procedure, compared to one patient (3%) in the ketamine group (p = 0.58).

The medical procedures requiring procedural sedation are summarized in Table 1.

Table 1. Type of procedure performed in both groups

Procedure; n (%)	Etomidate group n=25	Ketamine group n=30	p
Reduction of a dislocation	5 (20)	11 (36.7)	0.08
Wound care	6 (24)	5 (16.7)	0.73
Chest tube (thoracic drain)	6 (24)	4 (13.3)	0.49
Incision and drainage of a cutaneous abscess	3 (12)	6 (20)	0.27
Central venous catheter	2 (8)	3 (10)	0.64
Lumbar puncture	3 (12)	1 (3.3)	0.3

The mean duration of procedures was 4.93 ± 1.55 minutes in the etomidate group and 5.6 ± 1.8 minutes in the ketamine group (p = 0.61). Forty-one patients achieved an alertness scale score of less than 2 within 5 minutes, including 19 patients in the etomidate group and 24 patients in the ketamine group (Table 2). Four patients awakened during the medical procedure: three in the etomidate group and one in the ketamine group (p = 0.3). A single bolus of morphine was administered to these four patients to allow completion of the procedure without pain.

No patient exhibited hemodynamic or respiratory instability during the procedures. There was no significant difference in mean arterial pressure or respiratory rate between the two groups (p = 0.3) (Figure 2).

Table 2. shows the timing related to procedural sedation in both groups.

	Etomidate group n=25	Ketamine group n=30	p
Duration of the procedure (min); mean ±SD)	5.2 ± 1.4	5.6 ± 1.8	0.3
Sedation time (min); mean ±SD)	4 ± 2	4 ± 1.8	0.8
Recovery time (min); mean ±SD)	12 ± 3	13.5 ± 4	0.2
Effective sedation duration (min); mean ±SD)	8,6± 3	10 ± 3	0.2
Awakening time (min); mean ±SD)	4 ± 2.7	4.3 ± 2.3	0.7

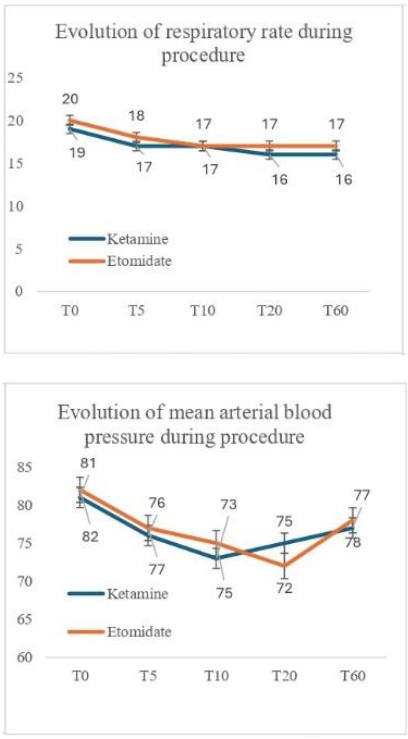

Figure 2: Variation in respiratory rate arterial pressure during the procedure in both groups

Occurrence of Adverse Events

Thirty-five patients (63.6%) experienced adverse events: 12 patients (48%) in the etomidate group and 23 patients (76%) in the ketamine group (Table 3).

Table 3: Adverse Events Reported in Each Group

Adverse effects; n (%)	Etomidate group N=25	Ketamine group N=30	p
Agitated awakening	5 (20)	10 (33.3)	0.2
Laryngospasm	1 (4)	2 (6.7)	0.8
Desaturation <90%	1 (4)	1 (3.3)	0.8
Apnea lasting 30 seconds	0	1 (3.3)	0.7
Nausea	1 (4)	8 (26.7)	0.03
Hallucinations	2 (8)	6 (20)	0.2
Cough	2 (8)	4 (13.3)	0.6
Myoclonus	4 (16)	1 (3.3)	0.1
Vomiting	2 (8)	3 (10)	0.7

Among the 10 patients in the ketamine group who experienced agitated awakening, six required a 2 mg bolus of midazolam to control the agitation.

Amnesia of the Painful Episode and Dreams During the Procedure:

Seven patients (12.7%) retained a complete memory of the painful procedure, including six in the etomidate group (p=0.03). During the procedure, 32 patients (58.1%) reported experiencing dreams (Table 4).

Multivariate Analysis

Our multivariate analysis showed that only amnesia of the painful episode was significantly higher in the etomidate group of patients, with an odds ratio (OR) of 0.1, 95% confidence interval [0.012; 0.980] (p = 0.04).

DISCUSSION

The results of our study revealed that etomidate and ketamine are two comparable agents in terms of efficacy for procedural sedation in emergency settings. Their rapid onset of action, ability to ensure quick recovery, hemodynamic and respiratory profiles make them preferred choices for clinicians.

Table 4: Dreams and Recall of the Procedure in Both Groups

	Etomidate group N=25	Ketamine group N=30	p
No memory; n(%)	17 (68)	19 (63.3)	0.03
Vague memory; n(%)	2 (8)	10 (33.3)	
Complete memory; n(%)	6 (24)	1 (3.3)	
Pleasant dream; n(%)	5 (20)	11 (36.7)	0,68
Unpleasant dream; n(%)	3 (12)	13 (43.3)	0.68

Our findings are consistent with those reported in the literature. The study by Salen et al. compared the efficacy of etomidate and ketamine in aligning dislocations and observed a similar success rate in both groups. Although two failures were reported in the etomidate group (n = 34), no failures occurred in the ketamine group (n = 46). These results suggest that both agents are comparable in terms of efficacy and management of immediate complications (9).

Ketamine, widely used in emergency medicine for procedural sedation, is recognized for its dissociative, analgesic, and anesthetic effects. It provides sedation, analgesia, and amnesia while preserving hemodynamic and respiratory stability (10). Thanks to its rapid onset and relatively short duration of action, it is particularly suitable for brief and painful procedures. In general, its effects last between 15 and 30 minutes (11).

When administered at low doses, ketamine induces analgesia and mild disorientation. Once

the dissociative threshold is reached, further increases in ketamine do not impact the level of sedation (12).

Etomidate, on the other hand, offers several advantages: a simple dosing regimen, rapid onset, short duration of action, rapid metabolism, and hemodynamic stability (13). Its action begins immediately and generally lasts between 5 and 15 minutes (14). However, etomidate does not possess analgesic properties and often requires co-administration of a short-acting opioid, which may increase the risk of respiratory depression (15).

In our study, the mean sedation time was 4 minutes in both groups ($p = 0.8$). These results are similar to those found in the literature. In the study conducted by Dişel et al. comparing the efficacy of etomidate versus ketamine for dislocations alignment, the sedation time was 4.3 minutes for the etomidate group and 2.2 minutes for the ketamine group ($p < 0.001$) (16).

Our study showed that both drugs can cause adverse effects, which is consistent with available data in the literature. Newton et al. observed that 21.7% of patients receiving ketamine-based procedural sedation experienced side effects, including emergence agitation (13%), vomiting (4%), myoclonus (4%), and hypersalivation (2%) (17). Nevertheless, etomidate may be responsible for myoclonus, adrenal suppression, nausea, and vomiting (18).

Furthermore, etomidate was sometimes associated with more pronounced awakening and a clearer memory of the procedure, a phenomenon we observed in 12.7% of patients who reported complete recall of the painful event. This difference between groups was statistically significant ($p = 0.03$), confirming the increased risk of procedural recall in patients who received etomidate.

A study by Ruth et al. found that among patients who received etomidate before a painful procedure, 69% had no memory of the event, 27% had partial recall, and 4% had complete recall ($p = 0.03$). These results are in line with our findings, although the proportion of complete recall in our population appears slightly higher (19).

Our study has several limitations. The main weakness is undoubtedly the small sample size. Additionally, at the time of the study, we did not have access to capnography, an essential tool for monitoring procedural sedation.

On the other hand, one of the strengths of the study lies in the originality of the work, which was conducted in an emergency setting and focused on addressing pain associated with medical procedures, a key mission for emergency physicians.

CONCLUSION

Etomidate and ketamine are effective agents for procedural sedation, with similar safety and efficacy profiles. However, the choice between these two medications should consider the specific clinical situation, particularly the duration of the procedure and the patient's post-procedural comfort. Although etomidate has a very rapid onset of action and is unlikely to cause severe hemodynamic or respiratory effects, the risk of

procedural recall remains an important factor, especially for painful procedures. Further research is needed to better understand the factors influencing procedural recall and to develop strategies aimed at minimizing this while maintaining effective and safe sedation.

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Evaluation of non-technical skills among emergency medicine residents in the management of severe trauma: a prospective study using simulation

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Abstract

Background: Learning through simulation is not mainly about technical skills. Non-technical skills, which are part of the prerequisite competencies for professionals working in emergency care, can be worked on through simulation as well.

This study aimed to evaluate the learning of non-technical skills in the care of a severe trauma patient and to study the retention of these non-technical skills after one month of simulation sessions.

Methods: We conducted a prospective, observational, descriptive, and single-center study carried out at the Northeast SAMU01 Emergency Care Teaching Center (CESU01) over a period of one year.

The use of a hetero-evaluation score of non-technical skills by the Anesthetists' Non-Technical Skills (ANTS score) was carried out by an observing instructor for all participants during the simulation session and one month later.

Results: We included 30 residents. The average age was 28 years, with a sex ratio of 4. Twenty-one residents (70%) had already benefited from simulation training. Participants significantly improved their situational awareness skills (3.6 vs 3.95, p = 0.026); decision-making (3.41 vs 3.52, p = 0.043); and teamwork (1.72 vs 2.06, p = 0.003) between the first session and one month later. The comparison of the evolution of different non-technical skills in the two groups," prior simulation training" and "no prior simulation training," showed a significant difference concerning the means at 01 month in the group "before training by simulation" (3.42 vs 3.92 with p = 0.002).

Conclusion: Health simulation is therefore a major educational tool in the learning of non-technical skills in emergency medicine

Keywords: Non-Technical skills, Simulation, ANTS, Emergency Medicine, Traumatology

INTRODUCTION

Medical simulation is becoming an increasingly important part of emergency medicine education, enabling the mechanisms involved in understanding clinical situations, reasoning, and decision-making to be analysed and improved (1). In a context of increasing the flow of patients to the emergency room, with its demonstrated impact on the quality of care and mortality (1), the performance of teams becomes a major issue.

The quality of care in terms of safety and effectiveness is directly linked to the non-technical skills (NTCs) of caregivers, which contribute to the efficient and safe realization of technical skills (2). In crises, these NTCs are grouped under the term "Crisis Resource Management" (CRM), defined as "the set of non-technical skills that aim to coordinate and use all available resources to optimize patient care and safety" (3).

Research on the identification of NTCs distinguishes individual (emotion management, fatigue, medical reasoning, communication, decision-making, cognitive load management) and collective (cooperation, conflict management, workload, and synergy with the leader) skills (4). While another approach classifies NTCs in interpersonal (leadership, communication) and cognitive (situational sensitivity, planning) skills (5-6).

Although the importance of NTCs is recognized in the quality of care (7), few studies have been conducted on their simulation learning in emergency medicine. Several rating scales have been developed, such as the Anaesthetist's Non-Technical Skills (ANTS) or the TEAM scale, based on assessment grids assigning an overall score to an observed performance (8-9).

Our study had two main objectives: first, to evaluate the acquisition of NTCs in the management of severe trauma by the ANTS score, and second, to study the retention of these skills one month after the simulation sessions.

METHODS

This was a prospective, descriptive, monocentric study conducted at the Emergency Care Education Center of SAMU 01 North East (CESU01) over a period of one year (January to December 2021).

We included emergency medicine residents who participated in simulation sessions organized as part of the simulation days at CESU01. Recruitment was carried out voluntarily. Participants gave their oral consent to participate and the right to image. Residents who declined to participate were not included, and those who did not participate in the one-month assessment were excluded. The assessment of the non-technical skills was carried out by using the ANTS (Anaesthetists' Non-Technical Skills) score, which was administered by an observing instructor to all the participants during the initial simulation session and one month later. (Appendix)

The ANTS score evaluates 15 competencies according to 4 categories: Task management, teamwork, situational awareness, and decision making.

For each skill, a score of 1 to 4 is assigned: 1 (poor), 2 (marginal), 3 (acceptable), 4 (good).

