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CASE REPORT

Diagnosis and management of rabies encephalitis in two patients in northwest Africa: A case series

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Abstract

In persons bitten by a stray dog, prompt administration of post-exposure rabies vaccination, anti-rabies immunoglobulin, and wound care can save lives. However, rabies is often fatal once the patient develops signs and symptoms. Here, we describe two fatal cases of rabies following a long delay after dog bites.

KEYWORDS

case series, hydrophobia, rabies, stray dogs, West Africa

1 | INTRODUCTION

Rabies is an acute encephalomyelitis caused by ribonucleic acid (RNA) virus belonging to the *Lyssavirus* genus, *Rhabdoviridae* family.¹ About 99% of the transmission of the virus to humans are due to the breach of the skin-mucosal barrier by biting, scratching, or licking of infected animals, most often dogs.² Human-to-human transmission is rare.³

Rabies is a zoonosis that continues to be an important public health problem in many developing countries.^{4,5} Today, it is still considered a neglected tropical disease despite the fact that it causes more than 59,000 human deaths each year in the world, particularly in Asia and Africa, where more than one-third of annual human deaths due to rabies occurs in each of these continents (>20,000 deaths in

India alone and >20,000 in West and Central Africa), as well as in the Middle East (reliable data not available).^{6–10} Once declared clinically, it is inevitably fatal.^{4,5} In most of Africa, especially in West and Central African countries, rabies notification is not mandatory, and epidemiological data are scarce.^{9–11} In Mauritania, enzootic rabies, which is known to have existed for a very long time, periodically affects animals and humans. Cases of death have been reported on several occasions. The first reported cases occurred in 1963 in Nouakchott (Trarza region). A man died of rabies after a cat bite in the throat, and a woman died of rabies after a dog bite.¹² Since then, sporadic cases of human rabies have been reported in Mauritania in 1967, 1968, 1973–1975, and 1980.¹² None of these cases have been confirmed with laboratory diagnosis. We report two cases of rabies encephalitis occurring after being bitten by stray dogs.

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2 | CASE PRESENTATION

2.1 | Case 1

A 65-year-old man residing in a rural town of Tintane, southern Mauritania, consulted at the Kiffa Hospital Center on December 2, 2018, for hiccups and hydrophobia. Recent past history of the patient suggested no significant medical problem, except for a scar from a bite by a stray dog on the palm of the right hand that occurred on October 9, 2018. Immediately after the bite, the patient washed the wound with soapy water and did not seek any medical treatment. Two months later, on December 2, 2018, he started complaining of headache, fever, and hiccups which required consultation at the health center of Tintane, where diagnosis was not established. The symptomatic treatment he received (paracetamol, i.e., acetaminophen) did not have any effect on his symptoms. Faced with the appearance of anxiety and agitation, the patient was referred to the Kiffa Hospital Center, a regional tertiary hospital. On admission, the patient was agitated and had hydrophobia, pharyngeal spasms, muscle contracture, and sialorrhea since 24 h. The values for routine clinical laboratory tests, including routine hematological examination (hemoglobin, complete blood count) and blood chemistry (blood glucose, blood urea nitrogen, creatinine, electrolytes, liver function tests), were within normal range. The diagnosis of rabies encephalitis was made on the basis of the typical clinical presentation. A laboratory confirmation of rabies was not performed due to a lack of technical facilities in the country. A symptomatic treatment based on phenobarbital (10 mg/kg via intravenous [IV] route administered over 15–30 min), diazepam (0.2 mg/kg IV), and paracetamol (15 mg/kg IV every 6 h) was initiated immediately after admission. However, the patient died 2 h after admission to the hospital. The investigation around the case revealed two additional undeclared human rabies cases in the town where the deceased patient came from, possibly due to bites of the same rabid stray dog. We were not able to obtain further information about these undeclared, possible cases of human rabies in Tintane.

