The challenge in diagnosing human rabies: A case report

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Abstract

Introduction

Rabies is a zoonotic disease caused by a neurotropic virus of the Lyssavirus genus. Human rabies can manifest in either encephalitic (furious) or paralytic (dumb) forms. The diagnosis is still challenging and often delayed. Viral infection must be considered and treated soon after viral transmission; failure to diagnose and intervene will usually result in disease progression and death.

Case presentation

We report a case of a 61-year-old female, with no past medical history, who visited the Emergency Department (ED) initially for sleep disorders, restlessness, anxiety, refusal of food and watery disgust. The investigations were normal, and the patient was discharged with symptomatic treatment. Her condition worsened after 24 hours, and she presented a cardiac arrest. After resuscitation and return of spontaneous circulation, her physical exam was without abnormalities. Laboratory exams and imaging investigations were normal. The diagnosis was a severe septic shock, treated with empirical antibiotics. A multiple organ failure syndrome has rapidly appeared, and the outcome was fatal.

Upon re-interviewing the family, it turned out that the patient was raising around 20 cats and that she was a victim of an accidental bite by one of her cats 3 weeks before admission. No medical advice was sought, and the family reported a completely healed wound. The patient did not receive any vaccination or serotherapy. Rabies serology came back positive. The diagnosis was confirmed after brain biopsy.

Conclusion

Human rabies is a challenging disease, with a complex neuropathogenic mechanism. The infection can be treated after recognized exposures. However, medical management, once the clinical disease develops, has almost universally proved to be unsuccessful, resulting in fatal outcomes.

Keywords: Encephalitis, Rabies, Diagnosis, Challenge.

INTRODUCTION

Rabies is a zoonotic disease caused by a neurotropic virus of the Lyssavirus genus. The virus is transmitted from animals to humans by bite, scratch or direct exposure of mucosal surfaces to saliva from an infected animal (1). Human rabies can manifest in either encephalitic or paralytic forms (2). The clinical stages are incubation, prodrome, acute neurological signs, coma, and inevitable death. The diagnosis is still challenging and often delayed, particularly the paralytic form (3).

Infection with the virus must be considered and treated soon after viral transmission; failure to diagnose and to intervene will usually result in disease progression and death (2).

We report a case of a patient who presented to the Emergency Department (ED) with a .

Observation

A 61-year-old female with no past medical history presented to our ED for sleep disorders, restlessness, anxiety, refusal of food, and watery disgust for two days. On admission, the patient was agitated, and the laboratory investigations were normal. Due to the pandemic context of COVID-19, a PCR test was performed and was negative. A brain and chest CT scans were normal. The patient was discharged with symptomatic treatment.

After 24 hours, her condition worsened; she had abdominal pain, and her consciousness altered. Upon arrival, the patient presented with cardiac arrest resuscitated within two minutes. After the return of spontaneous circulation, the physical examination found a normal temperature, blood pressure was 100/58 mmHg with 1mg/h of adrenaline, no peripheral signs of shock and normal respiratory parameters. No neurological signs were noted. The ECG did not show arrythmias or electrical signs of myocardial ischemia. Initial diagnosis was septic shock. The patient received empirical antibiotic therapy, catecholamine. Cerebrospinal fluid analysis was performed and was normal. Faced with the absence of an obvious cause for the cardiorespiratory arrest, shock, and initial agitation, a toxicological assessment was requested and was negative. On the fifth day of hospitalization, the patient presented multiple organ failure and death.

Upon re-interviewing the family, it turned out that the patient was raising around 20 cats and that there was the notion of an accidental bite by one of her cats 3 weeks before admission. No medical advice was sought, and the family reported a completely healed wound. The patient did not receive any vaccination or serotherapy. Rabies serology came back positive, and the diagnosis was confirmed after brain biopsy.

DISCUSSION

Rabies is a neurotropic RNA virus transmitted to humans through the saliva of infected animals, usually from bites (4). The virus is almost invariably fatal after the onset of neurologic symptoms (2). The rabies virus reaches the brain by centripetal propagation

mediated by retrograde trans-neuronal transfer and the clinical stages of rabies are incubation, prodromes, acute neurological signs, coma, and death (3). The incubation period or eclipse phase can vary from weeks to years but lasts 1-3 months on average (5). The cause of this variation is probably multifactorial including the site of virus entry and the viral load, the species and strain of the infecting virus, and the immunological competence of the host (6). Nonspecific prodromal symptoms include malaise, headache, fever, anxiety, and agitation. Paresthesia, pain, and pruritus are the earliest neurologic symptoms (5). Two classical forms of rabies are generally recognized: furious (also called encephalitic) which develops in approximately 80% of cases, and paralytic, which occurs in approximately 20% of cases. The predicting factors associated with the development of either form remain unclear (7,8). Specific symptoms are described in each form. However, case definition can typically be established with certainty only when the disease reaches the acute neurological phase (6). The paralytic form of disease differs from the encephalitic form in that muscle weakness develops early, whereas progression to coma and death often take longer than with the encephalitic form (3). In our case, the patient presented with signs and symptoms that commonly occur in the encephalitic phase of rabies, including agitation, hyper-excitability, and hydrophobia.

Infection with rabies virus can be difficult to diagnose ante-mortem (3). Hydrophobia is the most characteristic and no clinical signs of disease are pathognomonic for rabies (9). Given that the differential diagnosis for altered mental status is broad (reflecting impairment of affect, behavior, or cognition), the workup should start with reversible and life-threatening causes as recalled by use of the mnemonic “rule-out the WHIMPS.” Each letter of this acronym signifies 1 or more of the following conditions: Wernicke encephalopathy, hypoglycemia, hypoxia, hypoperfusion of the central nervous system, and hypertensive encephalopathy, infections and intracranial processes, metabolic derangements (such as hyponatremia/ hypernatremia, hypocalcemia/hypercalcemia, and hyperammonemia), poisons, and seizures. The workup should start with taking a history, looking for clues to etiology and to temporal relation-ships with symptoms, and then proceed to a thorough physical examination and laboratory testing (an electrocardiogram, a complete blood count, a comprehensive metabolic panel, a toxicology screen, as well as measurement of levels of B12, ammonia, and thyroid-stimulating hormone, and a radiologic examination for intracranial lesions via computerized tomography or magnetic resonance imaging, a chest x- ray, and a urinalysis). Further diagnostic tests (such as electroencephalography and cerebrospinal fluid exam) may also be considered. In the appropriate setting (fever, flulike symptoms, or cerebrospinal fluid inflammation), microbiologic assays (spirochetes) would be recommended. In patients with a longer duration of altered mental

status symptoms, neuro-psychologic testing and functional imaging may be ordered. In addition to pursuing potential medical and neurologic etiologies, psychologic ones must be investigated (5). In our case, there was no reported history of bite or scratch, and the symptoms were not specific.

The management of clinical rabies in nonvaccinated patients is largely palliative, and death is invariably expected (2). The onset of rabies clinical symptoms, and death can be prevented by adequate post-exposure prophylaxis (PEP) including vaccines and, if required, rabies immunoglobulin (RIG) (9).

CONCLUSION

Human rabies is considered as a disease of complex neuropathogenic mechanisms and challenging diagnosis. The infection can be treated after recognized exposures; however, medical management once the clinical disease develops has almost universally proved to be unsuccessful, resulting in fatal outcomes.

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