The teaching consisted of two parts:

1. First part: 3 simulation days (3 teams and 3 scenarios per day for the first two days, 4 teams and 4 scenarios for the third)
2. Part 2: One month later, 3 other days were organized according to the same pattern.

Each team consisted of three emergency medicine residents playing their own roles. A facilitator intervened as a nurse. The scenarios covered different clinical situations in the management of a severe trauma:

- Severe head trauma with signs of intracranial hypertension
- Chest trauma with suffocating pneumothorax
- Haemorrhagic shock complicating complex pelvic trauma
- Spinal cord injury

The sessions followed the recommendations of the HAS (10) with a briefing, scenario development, and debriefing.

Statistical analysis

The data was analysed with SPSS version 22.0. For the descriptive study, we calculated absolute and relative frequencies for the qualitative variables, and means, standard deviations, and extreme values for the quantitative variables. For the analytical study, the comparison of averages for paired series was made by the Wilcoxon test, and the relationships between quantitative variables were studied by the Spearman correlation coefficient. The significance level was set at $p<0.05$.

Ethical considerations

The anonymity and security of the participants' personal data were respected. The oral consent of the participants and a request for image rights were collected. The authors state that they have no interest in the content of this study.

RESULTS

The final analysis included 30 residents, with a female-to-male ratio of 4:1. The mean age was 28 years (range: 26-32 years). The breakdown by year of residence was 10 (33%) in the first year, 4 (13%) in the second year, 8 (27%) in the third year, and 8 (27%) in the fourth year.

Twenty-one residents (70%) had already received medical simulation training before the study, but only 19 (63%) had prior knowledge of NTCs.

The vast majority (90%) considered it possible to learn NTCs through medical simulation, and all (100%) considered it possible to learn technical skills. Regarding the percentage of medical errors related to NTCs, 60% of participants estimated it at more than 70%.

The initial means of the ANTS score, as well as those after one month, are mentioned in Table 1.

Table 1: The mean of the ANTS score studied at the initial assessment and after 01 month of training

ANTS SCORE	Averages at initial assessment	Average after 01 month of training	P
Task Management	3.96	4.96	1
Teamwork	1.72	2.06	0.003
Awareness of the situation	3.60	3.95	0.026
Decision-making	3.41	3.52	0.043

At one month, participants significantly improved their situational awareness (3.6 vs 3.95; p=0.026), decision-making (3.41 vs 3.52; p=0.043), and teamwork (1.72 vs 2.06; p=0.003) skills.

Comparison based on previous training by simulation

In the group with previous training (n=21), significant improvement was observed in situational awareness (3.56 vs 3.94; p=0.034), decision-making (3.4 vs 3.57; p=0.039), and teamwork (1.23 vs 1.85; p=0.023). The total score also improved significantly (3.58 vs 3.92; p=0.002).

In the group without prior training (n=9), improvement was significant for teamwork (1.11 vs 1.95; p=0.001) and task management (4.26 vs 4.96; p=0.001). (Table 2)

Table 2: Mean baseline and one-month ANTS scores in the groups with and without prior simulation training

	Previous simulation training (n=21)			No previous simulation training (n=9)		
ANTS score	Initial averages	Mean after 01 month	P	Initial Averages	Mean after 01 month	P
Task Management	4.86	4.96	1	4.26	4.96	0.001
Teamwork	1.23	1.85	0.023	1.11	1.95	0.001
Awareness of the situation	3.56	3.94	0.034	3.67	3.75	0.512
Decision-making	3.4	3.57	0.039	3.33	3.65	0.511
Total	3.58	3.92	0.002	3.36	3.42	0.055

DISCUSSION

Our study included 30 emergency medicine residents, 77.4% of whom were women, with an average age of 28 years. Although 70% had already received simulation training, only 63% knew about NTCs before the study, which is in line with the results of a 2016 French study (11) where almost all participants had no knowledge of NTCs despite prior simulation experience.

One month after the initial training, participants significantly improved their situational awareness, decision-making, and teamwork skills. These results confirm those of the literature on the retention of NTC learning. Thomas et al. (12) showed that behavioral changes within teams were retained six months after sessions without the need for a recall. Other studies (13-14) have shown that benefits on patient management persist 18 to 24 months after simulation training with CRM.

However, the study by Miller et al. (15) was inconsistent with previous results: participants had their non-technical skills regain their initial values one week after the simulation training. In light of these results, retention of non-technical skills appears to be variable. It was mostly studied in the medium term. Further studies on this subject would be of interest.

Subgroup analysis revealed that participants with prior simulation experience significantly improved their situational awareness, decision-making, and teamwork, while those without prior experience made particular progress in teamwork and task management. These results

are consistent with a French study (16) showing a significant improvement in teamwork and situational awareness in the previously untrained group.

Crisis Resource Management (CRM), as might be expected, crises in medicine can generate significant stress within a medical team. In the medical field, the same CRM skills as those identified in aeronautics have been recognized as fundamental and as improving the quality of teamwork (17,18).

In the United States, over the past fifteen years, courses have been developed for emergency physicians on communication and coordination of teamwork, "Emergency Team Coordination Course," using high-fidelity simulation as a learning tool (19).

Now more than ever, the medical community recognizes the importance of CRM skills in patient care and quality of care (20).

Thus, according to the recommendations of the High Health Authority (HAS) in 2012, the acquisition and evaluation of CRM skills by practitioners is essential (10). In 2015, the HAS created the "CRM health" sessions as part of the Continuous Improvement Program for Teamwork (PACTE). These sessions aim to raise awareness among practitioners about the principles of CRM in medicine.

Through our study, we show the need to set up training through medical simulation, including the teaching of non-technical skills. Given the concerns of young learners, the teaching of these skills in initial training would probably be more effective when technical skills are acquired. Learning of gestures could be proposed on procedural simulators (task-trainers). A summative evaluation could be carried out at the end. Learning of soft skills could take place in a second stage with the students who have passed this assessment.

CONCLUSION

Simulation learning is not limited to technical skills. NTCs, essential to the quality and safety of emergency care, can also be developed through this means. Our prospective study showed that one month after the initial training, participants significantly improved their situational awareness, decision-making, and teamwork. Subgroup analysis revealed differences in learning based on prior simulation experience. These findings underscore the importance of integrating NTC education into simulation training programs, ideally after the acquisition of technical skills in initial training. The implementation of a CRM-type program could optimize this learning. Further multicentred studies would be needed to assess the learning of NTCs in continuing education, the retention period of the acquired skills, and the optimal time to offer refresher training.

Conflicts of interest: *We declare that we have no conflicts of interest*

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Appendix

Anesthesiologist's Nontechnical Skills (ANTS) Global Rating Scale

Subtopics	Elements	Partial Rating (1-4)	Global Category Rating (1-4)
Task Management			
	Planning and preparing		
	Prioritizing		
	Providing and maintaining standards		
	Identifying and utilizing resources		
Team Working			
	Coordinating activities with team		
	Exchanging information		
	Using authority and assertiveness		
	Assessing capabilities		
	Supporting others		
Situation Awareness			
	Gathering information		
	Recognizing and understanding		
	Anticipating		
Decision-making			
	Identifying options		
	Balancing risks and selecting options		
	Reevaluating		
	TOTAL POINTS (total of global ratings)		

Rating Options		Descriptor
Good	4	Performance was of a consistently high standard, enhancing patient safety; it could be used as a positive example for others
Acceptable	3	Performance was of a satisfactory standard but could be improved
Marginal	2	Performance indicated cause for concern, considerable improvement is needed
Poor	1	Performance endangered or potentially endangered patient safety, serious remediation is required

- Subject Number _____ Date _____

Severity factors of epistaxis: A retrospective study of 60 cases.

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Abstract

Objective: Studying the severity factors of epistaxis.

Methods: Retrospective study involving patients hospitalized in the emergency department and ENT (Ear, Nose, and Throat) department for epistaxis over a period of 5 years (2018-2022). Based on the recommendations of the French Society of Otorhinolaryngology in 2015, we considered epistaxis severe when there was a sudden blood loss leading to acute anemia or signs of hypovolemic shock.

Results: Our study included 60 patients. Epistaxis was considered severe in 12 patients (20%). We found that female sex, black race, and patients with heart failure are severity factors for epistaxis.

Conclusion: Epistaxis is a common condition often considered benign, but in some cases, it can be serious. It is essential for clinicians to recognize forms that are initially or subsequently severe and to initiate optimal management to improve prognosis.

Keywords: epistaxis, severe, serious, shock state

INTRODUCTION

Epistaxis is one of the most common emergencies encountered in otorhinolaryngology (ENT) [1]. While it is often trivial, it can also pose a serious threat to life. This severity may stem from its volume or recurrence. Several factors can influence the severity of epistaxis, including patient characteristics, etiology, and the nature of management [2]. The role of the clinician is crucial in presuming the "dangerous" forms of initial or secondary epistaxis and initiating early, comprehensive, and effective management to improve prognosis.

This study aims to investigate the severity factors of epistaxis.

METHODS

1. Material

This is a retrospective study of patients hospitalized for epistaxis in the emergency and/or ENT departments of the Gabes University Hospital over a period of 5 years (from 2018 to 2022).

We included in this study patients requiring hospitalization for epistaxis due to: - The abundance of epistaxis: we do not have a figure specifying the amount of blood lost. It is thanks

to the data from the interview, the clinical examination, and the biological parameters that we subjectively determined the abundance of the state of health. We considered that:

An epistaxis is of low abundance: any epistaxis

• that helps spontaneously or with bidigital compression.

• An epistaxis is of high abundance: any epistaxis responsible for a state of shock or a drop in the hemoglobin level of more than 2g/dl.

• Epistaxis is of average abundance: any epistaxis that does not meet the criteria for epistaxis of low abundance or high abundance.

In this case, we hospitalized patients with epistaxis of high abundance.

- Repetition of epistaxis: we hospitalized patients with more than two episodes of epistaxis of average abundance in the last 24 hours preceding their admission.

- The need for posterior packing

- Retention on general condition: secondary to anemia: skin and mucous membrane pallor, asthenia, palpitations.

- Living far from the hospital without the possibility of close monitoring for patients with epistaxis of average abundance.

We excluded patients consulting for benign epistaxis in the emergency room without the need for hospitalization.

2. Methods

Based on the recommendations of the French Society of Otorhinolaryngology (SFORL) [3], we considered epistaxis to be severe in the presence of one of the following signs:

- sudden blood loss causing acute anemia

- signs of hypovolemic shock manifested by:

• Arterial hypotension (systolic blood pressure <90mmHg, with pinched differential)

• Tachycardia

• Impaired consciousness and/or polypnea and/or cyanosis of the lips and extremities and/or mottling

We defined recurrent epistaxis as any recurrent epistaxis after the performance of an effective local hemostasis procedure and after etiological treatment:

- The local hemostasis procedure must include at least an anterior packing +/- associated with a posterior packing.

-Etiological treatment may be:

• Regulation of high blood pressure

• Correction of a hemostasis disorder

• Reduction of a fracture

• Cauterization of a bleeding blood vessel

• Treatment of rhinosinusitis

• Removal of a bleeding tumor lesion

We studied the severity and recurrence factors of epistaxis: age, sex, race, season, revelations of hypertension, diabetes, renal failure, and heart disease, smoking, taking anticoagulants, the location of the murmur, hemodynamic parameters,

hemoglobin levels, PT percentage, etiology of epistaxis, and the nature of the treatment.

3. Statistical analysis

We used SPSS 22 in data collection. We checked the normality of quantitative variables by the Shapiro-Wilk test.

-For the comparison of qualitative variables, we used the Chi-square test.

-For the comparison of quantitative variables, we used the Student test if the normal distribution was verified and the non-parametric Mann-Whitney test if it was not verified.

We performed a univariate and multivariate analysis, considering that the test is significant for any $p < 0.05$.

RESULTS

Our study included 60 hospitalized patients with epistaxis. The mean age of the patients was 59.2 years (range: 10 to 93 years; SD=21.2 years). Patients over 60 years old represented 50% of the population. The cohort comprised 38 male patients (63.3%) and 22 female patients. White patients accounted for 80% of cases, while black patients represented 20% of cases. Hypertension was present in 55% of cases, and diabetes in 18% of cases. Four patients had heart failure, and three patients had renal insufficiency. Two patients underwent endonasal surgery: one septoplasty and one tubinectomy.

Epistaxis was post-traumatic in two patients. Thirty-three-point three percent (33.3%) of patients were on antiplatelet therapy such as Lysine Acetylsalicylate (Aspegic*), 5% were on clopidogrel (Plavix*), and 5% were on vitamin K antagonists (Sintrom*). A history of smoking was observed in 23.3% of patients. Most admissions occurred in the winter season, accounting for 36% of cases.

At admission, all patients had active bleeding from the nasal cavities and/or oropharynx. Anterior epistaxis was present in 73.3% of cases, and bilateral epistaxis was seen in 43.3% of cases.

Epistaxis was considered severe in 12 patients (20% of cases). General causes of epistaxis were predominant (58%), followed by essential epistaxis (25%) and local causes (17%). Traumatic causes (6 patients) dominated local etiologies of epistaxis, followed by inflammatory causes (3 patients), then tumoral causes (one patient). Hypertension (41.7% of patients) dominated the general causes of epistaxis. Hemostatic disorders due to medication represented 16.7% of etiologies.

Before hospitalization, bidigital compression was performed in most patients (96.7%), and anterior packing was done in 24 patients (40%).

At admission, patients with profuse epistaxis, poor general condition, or hypovolemic shock were admitted to the intensive care unit. A general hemostatic agent (Dicynone*) was administered to 91.7% of patients. Four patients were given tranexamic acid (Exacyl*). Vitamin K was administered intramuscularly at a dose of 10 mg in 12 patients. Most patients (85%) received antibiotic prophylaxis. Red blood cell transfusion was performed in 3 patients with hemoglobin levels below 8g/dl and in 4 patients with levels below 10g/dl in a fragile condition (coronary and

diabetic patients). The average number of red blood cell units transfused was 1.8. Fresh frozen plasma (FFP) transfusion was performed in one patient with a prothrombin percentage below 35%.

Bilateral anterior nasal packing was performed in 44 patients (73.3% of cases), and anterior-posterior double packing was done in 16 patients (26.7% of cases). Bipolar cautery under local anesthesia was performed in one patient. One patient required embolization of the right maxillary artery for persistent unilateral epistaxis.

Blood pressure regularization was necessary in 27 patients. Discontinuation of anticoagulation with a switch to an anticoagulant (Heparin) was required in two patients. These patients received Vitamin K supplementation. Recurrence of bleeding was observed in 36 patients (60%). These patients required reinsertion of anterior packing in 55% of cases (33 patients). Repositioning of posterior packing was performed in two patients.

The average length of hospital stay was 4.67 days (ranging from 2 to 14 days; SD=2 days). After discharge, two patients required readmission due to recurrence of epistaxis. The time between discharge and readmission was 2 days for one patient and 7 days for the other.

Upon studying the severity factors of epistaxis, we found that female sex is a risk factor for the severity of epistaxis: 36.4% of females had severe epistaxis compared to 10.5% of males, and this difference was significant (p=0.022). Similarly, the black race was considered a severe factor for epistaxis, as 50% of black patients had severe epistaxis compared to 12.5% of white patients, and this difference was significant (p=0.02). We also observed that 75% of patients with heart failure had severe epistaxis compared to 16% of patients without heart failure, and this difference was significant (p=0.023). Regarding other factors such as anticoagulant use, site of bleeding, hemodynamic parameters, laboratory data, and etiology of epistaxis, no significant difference between patients with and without severe forms of epistaxis was observed (Tables 1,2).

Table 1: Risk Factors for Severity of Epistaxis (Qualitative Variables)

Risk Factors		n/N	(%)	P
Age	<60 years	5/30	16.7	0.51
	=60 years	7/30	23.3	
Sex	Male	4/38	10.5	**0.02**
	Female	8/22	36.4	**2**
Race	Black	6/12	50	**0.02**
	White	6/48	12.5	
Season	Winter/Spring	10/43	23 ;3	0.31
	Autumn/ Summer	2/17	11.7	
Hypertension	Yes	9/33	27.3	0.19
	No	3/27	11.1	
Heart Failure	Yes	3 /4	75	**0.02**
	No	9/56	16	**3**
Diabetes	Yes	1/11	9.1	0.43
	No	11/51	21.5	
Renal Insufficiency	Yes	2/3	66.7	0.09
	No	10/57	17.5	
Anticoagulant Use (VKA)	Yes	1/3	33.3	0.49
	No	11/57	19.2	
Antiplatelet Use (Aspirin*)	Yes	5/20	25	0.49
	No	7/40	17.5	
Antiplatelet Use (Plavix*)	Yes	1/3	33.3	0.49
	No	11/57	21.5	
Anterior/Posterior Bleeding	Anterior	8/44	18.2	0.77
	Posterior	1/3	33.3	
	Anterior-Posterior	3/13	23.1	
Unilateral/Bilateral Bleeding	Unilateral	7/34	20	0.73
	Bilateral	5/26	19.2	
Etiology	Local	1/10	10	0.66
	General	8/35	22.9	
	Essential	3/15	20	

VKA: Vitamin K Antagonists; AAP: Antiplatelet Agent

In the multivariate analysis, we did not find any severity or recurrence factors.

Table 2: Severity risk factors for epistaxis (Quantitative variables)

Risk Factors	Severe Epistaxis	No Severe Epistaxis	p
SBP (mmHg)	140 (ET=34)	136 (ET=28)	0.33
DBP (mmHg)	76 (ET=14)	77 (ET=16)	0.69
MAP (mmHg)	97 (ET=14)	96 (ET=19)	0.93
TP (%)	86 (ET=10)	95 (ET=11)	0.67
INR	1.19 (ET=0.27)	1.04 (ET=0.22)	0.17

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure; PT: Prothrombin Time; INR: International Normalized Ratio

DISCUSSION

Epistaxis is a common ENT emergency. Usually benign, but it can be severe in certain cases, jeopardizing the patient's life prognosis. The vast majority of epistaxis cases do not require hospitalization, and invasive treatment is only necessary in 6% of cases [3]. There has been a persistent problem with assessing the severity of epistaxis, which has traditionally been based on subjective criteria. In most studies, epistaxis was classified based on its abundance or recurrence [4]. There is no clear definition of severity in the literature, often relying on subjective criteria such as estimating the volume of bleeding (mild, moderate, or severe epistaxis) or localization (anterior and/or posterior), with posterior epistaxis being considered severe or potentially more severe. Some authors [5] believe that hospitalization due to spontaneous epistaxis may be considered a sign of severity. However, there may be a bias, as admission may be related to the patient's fragility (elderly, comorbid patient) rather than solely to the epistaxis itself. Nonetheless, hospitalization typically implies some clinical instability, often requiring invasive treatment, including surgery [6]. Thus, in reality, all cases subjectively deemed "severe" or "serious" epistaxis inevitably require hospitalization.

In a study by André et al. [7], they classified spontaneous epistaxis as "severe" if admitted with anterior nasal packing for 48 with epistaxis cessation by day 3 of hospitalization and as "serious" if hospitalized for >3 days requiring double hours balloon packing, or if significant decompensation with hemoglobin levels <10 g/dL requiring red blood cell transfusion, or if invasive surgical treatment and/or selective arterial embolization were necessary under arteriography.

In our study, we relied on the 2015 SFORL recommendations [3], which consider epistaxis severity to be evaluated based on clinical, hemodynamic, and biological criteria:

Anterior-posterior epistaxis and/or bilateral epistaxis suggest severe epistaxis and warrant investigation for signs of hypovolemic shock.

Hemorrhagic shock is absolute hypovolemia secondary to sudden and significant blood loss, also resulting in acute anemia [8].

The diagnosis of shock is made based on the following signs [9] (Level 4 evidence):

-Low blood pressure (systolic blood pressure <90 mmHg, with pinched differential)

-Tachycardia

-Altered consciousness and/or tachypnea and/or cyanosis of the lips and extremities and/or mottling

The most commonly described risk factors for severe epistaxis in the literature include age, male sex, summer season, hypertension, and anticoagulant use.

In most studies, advanced age has been a severe factor for epistaxis. In this context, Hadar et al. [2] found that age (OR 1.02; CI 1.01-1.023) was significantly correlated with clinical symptoms of epistaxis severity. However, André et al. [7] found no significant differences in epistaxis severity between patients over 60 and those under 60 years old. Paradoxically, the average age was slightly lower in the severe epistaxis group in their study.

In our study, we found that 23.3% of patients over 60 years old had severe epistaxis compared to 16.7% in patients under 60 years old, but the difference was not significant.

Male sex has been a significant factor in several studies. Hadar et al. [2] found that male sex (OR 2.07; CI 1.59-2.69) was significantly correlated with severe epistaxis symptoms. This male predominance might be explained by estrogen protection in females against epistaxis. The preventive role of estrogen in epistaxis recurrence was reported by Daniell in 1995 [10]. However, in our study, paradoxically, we found that women were more likely to have severe epistaxis (36.4% vs. 10.5% in men). This could be explained by sampling bias, as only patients requiring hospitalization were studied, not all patients with epistaxis.

Several studies have found a higher incidence of hospital admissions due to epistaxis during winter, likely due to decreased humidity and increased dryness, leading to drier nasal mucosa and increased bleeding tendency. For instance, Min et al. observed that nosebleeds typically occur in winter and spring when there's a significant temperature difference between indoor and outdoor areas, causing obvious nasal blood vessel contraction and relaxation, resulting in dry nasal mucosa and an increased risk of nasal blood vessel rupture. Low temperature and dryness are risk factors for nosebleeds.

Hypertension is generally considered a severe factor for epistaxis. In a meta-analysis [14], the relationship between epistaxis severity and hypertension was controversial. While hypertension was considered a bleeding risk factor, it was not determined whether it was the cause, as biases caused by sex and age were not excluded. In another study, Hadar et al. [2] found that hypertension (OR 1.76; CI 1.27-2.45) was significantly correlated with severe epistaxis symptoms. The British Rhinological Society's multidisciplinary consensus considers only hypertension [15] as a major risk factor for severe clinical progression. However, it should be noted that measuring hypertension during an epistaxis episode may not be reliable, as it is a stressful event.

A meta-analysis by Jin Min et al. in 2017 of 10 studies showed an increased odds ratio for epistaxis in patients with hypertension (OR = 1.253; 95% CI: 1.080-1.453) [14]. A retrospective cohort study in 2020 by Byun et al. demonstrated hypertension as a significant risk

factor for epistaxis with an adjusted risk ratio of 1.47 (95% CI: 1.30-1.66). They also found that hypertensive patients were more likely to require posterior nasal packing [15]. Another retrospective review by Sethi et al. in 2017 showed that hypertensive patients presenting to the emergency department were more likely to require nasal packing (41.2% vs. 30.3%, $p < 0.001$) [16]. Hayoung et al. [17] demonstrated that hypertensive patients were more likely to visit the emergency department for epistaxis and undergo posterior nasal packing compared to non-hypertensive patients.

In our study, hypertensive patients were more likely to have severe epistaxis (27.3% vs. 11.1% in non-hypertensive patients), but the difference was not significant (p=0.19). When comparing SBP, DBP, and MAP at admission between patients with severe epistaxis and those without, no significant difference was found.

The role of anticoagulant use in the occurrence of severe epistaxis is controversial from one author to another and from one product to another. Hadar et al. [3] found that the use of antiplatelet agents or anticoagulation (OR=2.53; CI=1.93–3.33, OR=1.65; CI=1.11–2.44, respectively) was significantly correlated with severe clinical symptoms of epistaxis. The British Rhinological Society's multidisciplinary consensus considers anticoagulant therapy to carry a higher risk of severe syndrome [18]. Studies have examined the association between the use of different types of anticoagulant/antiplatelet drugs and the risk of epistaxis. Conventional medications (e.g., warfarin; enoxaparin) were significantly associated with more severe nosebleeds than new-generation oral anticoagulants (e.g., Apixaban, Rivaroxaban) [19, 20]. Tunkel et al. consider that although anticoagulants increase the severity and frequency of epistaxis, other preventive and therapeutic measures should be considered before stopping these medications unless bleeding is severe [21]. In this context, saline nasal sprays and nasal emollients are recommended as first-line preventive measures despite the lack of evidence, as they have shown significant improvement in epistaxis with these moisturizing agents [22, 23].

Contrary to previous studies, Gavin et al. did not find that anti-thrombotic use was a severity factor for epistaxis [24].

Another study found that the incidence of nosebleeds increased with increased use of oral anticoagulants, but the number of patients requiring hospitalization did not increase [25].

In a study by André et al. [7], they found that the use of hemostasis-altering medications does not appear to be a significant severity factor, unlike Soyka's study, where aspirin use appears to be a severity factor for epistaxis [26].

In our study, we compared the frequency of severe epistaxis based on the nature of each type of anticoagulant (VKAs, AAPs, or anti-thrombotic), and no significant difference was found regardless of the product used. Additionally, comparing PT and INR between the two patient groups found no difference

despite TP being lower in patients with severe epistaxis (86% vs. 95%).

In a study by Chaaban et al., in addition to hypertension, elevated blood lipid levels, especially LDL, grade III retinal arteriosclerosis, hyperglycemia, heart failure, and obstructive sleep apnea syndrome were found to be severity factors for epistaxis [27]. This may be explained by endothelial vascular alteration due to arteriosclerotic phenomena leading to impaired vascular repair and persistent epistaxis.

In our study, we found that patients with heart failure were more likely to have epistaxis compared to patients without it (75% vs. 16%), and the difference was significant (p=0.023). However, for other factors (diabetes, renal failure), no significant difference was found.

This study has the advantage of determining the severity and recurrence factors of epistaxis, but its limitation was the sampling bias, as only severe forms of epistaxis were included in the study due to a lack of data. This could affect the results of the analytical study.

CONCLUSION

Severe epistaxis is much less common than its benign form. Understanding it based on clinical and biological criteria is essential to initiate early and appropriate management. Age, sex, and patient comorbidities (such as hypertension, heart failure, and anticoagulant use) are always severity factors.

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Chest computed tomography findings in organizing pneumonia

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Abstract

Background: Organizing pneumonia (OP) is a non-specific clinicopathological entity characterized by intra-alveolar buds of granulation tissue consisting of fibroblasts and connective tissue. OP is often secondary to infections, drug reactions, autoimmune diseases, or radiation therapy. Chest computed tomography (CT) is pivotal in the evaluation of suspected OP, often demonstrating characteristic findings. Our study aimed to illustrate major imaging characteristics and patterns of OP.

Methods: We conducted a prospective study including all patients hospitalized in the infectious disease department for OP between 2018 and 2024. The diagnosis of OP was based on histopathology (lung biopsy).

Results: We encountered 35 cases of OP, including 19 women and 16 men. The mean age of patients was 76±18 years. Chest X-ray showed multiple alveolar opacities, which were often migratory, in 20 cases, a heterogeneous excavated nodule in one case, and an invasive alveolar opacity in 14 cases. The thoracic CT scan showed multifocal parenchymal condensations in 34% of the cases, single or multiple nodules in 11% of the cases, and "reversed halo sign" in 25% the cases. Arciform condensations (40%), crazy paving (3%), and fibrosis (6%) were reported. The migratory aspect of the lesions and the regression under steroids were specific and present in 49% of the cases.

Conclusion: Organizing pneumonia is a heterogeneous condition with diverse clinical and imaging presentations. Chest CT plays a crucial role in detecting typical radiological features that aid in diagnosis. Recognizing these imaging patterns, along with clinical correlation, can facilitate early diagnosis and appropriate management, improving patient outcomes.

Keywords: Organizing pneumonia; Computed Tomography; Lung diseases; Diagnostic imaging

INTRODUCTION

Organizing pneumonia (OP) is a non-specific clinicopathological entity characterized by intra-alveolar buds of granulation tissue consisting of fibroblasts and connective tissue, typically resulting from an aberrant healing response to lung injury [1,2]. Although it can be idiopathic, referred to as cryptogenic

organizing pneumonia (COP), OP is often secondary to infections, drug reactions, autoimmune diseases, or radiation therapy [3,4]. Clinically, patients present to the emergency department for subacute symptoms including cough, dyspnea, fever, and malaise, often leading to initial misdiagnosis as bacterial pneumonia [5].

Chest computed tomography (CT) is pivotal in the evaluation of suspected OP, commonly demonstrating characteristic findings such as patchy peripheral or peribronchial consolidations, ground-glass opacities, and the classic “reverse halo” sign (also known as the atoll sign) [6,7]. While these radiologic features are not pathognomonic, they can strongly support the diagnosis and guide further diagnostic or therapeutic decisions, particularly in differentiating OP from other interstitial and infectious lung diseases [8]. Our study aimed to illustrate major imaging characteristics and patterns of OP.

METHODS

We conducted a prospective study including all patients hospitalized in the infectious disease department for OP between 2018 and 2024. Some patients underwent a chest X-ray, and others had a chest CT.

The diagnosis of OP was based on histopathology (lung biopsy). Cryptogenic origin was confirmed after negative immune serologies, bronchoalveolar lavage searching the infectious agents, environmental surveys, and a precise questionnaire about drug and toxic consumption.

RESULTS

In total, 35 cases of OP were identified, including 19 women and 16 men. The mean age of patients was 76±18 years. The most common symptoms were dyspnea, cough, anorexia, fever, and occasional hemoptysis. OP was cryptogenic in 12 cases, infectious in 14 cases, toxic in 2 cases, associated with systemic pathology in 4 cases, post post-therapy in 3 cases.

Chest X-ray showed multiple alveolar opacities, which were often migratory, in 20 cases, a heterogeneous excavated nodule in one case, and an invasive alveolar opacity in 14 cases (Figures 1 and 2).

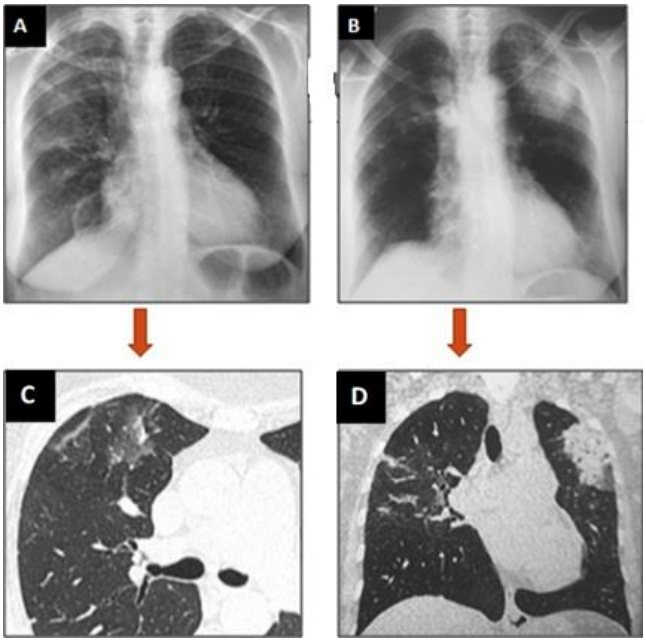

Figure 1: Patient's X-ray (A, B) and chest computed tomography scan (C, D) demonstrating ground-glass hyperdensity and migratory pulmonary condensations.

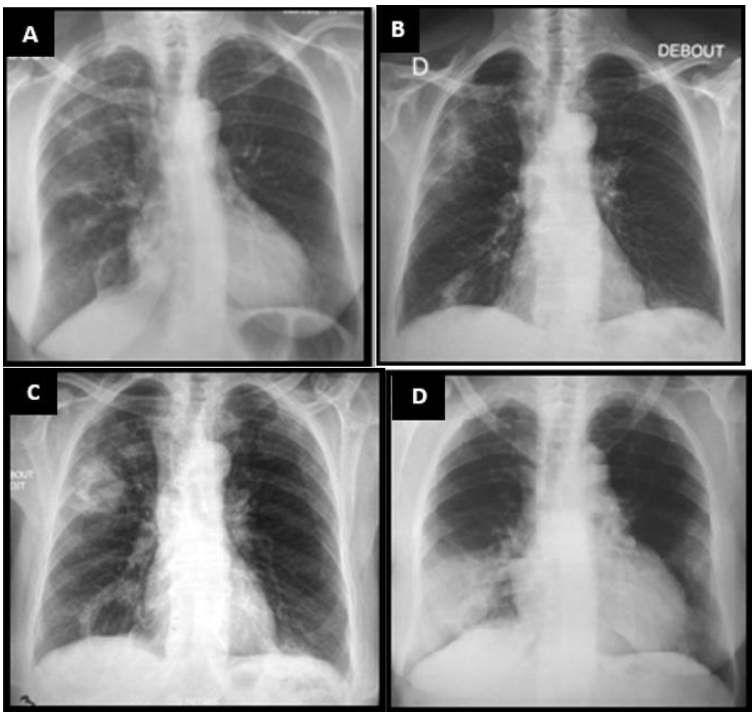

Figure 2: Different radiological patterns of organising pneumonia on chest X-ray: Migrating alveolar opacities (A, B), excavated nodular opacity (C), and invasive alveolar opacity (D)

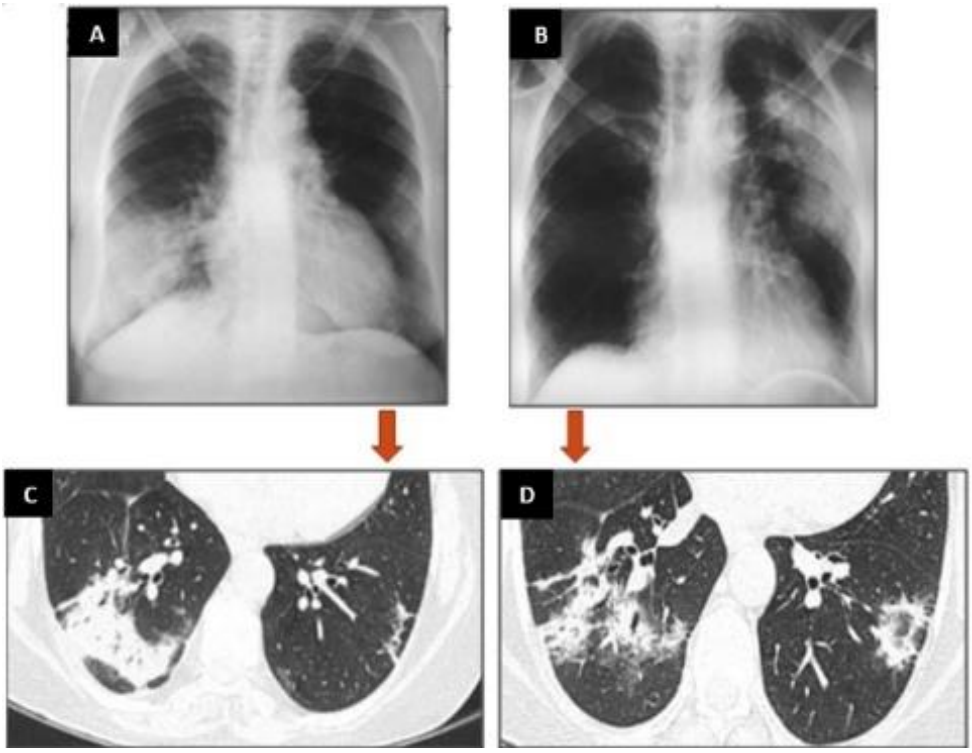

Figure 3: Chest X-ray and computed tomography scan demonstrating curved condensations and reversed halo sign.

The thoracic CT scan showed multifocal parenchymal condensations in 34% of the cases, single or multiple nodules in 11% of the cases, and "reversed halo sign" in 25% the cases (Figure 3).

Arciform condensations (40%), crazy paving (3%) (Figure 4), and fibrosis (6%) were reported. The ground-glass hyperdensity was the most common sign in 51% of cases.

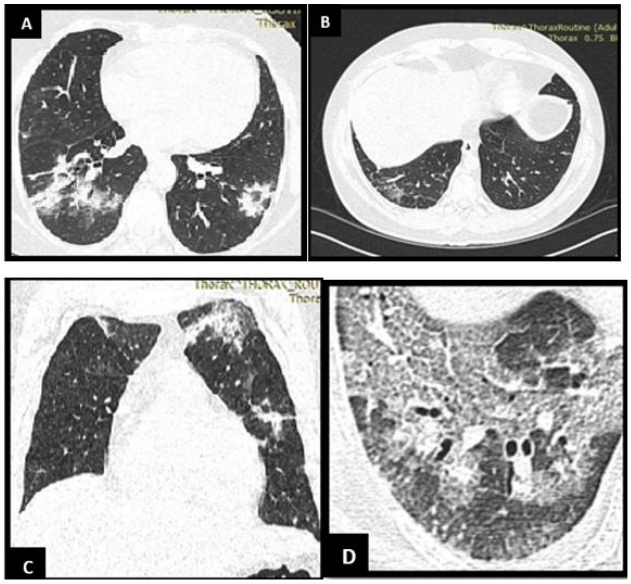

Figure 4: Different radiological patterns of organizing pneumonia on chest computed tomography scan: Multifocal parenchyma condensations (A), frosted glass hyperdensity (B), arciform condensations (C), and crazy paving (D)

Condensation's distribution was generally sub-pleural or peribronchial. The migratory aspect of the lesions and the regression under steroids (Figure 1) were specific and present in 49% of the cases.

DISCUSSION

Our study provides valuable insight into the clinical and radiological variability of organizing pneumonia, emphasizing the diagnostic importance of chest CT in conjunction with histopathological confirmation. The demographic and clinical characteristics of our cohort are consistent with previously published data, with a slight female predominance and a mean age above 70 years [1,4]. The most frequent symptoms, dyspnea, cough, anorexia, and fever, reflect the non-specific and subacute nature of OP, often leading to initial diagnostic confusion with infectious or neoplastic lung diseases [9]. In our series, COP accounted for 34% of cases, while the remaining forms were secondary to identifiable causes such as infections, systemic diseases, drugs, or post-therapy complications. This distribution aligns with previous reports indicating that secondary OP may be more frequent in hospital-based populations due to referral bias or underlying comorbidities [5].

Radiologically, chest X-ray findings in our cohort were variable and often misleading, underlining the limited specificity of plain radiography in OP. Migratory alveolar opacities were frequent, a hallmark feature that should raise suspicion of OP when present in a compatible clinical context [8]. However, the more heterogeneous presentations, including excavated nodules or invasive-looking consolidations, highlight the importance of advanced imaging.

High-resolution computed tomography was significantly more informative, revealing a broad spectrum of abnormalities. The most common findings were ground-glass opacities (51%), arciform/subpleural condensations (40%), and reversed halo sign (25%), consistent with classical imaging patterns described in OP [6,7]. Although the "crazy paving" pattern and fibrosis were less common in our study, their presence has been

previously documented, especially in chronic or evolving forms of OP [10].

The subpleural and peribronchial distribution lesions seen in our patients reflect the pathophysiological tendency of OP to follow the small airways and alveolar ducts. The migratory nature of lesions, observed in nearly half of the cases, as well as their favorable response to corticosteroids, are highly characteristic features of OP and can be diagnostically helpful in differentiating it from infections, malignancies, or vasculitides [2].

Histological confirmation through lung biopsy remains the gold standard for diagnosis, especially in atypical or non-responsive cases, as was the case for all patients in this cohort. The systematic exclusion of secondary causes, through immunologic testing, bronchoalveolar lavage, environmental and drug exposure history, allowed us to accurately distinguish COP from secondary forms [4].

CONCLUSION

OP is a heterogeneous condition with variable clinical and radiological presentations, often mimicking other pulmonary diseases. This study reinforces the value of chest CT scanning as an essential diagnostic tool in suspected OP in the emergency setting. The CT scan provides specific patterns that, in the right clinical context, can strongly suggest the diagnosis even before histopathological confirmation. However, biopsy remains indispensable, especially when radiologic features are atypical. A multidisciplinary approach is crucial for accurate diagnosis and appropriate management.

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Author contributions : (I) Conception and design: WF, FH, MK; (II) Administrative support: WF, FH; (III) Provision of study materials or patients: WF, FH, AK; (IV) Collection and assembly of data: FH, ZM; (V) Data analysis and interpretation: WF, FH, MK, AK; ZM (VI) Manuscript writing: WF, FH; (VII) Final approval and revision of manuscript: All authors.

Conflict of interest statement: The authors have no conflict of interest to declare.

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Suppurative infection of the central nervous system secondary to Streptococcus constellatus: about three cases

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Abstract

A brain abscess or empyema is a severe neurological infection with a high mortality rate. Rarely, Streptococcus species other than S. pneumoniae were responsible for brain abscesses or empyema. A few case series were reported in the literature.

We present three cases of severe empyema and abscess induced by S. constellatus in three immunocompetent individuals. A 12-year-old girl presented with febrile meningeal syndrome. The CT scan showed a brain abscess and empyema associated with hemispheric edema. She underwent surgery for empyema evacuation and frontal lobectomy with a decompressive flap bone. A 52-year-old man presented with right-hemisphere heaviness, headache, and fever. Cerebral MRI showed an abscess of the left semi-oval center with signs of ventriculitis. He underwent neurosurgical drainage. A 14-year-old child admitted with right frontal swelling and osteitis in the context of fever. Cerebral MRI showed a right hemispherical subdural collection and thrombophlebitis of the superior sagittal sinus.

The outcome was good only for the two children. Although S constellatus can cause serious infections in patients with underlying diseases and immunosuppression, physicians need to consider S constellatus infection in immunocompetent patients in the context of empyema and abscess.

Early neurologic drainage and antibiotics must be installed on time to have a good outcome.

Keywords: Streptococcus constellatus; Abscess; Brain; Empyema, Outcomes

INTRODUCTION

Brain abscesses and empyema are life-threatening infections(1). Intracranial infections may result from contiguous infections, such as mastoiditis or acute otitis media, or from hematogenous dissemination from an infectious source (2,3). S. pneumoniae is the most common etiologic agent of central nervous system infection (4,5). *Streptococcus constellatus (S. constellatus)* is an uncommon type of viridans streptococci(4). It is a gram-positive cocci of the *Streptococcus anginosus* group (SAG), formerly the *Streptococcus milleri* group (4,6,7). SAGs are commensals of mucosal membranes (the oral cavity, pharynx, gastrointestinal tract, and genitourinary tract) (8), known for their ability to form abscesses, namely in immunocompromised patients (4-6). Few case series are reported in the literature (6). We report three cases of severe empyema and abscess caused by *S. constellatus* in three immunocompetent hosts.

CASE REPORT 1

A 12-year-old girl presented to the emergency department with febrile meningeal syndrome, with a fever of 40°C, headache, nausea, and vomiting. She has no previous medical history. On physical examination, she was conscious (Glasgow Coma Scale =15/15), with a heart rate of 119 beats per minute (bpm), a blood pressure of 91/40 mmHg, a respiratory rate of 26 cpm, and a pulse oximetry of 96%. Laboratory examination revealed 39,000/mm^3 leukocytosis (reference values are 4,000 to 10,000/mm3), with a predominance of neutrophils (20,000/mm^3), and 424,000/mm^3 platelets count (reference values are 150,000 to 450,000/mm^3), 80 U/L aspartate transaminase (reference values are 5 to 45 U/L), 101 U/L alanine transaminase (reference values are 7 to 56 U/L), and 170 mg/L C-reactive protein (reference values are < 3 mg/L) levels were above the reference limits. Renal function and electrolyte levels were in normal ranges. A cerebral computed tomography scan, urgently performed, objectified a right parietal brain abscess and empyema associated with a significant right hemispheric edema responsible for subfalcal involvement, and a right frontal sinusitis with lysis of its posterior wall (Figure 1A). Due to sepsis, the patient was admitted to the intensive care unit, where the sepsis protocol was performed. A blood sample was collected, and broad-spectrum intravenous antibiotics (cefotaxime, vancomycin, and metronidazole) were administered. Despite this early management, her respiratory and neurological condition had deteriorated, and the mechanical ventilation was indicated. She underwent a surgical evacuation of empyema and abscess with a decompressive bone flap. Her samples were sent to culture. Gram stain revealed gram-positive cocci, *Streptococcus constellatus*, sensitive to Cefotaxime. Within one day after surgery, the first control CT scan revealed a decrease in edema (Figure 1 B). On day 2, the evolution was unfavorable with neurological deterioration with the onset of right anisocoria due to an increase in cerebral edema and in midline deviation (0 mm *vs* 5 mm), and the presence of temporal involvement (Figure 1C). She underwent

a second surgery with flap bone enlargement and frontal lobectomy (Figure 1D). Cerebral MRI showed signs of meningoencephalitis without cerebral thrombophlebitis (Figure 1E). She was extubated on day 7, but hemiparesis persisted.

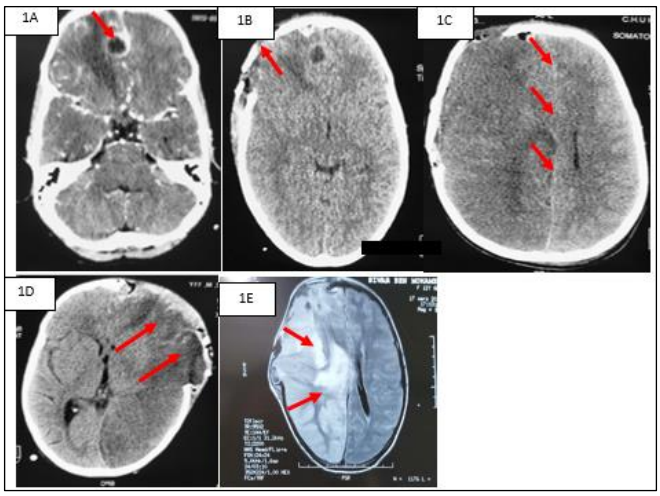

Figure 1: 1A: Injected CT scan: parietal brain abscess. **1B**: control brain CT scan after surgery. **1C:** Control brain CT scan after neurological worsening: increase in cerebral edema, increased midline deviation by 10 mm. **1D:** Control brain CT scan after the second surgery: flap enlargement and frontal lobectomy **1E:** MRI T2FLAIR: signal anomaly in the cortical zone and in the right frontoparietal white matter not systematized in FLAIR hyper signal with a restriction of the Apparent Diffusion Coefficient.

Figure 1: Injected brain CT-scan (1A): parietal brain abscess, Control brain -CT-scan after surgery (AB), Control brain CT-scan after neurological worsening, increase in cerebral edema, increased midline deviation by 10mm) (1C); control brain CT-scan after the second surgery: flap enlargement and frontal lobectomy (1D); MRI T2FLAIR: signal abnormality in te cortical zone and in the right frontoparietal white matter

CASE REPORT 2

A 52-year-old man with no previous history was admitted to the neurosurgery department with right-hemisphere heaviness, headache, and a fever (38.5°C). On admission, the patient was unconscious (Glasgow Coma Scale = 9/15) with aphasia, right facial paralysis, and right hemiplegia. The brain CT-scan (Figure 2A) showed a left frontal intracranial expansive process exerting a mass effect on the medial structures. Laboratory examination revealed 13,400/mm^3, leukocytosis, 199,000/mm^3 platelet count, and 298 mg/L C-reactive protein. Renal function and electrolyte levels were in normal ranges. Because of impairment of his consciousness and respiratory condition, related to aspiration pneumonia, the patient was admitted to intensive care. He underwent mechanical ventilation. With the onset of septic shock, noradrenaline infusion and antibiotics (cefotaxime and metronidazole*)* were administered. Cerebral MRI showed a pyogenic abscess (26x22 mm) of the left semi-oval center fissured in the lateral ventricle with signs of ventriculitis, and sub-factorial and temporal involvement (Figure 2B). Neurosurgical drainage of the empyema revealed a purulent liquid where *Streptococcus constellatus*, sensitive to cefotaxime, was identified.

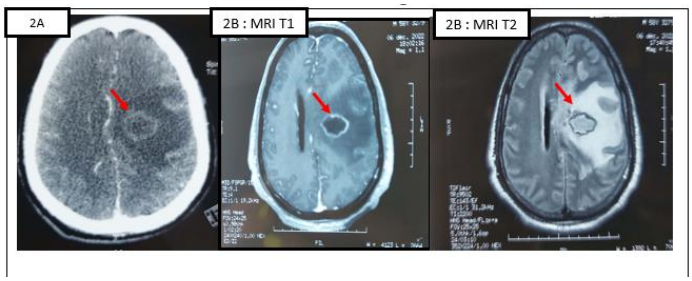

Figure 2: Injected brain CT-scan showing brain abscess 2B: MRI: intracranial expansive process of the left oval center in hypo signal T1 and hypersignal T2 with a restriction of the diffusion delimited by an irregular wall in hyper signal T1 and hypo signal T2 being enhanced after gadolinium injection, and measuring 27x18x27 mm. There is an important edema in glove-finger shape with a mass effect on the left ventricle and a contralateral hydrocephalus (MRI Aspect of pyogenic abscess with signs of ventriculitis and subfalcial and temporal involvement.

The chest radiograph, the transthoracic echocardiogram, and the ultrasonography of the abdomen were normal. The outcome was unfavorable, with alteration of his hemodynamic state leading to death.

CASE REPORT 3

A 14-year-old child, with no prior medical history, was admitted to the neurosurgery department with right frontal swelling with osteitis, as shown in the first CT scan (figure 3A) in the context of fever. Laboratory examination revealed 19,500/mm^3 leukocytosis, 264,000/mm^3 platelet count, and 298 mg/L C-reactive protein. He underwent surgery for the evacuation of the right frontal collection with osteitis. Figure 3B shows the post-surgery result of the CT scan. On day 2 post-surgery, the onset of a deterioration in his state of consciousness, right anisocoria, left hemiplegia, and aphasia led to mechanical ventilation. Cerebral MRI showed a right hemispherical subdural collection of 5 mm FLAIR hypersignal and diffusion with a low Apparent Diffusion Coefficient with right temporal involvement, superior sagittal sinus thrombophlebitis, and pansinusitis (Figure 3C). He underwent emergency surgery to evacuate the subdural collection. A broad-spectrum antibiotic therapy including *cefotaxime*, *vancomycin*, and metronidazole was administered. The bacteriological sample identified a *Streptococcus constellatus* sensitive to *cefotaxime*. On the sixth day, he developed a convulsive status epilepticus when the sedation was stopped. The control computed tomography scan (Figure 3D) showed the onset of ischemic lesions in the right hemispheric brain with an increase in cerebral edema and midline deviation (9 mm vs 7mm), and central involvement, requiring a second neurosurgical drainage (Figure 3E). The outcome was favorable, but he remained with left hemiplegia.

DISCUSSION

Here, we report three cases of extensive brain abscess and empyema due to S. constellatus in immunocompetent patients. In all cases of S. constellatus abscess reported in the literature, there was either underlying pathology or a history of immunosuppression (6). S constellatus is an

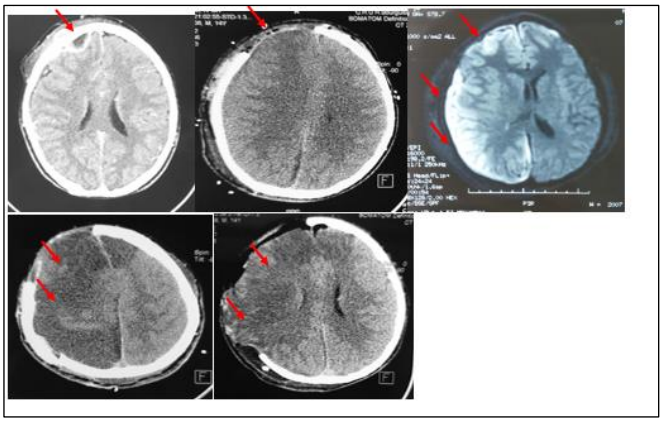

Figure 3: 31: right frontal swelling with osteitis; 3B: post-surgery brain CT-scan; 3C: Cerebral MRI: right hemispherical subdural collection of 5mm FLAIR hypersignal and Diffusion low apparent Diffusion Coefficient with right internal temporal engagement; 3D: development of ischemia in the right hemisphere with an increase in cerebral edema and in the midline deviation (9 vs 7 mm); 3E: post-surgery brain CT-scan. .

oropharyngeal commensal that colonizes the mouth and the upper airways. It can be pathogenic in patients with certain predisposing factors and

therefore responsible for a broader range of purulent infections, including odontogenic, pleura-pulmonary (9), intra-abdominal, genitourinary, soft tissue, and central nervous infections(8,10). S. constellatus is an extremely rare causative agent of brain abscesses in immunocompetent patients (2,11). Brain parenchymal infection usually occurs through hematogenic path (2,11) or contiguous spread (12). In our cases (13), we hypothesized that the infection route was pansinusitis, not well-treated. In most cases, brain abscesses were caused by a contiguous spread of infections, such as sinusitis or otitis. Orbital and dental infections are potential other causes of brain abscesses (13). One further complication was also noticed in our cases, thrombophlebitis, as seen in our third case. This complication was reported in a few cases (13,14).

The most frequent symptoms of intracranial abscesses are fever and headache. Sensory loss and disorientation may also occur. The neurological symptoms and signs depend on the abscess location and can range from an asymptomatic disease to coma, and at times, may even lead to death. Frontal and temporal lobe abscesses may manifest as behavioral changes that can be misdiagnosed as psychiatric disorders. Clinical manifestations become more evident as the abscess grows and the surrounding swelling increases. Imaging studies using CT or MRI aid diagnosis(2,6), as done in our patients, and may show signs of sinusitis or complications such as thrombophlebitis, present in the third patient. For these infections, the treatment protocol consists of ceftriaxone or cefotaxime for at least two weeks. This is the best antibiotic choice, thanks to its distribution in the neural tissue. Intravenous metronidazole and clindamycin can be concurrently prescribed for up to six weeks when anaerobic bacteria are found, especially in polymicrobial abscesses. Vancomycin is the option when resistance or allergies are evidenced or to treat Staphylococcus (7). In our patients, we used cefotaxime as the first-line treatment of community meningitis, associated with metronidazole to treat anaerobic bacteria, possibly due to concurrent infection by S. constellatus (7). In two of our cases, Vancomycin was empirically administered and then stopped adapting to the antibiogram.

CONCLUSION

The foremost lesson to be learned from the current cases is that cultures and antibiograms are the best cues for making diagnoses and selecting accurate therapies. The ability of S. constellatus to form an abscess is another important finding, not only in patients with underlying diseases and immunosuppression. Physicians must consider S constellatus infection in immunocompetent patients in the context of empyema and abscess. Early neurologic drainage and antibiotics must be promptly done to ensure good outcomes.

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Catastrophic antiphospholipid syndrome: literature review and case report

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Abstract

Catastrophic antiphospholipid syndrome (CAPS) is a rare and life-threatening condition characterized by the simultaneous occurrence of multiple thrombotic events, predominantly affecting microcirculation. We report a case of CAPS in a 55-year-old male patient with no notable pathological history who presented with diffuse abdominal pain and subsequently developed neurological and renal manifestations. This case report is complemented by a comprehensive literature review of CAPS, highlighting its epidemiology, clinical manifestations, diagnostic criteria, and treatment options.

Our literature review included a thorough search of various databases and search engines, including PubMed/Medline, Google Scholar, and Cochrane, in both English and French. We adhered to patient data protection guidelines, ensuring confidentiality throughout the report.

CAPS is associated with a significant morbidity and mortality rate, with a high short-term mortality rate, particularly in the acute phase. Prompt recognition and early initiation of treatment, such as the "Triple Therapy" approach involving intravenous heparin, oral anticoagulation, and corticosteroids, are crucial for improving patient outcomes. In refractory cases, Rituximab and Eculizumab have shown promise as alternative treatment options.

Our case report underscores the importance of timely diagnosis and appropriate management of CAPS. Further research and collaboration among healthcare professionals are warranted to enhance our understanding of this complex syndrome and improve patient care.

Keywords: Catastrophic antiphospholipid syndrome, thrombosis, microcirculation, autoimmune.

INTRODUCTION

Antiphospholipid syndrome (APS) or Hughes syndrome is a clinical and biological entity characterized by the association of thromboembolic (venous and/or arterial) and/or obstetric manifestations and long-lasting antiphospholipid antibodies (lupus-like circulating anticoagulant; IgG or IgM anti-B2 glycoprotein I or IgG or IgM anti-cardiolipin antibodies) (1,2). Less than 1% of patients with APS develop a rare and severe variant known as

the catastrophic variant, or CAPS or Asherson syndrome. This entity is characterized by the occurrence of multiple microcirculatory thromboses within a short period, often leading to a multivisceral failure. CAPS commonly occurs in young women during primary APS (60%) (3). The prognosis is poor, with a high mortality rate estimated at 30% in the acute phase and 34% at one year (3).

This case report presents a unique instance of primary CAPS diagnosed early in a 55-year-old male patient without any apparent triggering factors. The patient showed a favorable outcome with dual therapy. Additionally, the literature on this condition is reviewed to provide a comprehensive understanding of CAPS.

METHODS

We report an observation of catastrophic antiphospholipid syndrome, with a literature review of the existing literature on this topic.

To gather relevant information, a thorough search was conducted using various databases and search engines, including PubMed/Medline, Google Scholar, and the Cochrane database. The search encompassed both English and French sources, with a focus on accessing full-text articles or published abstracts.

Throughout the process, strict adherence to patient data protection regulations was maintained. The confidentiality and anonymity of the patient were carefully preserved, ensuring that no identifying information was disclosed at any point from data collection to publication.

RESULTS

We present a case study of a middle-aged Tunisian man, Mr. A.B, who had no significant medical history and was admitted to the emergency department due to persistent diffuse abdominal pain for the past 7 days without any gastrointestinal or urinary tract-associated symptoms.

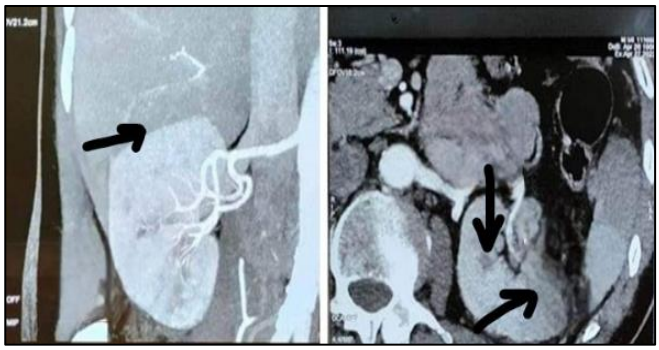
On physical examination, the patient's hemodynamic, respiratory, and neurological status were stable with tachycardia at 110 bpm; no fever was documented upon initial examination.

He presented with diffuse abdominal tenderness without guarding or contracture, free hernial orifices; the rectal exam was without abnormalities.

Upon further investigations:

- EKG: RRS 85 bpm; axis 60°; no repolarization disorders; LVH (Sokolow index 40)
- Biology:
  - Hb= 16 g/dl; WBC= 15000/mm3 with 75% PNN; platelets= 198000
- Creatinine: 97 µmol/l (clearance=74 ml/Mn).
- Na+=137 mmol/l; K+= 4.7 mmol/l; Cl- = 98.73 mmol/l. CRP = 41 mg/l; blood calcium = 2.64 mmol/l; Procalcitonin = 0.05 ng/ml
- ALT = 164UI/L (5×ormal values); ASAT = 62UI/L; BT/BD=6/1; GGT= 58 UI/L; PAL 99 UI/L. CBEU: Hu +++; Alb: +; Leu: 17/mm3.
- Blood cultures were negative.

A contrast injection abdominal pelvic CT scan revealed multiple foci of infarction in both kidneys and the spleen, direct images of clot in a superior polar branch of the left renal artery, and in the middle part of the superior mesenteric artery.



Figures 1+2: CT scans showing foci of infarction in both kidneys and the left renal artery.

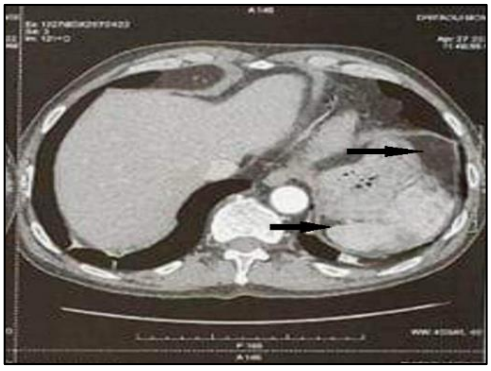


Figure 3: CT section showing foci of infarction in the spleen.

Given the arterial location of the emboli, a TEE and a TTE were performed to look for a cardiac origin, and concluded that the left atrium was filled to 3 thrombi, one of which was floating, measuring 8×8 mm; the cavities were not dilated; there was no valvular disease; and there was no image suspicious of infectious endocarditis. The patient was put on effective anticoagulation: UFH at PSE combined with methylprednisolone (1mg/kg/d). After 3 days, the patient became confused with the onset of right hemiplegia and dysarthria. A cerebral CT scan concluded that there was an area of non-systematic hypodensity in the left frontal subcortical white matter. A cerebral MRI-MRA had concluded with a recent ischemic stroke in the left superficial middle cerebral territory.

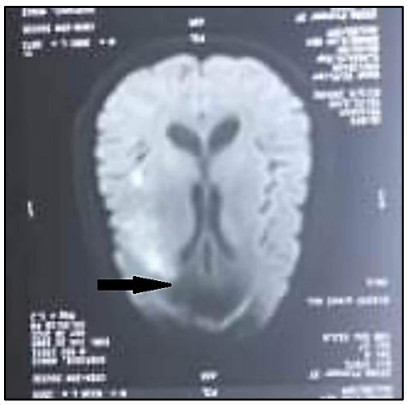


Figure 4: MRI slide showing left superficial middle cerebral ischemic stroke

While the goal of anticoagulation was achieved, the patient's neurological condition worsened around the 7th day of treatment, with a GCS of 12/15, with the onset of left hemiparesis. A cerebral CT scan confirmed the presence of an ongoing ischemic stroke in the territory of the right superficial middle cerebral artery. The contralateral first stroke showed a stable appearance without hemorrhagic transformation. Given the multiplicity of thromboses and their unusual anatomical location, especially in the abdomen, further investigation was conducted to identify a systemic origin.

The etiological work-up included a thorough physical examination, which did not reveal any vascular abnormalities upon auscultation of various vascular axes. Ophthalmological examination yielded normal results. Tests for rheumatoid factor RF, anti-cyclic citrullinated peptide (anti-CCP) antibodies, and

cryoglobulinemia were negative. The levels of complement components C3 and C4 were within the normal range. Proteinuria was absent in the 24-hour urine sample. Serological tests for viral hepatitis B and C, syphilis, and HIV were negative. Protein C, protein S, and antithrombin III levels were normal. Furthermore, there was no indication of resistance to activated protein C or the presence of the factor V Leiden mutation.

The activated partial thromboplastin time was not prolonged, and levels of fibrinogen and homocysteine were within the normal range.

The immunological work-up found:

- aCL antibody: IgM positive at 93 MPL/ml, IgG negative; IgA negative.
- aB2GPI antibody: IgM positive at 133 IU/ml, IgG negative; IgA negative.
- LA: positive.
- Anti-nuclear antibodies; anti-native DNA; anti-neutrophil cytoplasm negative.

Biological control at 12 12-week intervals still found positive aCL, thus the diagnosis of primary APLS was retained.

Given the rapidity and multiplicity of thrombotic events, the diagnosis of CAPS was retained. The patient is currently on warfarin (INR=3) and Atorvastatin 40mg with a good clinical evolution: GCS: 15/15; regression of neurological deficit and dysarthria. No new thrombotic events were noted.

DISCUSSION

APS is now recognized as the most common cause of acquired thrombophilia (4). APS is a thrombogenic autoimmune disorder whose pathophysiological mechanisms are not yet well understood. In vitro studies have shown that antiphospholipid antibodies (aPL) have pro-thrombotic properties and effects on platelet activation (2).

APS is defined by the combination of at least one clinical and at least one biological criterion among those listed in Table 1, persisting at least 12 weeks. (5,6)

Table 1: APLS diagnostic criteria

Clinical criteria	Biological criteria
Arterial or venous thrombotic events obstetric events: * Unexplained fetal loss after 10 weeks' gestation, * Premature delivery before 34 weeks' gestation * at least 3 unexplained early spontaneous miscarriages (before 10 weeks' gestation).	Presence of lupus anticoagulant (LA) IgG and/or IgM anticardiolipin antibodies (aCL), or IgG anti-beta 2 glycoprotein I (b2GP1) antibodies and/or IgM, confirmed at 12-week intervals. aCL and ab2GP1 by ELISA above the 99th percentile.

A literature review found publications of case reports or small case series, given the rarity of this condition. We chose to focus on the international registry, or "CAPS registry". The following table summarizes the epidemiological and clinical characteristics of these observations in the chronological order of their appearance.

The immunological work-up of our patient is marked by a triple positivity: IgM-positive anti-cardiolipin antibodies at 93 MPL units; IgM-positive anti-beta 2-glycoprotein I antibodies at 133 MPL units, and the presence of anticoagulant lupus.

Table 1. Review of the literature on the CAPS registry

Author/references	Year	Number of cases	Epidemiological and evolutionary criteria
Asherson RA (7)	1992	10	90% Females, mean age = 39years, 60% primary APLS, 30% SLE, organ involvement: 50% cerebral, 50% cardiac, 50% pulmonary, 60% abdominal, 50% skin, mortality =40%
Asherson RA (5)	2003	50	66% Females, mean age = 37years, 56% Primary APLS, 30% SLE, precipitating factor 22%, mortality50%
Cervera R (8)	2005	220	69% females, mean age = 38years, organ involvement: renal 70%, pulmonary 66% cerebral 60% cardiac 52% skin 47%, mortality 48%
Rodriguez-pinto I (9)	2016	500	69% females, mean age = 38years, 75% SLE, precipitating factor 65%, mortality 37%
Lopez-Benjume B (10)	2022	584	39 cases (6.7%) treated with eculizumab, first intention treatment in 6 cases, palliative 30cases, mortality rate = 5/39

Antiphospholipid syndrome (APS) encompasses both primary APS and secondary APS associated with other systemic diseases. Primary APS affects approximately 0.5% of the population, with a higher prevalence in women: 3.5 women/1man, with an average age of 34 years. It is characterized by arterial thrombosis and recurrent miscarriages. (11)

Secondary APS can occur in the context of various systemic diseases, such as scleroderma, Behçet's disease, Sjögren's syndrome, Dermatomyositis, neoplasia, hematological disorders, coagulation protein deficiencies, infectious diseases, or because of certain medications such as Phenothiazines (chlorpromazine, hydantoins), beta-blockers, interferon alpha, quinidine.

In our patient, no clinical or biological criteria for SLE were found. C3 and C4 supplements were normal. NAA, native anti-DNA, and neutrophil cytoplasm tests were negative. Serologies for hepatitis B and C were negative. Similarly, the tests for RF and Cryoglobulinemia were negative. The APTT was not prolonged. Biological control at a 12-week interval still found aCL, ab2GPI, and LA positive, thus the diagnosis of primary APS was retained.

Catastrophic antiphospholipid syndrome (CAPS), also known as Asherson syndrome, is a rare but severe manifestation of APS. While it affects less than 1% of APS patients, the number of reported cases has significantly increased over the years. In Tunisia, six cases of CAPS have been documented. CAPS is characterized by the simultaneous occurrence of multiple microcirculatory thromboses, often leading to multivisceral failure. Arterial or venous macro thrombosis can sometimes be associated (3,12).

In fact, it is the rapidity and multiplicity of thrombotic events that differentiate CAPS from classic SAPL (12). It can be distinguished from classic APS by the rapidity and multiplicity of thrombotic events. However, the rarity of CAPS poses challenges in systematic study and conducting randomized clinical trials. The CAPS Registry, comprising 1205 registered patients, provides valuable clinical, laboratory, and therapeutic data. CAPS predominantly affects young individuals, with a mean age of 38 years,

and women account for 69% of cases (13). It occurs equally in primary APS and APS associated with other autoimmune diseases, particularly systemic lupus (5). CAPS can also serve as an initial presentation of APS in approximately 50% of cases (14). Our case involved a primary CAPS in a 55-year-old man.

The clinical manifestations of catastrophic antiphospholipid syndrome are influenced by four factors: microcirculatory involvement, systemic inflammatory response syndrome (SIRS) manifestations, activation of coagulation inhibitors and lysis, and complement activation.

Thrombus development and the risk of recurrent thrombotic events are associated with high levels of lupus anticoagulant (LA) and anticardiolipin antibodies (aCL). CAPS can affect multiple organs, with renal involvement being the most common (73% of cases), often presenting as lumbar pain, fever, acute renal failure, proteinuria, hypertension, and microscopic hematuria (15). Our patient presented with bilateral low back pain and microscopic hematuria. The CT scan showed multiple foci of infarction in both kidneys, with a direct image of a clot in the left renal artery.

Neurological damage is also frequent, leading to encephalic suffering (40% of the cases), vigilance disorders, confusion, headaches, or seizures. Similarly, constituted cerebral microinfarcts were observed in 40% of cases (13). Our patient presented a confusional syndrome and two ischemic strokes in the territory of the superficial middle cerebral artery on each side.

Cardiac manifestations may include heart failure (44% of the cases), myocardial infarction (30%), valvulopathy (10%), intracardiac thrombi, and/or Libman-Sacks endocarditis (16). In our patient, 3 thrombi were found in the left atrium, one of which was floating.

Pulmonary manifestations such as acute respiratory distress syndrome (26%), intra-alveolar hemorrhage (12%), and pulmonary Edema (8%) can occur (13). Abdominal and digestive manifestations are less common (10%), with liver failure (9%) and jaundice (7%) observed in some cases (13,17–22). Our patient had hepatic cytolysis (5×normal values), CT scan showed splenic infarction and a clot pattern in the superior mesenteric artery.

Vascular thromboembolic events, including deep vein thrombosis (69%) and pulmonary embolism (26%), are common systemic manifestations (13). In our patient, the involvement was purely arterial.

Skin involvement (50% of the cases) can manifest as reticular livedo, acrocyanosis, skin necrosis, ischemic gangrene, and sub-nail hemorrhage (23). In our patient, no skin involvement was noted.

Infections, discontinuation or modification of antithrombotic therapy, surgery, and pregnancy can precipitate CAPS.

The biological disturbances include both long-lasting abnormalities associated with APS and non-specific abnormalities concurrent with the acute microangiopathy, such as thrombocytopenia <100,000/mm3 (46%), mechanical hemolytic anemia (35%), and signs of disseminated

intravascular coagulation (15%) (19,20). In the reported patient, there were no findings of anemia or thrombocytopenia.

Triggers have been identified in approximately 65% of cases, with the most common trigger being infection. Other triggers include surgical procedures or trauma, withdrawal of anticoagulation medication, SLE flares, and oral contraceptive drugs (13). CAPS should be differentiated from a thrombotic storm occurring outside of APS.

In the absence of histological evidence of vascular occlusion, our patient met the criteria for probable de novo CAPS. It was indicative of APS, and no triggering factors were found. Preliminary Classification Criteria for Catastrophic Antiphospholipid Syndrome are: (23,24)

- Evidence of involvement of three or more organs, systems, and/or tissues
- Development of manifestations simultaneously or in less than a week
- Confirmation by histopathology of small-vessel occlusion
- Laboratory confirmation of the presence of antiphospholipid antibodies

Regarding CAPS treatment, the grades of evidence are quite low in the absence of clinical trials, due to the extreme rarity of the syndrome. The gold standard treatment for catastrophic antiphospholipid syndrome (CAPS) is the "Triple Therapy" approach. It consists of three main components:

1. Anticoagulation: Intravenous heparin is administered during the acute phase, followed by long-term oral anticoagulation to prevent further blood clot formation.

2. Corticosteroids: High-dose intravenous methylprednisolone followed by oral prednisone is used to reduce inflammation and modulate the immune response.

3. Intravenous Immunoglobulin (IVIg) or Plasma Exchange: IVIg is the first-line treatment for critically ill patients, while plasma exchange may be used to remove antiphospholipid antibodies and procoagulant factors.

In refractory cases, additional therapies such as rituximab and eculizumab may be considered. However, evidence is still scarce, and there are only anecdotal case reports.

Treatment should also address any underlying factors contributing to CAPS. Overall, a multidisciplinary approach and individualized management are crucial for the successful treatment of CAPS. (9,25–31)

CAPS is associated with high morbidity and mortality. Overall mortality during the acute phase is close to 37% [8]. Short-term mortality is associated with the presence of neurological, cardiac, or pulmonary involvement, associated systemic lupus, and, above all, the absence of anticoagulant treatment. The prognosis of CAPS remains severe in the long term, with a 1-year mortality of around 34% (23).

Prevention of CAPS is essential and relies on adequate management of the perioperative period

when surgery cannot be avoided, prompt treatment and prevention by vaccination of infections, and education of patients with APS, particularly in the management of oral anticoagulants (27). Studies agree on the effectiveness of very prolonged anticoagulation.

Associated risk factors for thrombosis and atherosclerosis must be controlled. In our patient, he received dual therapy in the acute phase: UFH at PSE combined with methylprednisolone (1mg/kg/d) followed by a relay with warfarin. The aim was to achieve an INR close to 3 with a good clinical outcome. No new thrombotic events were noted.

CONCLUSION

In conclusion, catastrophic antiphospholipid syndrome (CAPS) is a rare and severe manifestation of antiphospholipid syndrome (APS) characterized by the rapid onset of multiple thrombotic events, often involving the microcirculation. CAPS can affect various organs and systems, leading to significant morbidity and mortality. It is essential to recognize the clinical features of CAPS promptly and differentiate it from classic APS or other thrombotic conditions.

Further research and clinical studies are needed to improve our understanding of CAPS, enhance early diagnosis, and identify more effective treatment strategies. Collaborative efforts among healthcare professionals, researchers, and patients are essential for advancing knowledge and improving the management and outcomes of CAPS patients.

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Generative AI use: An AI program (DeepL write) was used for linguistic correction and improving the coherence of the manuscript.

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Inspiratory dyspnea revealing a base of tongue abscess: a case report

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Abstract

Background: A base of tongue abscess is a rare but serious condition that can compromise vital prognosis due to upper airway obstruction and the septic syndrome it may cause.

Case presentation: **This case is about a** 62-year-old diabetic woman who presented with inspiratory dyspnea in the context of fever. On examination, she showed signs of respiratory distress, with an oxygen saturation of 78%, submandibular and supraclavicular retractions. Due to the impossibility of intubation, a tracheotomy was performed. Radiological exploration revealed an abscess at the base of the tongue, exerting a mass effect on the upper airways. The patient underwent endoscopic drainage of the abscess and was treated with cefotaxime, gentamicin, and metronidazole. After stabilization, the dental origin of the abscess was confirmed.

Conclusion: A base of tongue abscess is a diagnostic and therapeutic emergency to preserve vital prognosis.

Keywords: Abscess, Tongue, Dyspnea, Tracheotomy, Case Report

INTRODUCTION

A tongue abscess (TA) is an uncommon yet potentially severe condition because it can lead to airway obstruction. The tongue's unique anatomical, vascular, and muscular makeup, along with the natural antibacterial properties of saliva, play a role in its susceptibility to infection, play a key role in preventing infections. However, certain factors, such as the presence of foreign bodies or immunosuppression, can increase susceptibility to this infection. After respiratory stabilization, a cervical and facial CT scan was performed, revealing a hypodense mass measuring 45x37x35 mm at the base of the tongue, laterally shifted to the right, exerting mass effect on the airway, leaving a small patent opening. The mass did not enhance after contrast injection and was

thick wall that took up the contrast. These scan findings were consistent with a diagnosis of a base of tongue abscess. (Figure 1).

Tongue abscesses typically occur as a single, localized lesion in the front two-thirds of the tongue. However, abscesses in the posterior region, including the tongue's base, are often linked to conditions like infections of the lingual tonsils, infected thyroglossal duct cysts extending to the base, ectopic thyroid glands, or infections that spread from the roots of the upper molars. [1].

Abscesses at the base of the tongue demand special attention due to the risk of rapid respiratory failure. This condition can be life-threatening, as swelling in the tongue can quickly block the airway [2].

The available literature on this topic is primarily in the form of case reports, and the number of patient series remains limited. In this study, we present a rare case of acute dyspnea revealing a base of tongue abscess.

CASE PRESENTATION

This is a 62-year-old diabetic woman on insulin, brought to the emergency department by civil protection for progressively worsening inspiratory dyspnea over the past 24 hours in the context of fever.

Her medical history dates back one week, marked by the onset of febrile odynophagia, for which she was prescribed amoxicillin (3g/day) and Solumedrol (60mg/day). Initially, there was improvement in her symptoms, followed by a secondary deterioration. The patient became aphagic, with changes in her voice and the onset of inspiratory dyspnea, first with exertion, then at rest (without any history of foreign body aspiration).

On examination, the patient was agitated, cyanotic, tachypneic, with muffled speech, and febrile at 39°C. She exhibited inspiratory dyspnea with submandibular, suprasternal, and supraclavicular retractions. The respiratory rate was 40 cycles per minute, oxygen saturation in ambient air was 78%, blood pressure was 110/56 mmHg, and heart rate was 112 beats per minute. Pulmonary and cardiac auscultation were normal, and the Glasgow Coma Scale score was 13/15. The oropharyngeal and oral cavity examination showed no obstructive signs, only simple pharyngitis. The patient had poor oral hygiene.

Laboratory results revealed metabolic acidosis (pH=7.23; pCO2=60mmHg, HCO3=25; pO2=55mmHg), with a significantly elevated inflammatory marker (CRP=240g/L; 18,600 white blood cells/mm³). Blood glucose was 2.8g/L. Liver and renal function tests, as well as a chest X-ray, were normal.

Given the imminent respiratory distress, the patient was placed on non-invasive ventilation. However, her oxygen saturation did not improve, and the signs of inspiratory distress persisted. We decided to intubate the patient. During intubation, we observed an

inflammatory mass at the base of the tongue obstructing the pharyngo-laryngeal pathway. Due to the inability to intubate, we performed a surgical tracheotomy under general anesthesia between the second and third tracheal rings.

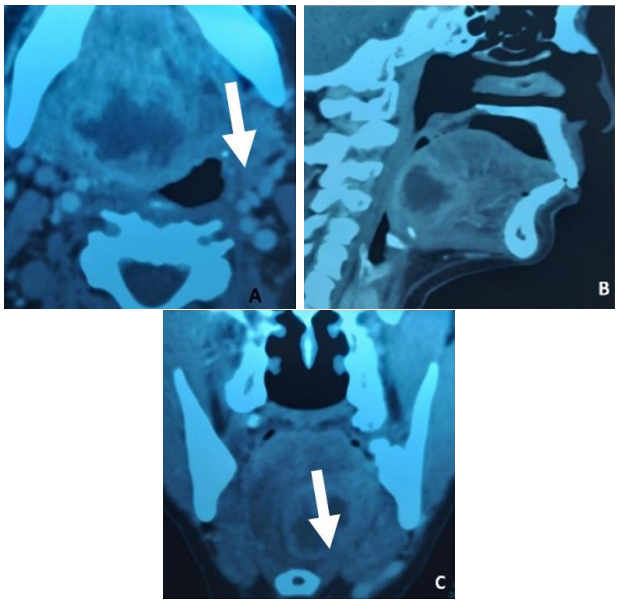

Figure 1: Cervicofacial CT scan with contrast injection; A: Axial section; B: Sagittal reconstruction; C: Coronal reconstruction.

An endoscopic drainage of the abscess was performed under general anesthesia. After puncturing the prominent area and collecting a sample for bacteriological examination, the abscess was flattened and drained.

Postoperatively, the patient was placed on intravenous antibiotics including cefotaxime (2g three times a day), gentamicin (160mg/day for 5 days), and metronidazole (500mg three times a day). The tracheostomy tube was removed after 48 hours, following an endoscopic assessment of the pharyngeal-laryngeal airway.

The bacteriological examination did not reveal any specific microorganism, while the histopathological examination concluded with a non-specific inflammatory reaction without evidence of epithelioid granuloma, caseous necrosis, or tumor cells.

The patient's progress was marked by gradual improvement of the odynophagia, resolution of the fever, stabilization of respiratory status, normalization of inflammatory markers, and stabilization of blood glucose levels. The patient remained on intravenous antibiotics for one week, followed by oral amoxicillin-clavulanic acid (3g/day) for an additional week. The dental origin of the tongue abscess was confirmed following a dental examination.

DISCUSSION

Tongue abscesses (TA) are relatively rare conditions in healthy individuals but are more commonly seen in those with compromised immune systems. This phenomenon can be attributed to the natural resistance of the tongue to infections, despite its constant exposure to various pathogens. The tongue has several defense mechanisms that play a crucial role in preventing infections. Among these mechanisms, the continuous mobility of the tongue helps facilitate its self-cleansing through saliva. Additionally, its thick, keratinized mucosa acts as an effective barrier against microorganisms. The muscle tissue of the tongue ensures a rich blood supply, which helps maintain proper immune function. Finally, the tongue benefits from an extensive lymphatic network and immune properties present in the

saliva, further enhancing its resistance to infections [3].

However, when these defense mechanisms are impaired, especially due to factors such as trauma, the presence of foreign bodies, or conditions related to immunodeficiency, the risk of infection and, consequently, the development of a tongue abscess significantly increases. Tongue abscesses can then form, affecting not only the structure of the tongue but also the overall well-being of the patient. A weakened immune defense allows bacteria or other pathogens to more easily infiltrate the tissues, leading to localized, sometimes severe infections.

The location of the abscess also plays a determining role in understanding its cause. Abscesses located in the anterior two-thirds of the tongue, also referred to as the "oral tongue," are typically unilateral and are frequently associated with direct trauma, such as accidental bites or injuries from sharp objects like fish bones. These infections often result from breaks in the mucosa, allowing bacteria to infiltrate the tissues. In contrast, abscesses in the posterior part of the tongue, particularly at the base, are often linked to infections of the lingual tonsils, infected thyroglossal duct cysts, or the spread of infections from the roots of the upper molars. These abscesses can be more challenging to diagnose due to their deeper location and potential to cause airway obstruction [4].

The diagnosis of TA relies on identifying specific characteristic symptoms. Patients often complain of painful swelling, difficulty swallowing, changes in voice, and localized tongue pain. High fever and inspiratory dyspnea can also be significant clinical signs. In severe cases, where airway obstruction is imminent, a tracheotomy may be required to restore normal breathing [5, 6]. A thorough clinical examination, including palpation, is essential for detecting the presence of an abscess, especially in the posterior region of the tongue, where these abscesses are harder to detect visually.

Several differential diagnoses must also be considered when a lingual abscess is suspected. These conditions include tumors, cysts, hematomas, hormonal disorders such as hyperpituitarism or hypothyroidism, anomalies like lingual thyroid, and conditions associated with ectopic lymphoid tissue [5]. To properly evaluate a tongue abscess, various imaging techniques can be used, such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). Ultrasound, although useful for differentiating abscesses from other vascular lesions, can be challenging to perform, particularly with an intraoral probe. Typically, a lingual abscess will appear as a hypoechoic lesion surrounded by a hyperechoic ring on ultrasound [5]. CT scans are particularly effective in visualizing abscesses in the posterior region of the tongue and in distinguishing external lesions from the tongue musculature [7]. MRI, on the other hand, provides excellent soft tissue resolution and is ideal for assessing the tongue and floor of the mouth, allowing for better observation of inflammatory processes

that appear as solid or cystic areas on radiological images [1].

The treatment of tongue abscesses requires several key steps, primarily ensuring the patency of the airways. If airflow is compromised, drainage must be performed. This can be done either through needle aspiration or surgical incision. If carcinoma is suspected, a biopsy of the abscess wall should be performed to rule out malignancy. It is important to note that aspiration alone is insufficient, and proper drainage must follow [1]. Abscesses smaller than 1 cm in size may sometimes be managed with medical treatment alone, without the need for surgical drainage [8]. Antibiotic therapy should be guided by Gram staining results and culture of the abscess drainage. Empirical treatment should target oral streptococci and anaerobic Gram-negative bacteria. Given the increasing resistance of certain Bacteroides strains to penicillin, alternative antibiotics such as clindamycin, ampicillin/clavulanic acid, or a combination of penicillin and metronidazole may be used. Once the patient's clinical condition stabilizes, a comprehensive dental evaluation is crucial to address any underlying dental infections that may have contributed to the development of the abscess [9].

In conclusion, while rare, tongue abscesses require prompt and appropriate management to prevent severe complications, including respiratory obstructions and systemic infections.

CONCLUSION

Lingual abscess is a rare infection that should be suspected in cases of acute tongue swelling. Delays in treatment may jeopardize the patient's life. Early treatment, including antibiotic therapy and abscess drainage, is crucial to prevent the risk of fatal asphyxiation.

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