2.2 | Case 2

A 13-year-old boy residing in Aioun city, southern Mauritania, was referred from Aioun hospital center on August 19, 2021, for better management of hyperthermia and psychomotor agitation. Past medical history indicated that a stray dog bit the patient on the left cheek and chest 3 weeks earlier (July 31, 2021). On admission, a scar at the site of the bite, restlessness, intermittent spastic

hypertonia, psychomotor agitation, persecutory delirium, fever, hydrophobia, and excessive salivation were observed. These symptoms were reported to occur since 36 h prior to admission. The diagnosis of rabies encephalitis was made based on clinical presentation. Symptomatic treatment (phenobarbital 10 mg/kg slow IV injection over 15–30 min; diazepam 0.2 mg/kg IV; paracetamol 15 mg/kg IV every 6 h) was administered without success. The results of routine clinical laboratory tests (hemoglobin, complete blood count, blood glucose, blood urea nitrogen, creatinine, electrolytes, and liver function tests) were within normal ranges. Due to the typical clinical manifestations of rabies encephalitis associated with a recent history of a dog bite, no other tests were performed to assess neurological manifestations. The patient was discharged against medical advice and died 2 days later. Upon contacting the family members of the deceased patient, it was found that another possible undeclared fatal case of rabies seemed to have occurred after a dog bite in Aioun, but further information was not available.

3 | DISCUSSION

Rabies is one of the deadliest infectious diseases with a 100% case-fatality rate once the signs are declared.^{4,5} In Mauritania, rabies has been known to exist, but reliable epidemiological data on rabies are absent. Many cases of rabies in developing countries are not diagnosed with laboratory confirmation and are often not even reported to health authorities.¹³ Bite victims often do not receive appropriate prophylactic care due to patients' ignorance, lack of awareness among health workers, lack of necessary biological products, or insufficient means to pay the cost of preventive treatment. The affected subjects usually die without appropriate care at home, without diagnosis being made. Even cases diagnosed in hospitals are rarely reported or may be wrongly attributed to other diseases. A careful review of our patients' history and presenting signs and symptoms does not favor a sudden onset of neurological disorders, ruling out diseases such as cerebral malaria, bacterial meningitis, acute encephalitis, or encephalopathy (hypertension), poliomyelitis, poisoning or toxicity (botulism, drugs, organophosphate), metabolic disturbances (hypoglycemia, thiamine deficiency), ischemic or hemorrhagic stroke, and subdural hemorrhage. Other diseases in the differential diagnosis characterized by an insidious onset of neurological symptoms include brain abscess, tetanus, autoimmune or other viral encephalitis, Guillain-Barré syndrome, neurosyphilis, tick paralysis, electrolyte imbalance, amyotrophic lateral sclerosis, diffuse gliomatosis, and lymphoma affecting the central nervous system.

In the two cases observed in our study, both presented hydrophobia, hypersalivation, and a recent history of a dog bite, with or without a visible trace of the bite wound at the time of hospitalization, in addition to other non-specific neurological signs and symptoms. The phase of agitation was quickly followed by coma and death. These characteristic features and poor prognosis helped to orient our diagnosis despite the absence of laboratory confirmation of rabies.

In two human cases of rabies observed in our hospital, the recent history of dog bite was the most important clue for the clinical diagnosis. The patients consulted a medical facility only at the appearance of the first signs of the disease when it is usually too late for treatment to be effective. The population largely remains ignorant of the risk of rabies in Mauritania and elsewhere.¹¹ In the literature, almost all studies conducted in different parts of the world showed that dog is the main vector in Africa, Asia, and Latin America.^{4,5,11,13} The incubation period observed in our two cases was 20 and 55 days, respectively. The incubation was longer in the first patient who was bitten once on the hand. The incubation period in the second patient, a child who was bitten on the cheek and chest, was shorter, probably due to a larger inoculum and the site of injury in richly innervated parts of the body near the brain. Indeed, once the peripheral nerves are infected after an infective bite, rabies virus is transported along the axons, undergoes replication before and also after reaching the brain, and spreads within the nervous system to the salivary glands. Factors such as a shorter distance between the site of the bite (e.g., face) and the brain, smaller body size in children, involvement of richly innervated parts of the body (e.g., hands, neck, face), multiple or deep bites, higher viral load, and virulent viral strains may lead to a shorter incubation time.^{4,5,14}

There are a variety of non-specific prodromal symptoms of rabies, including fever, chills, malaise, fatigue, insomnia, anorexia, headache, anxiety, and irritability, that last up to about 10 days, similar to those of many other viral diseases.⁴ The majority of patients with rabies encephalitis develop hydrophobia, a sign strongly suggestive of rabies, as in our patients. Initially, patients experience pain in the throat or difficulty in swallowing. Subsequently, during attempts to swallow, they experience contractions of the diaphragm and accessory muscles on inspiration. There may be associated features including twitching of neck muscle, vomiting, cough, grimacing, and seizures.^{4,5} In addition to these signs and symptoms which are often observed in cases of human rabies, complications may develop. These include cardiac (arrhythmias, heart failure, hypotension), pulmonary (pneumonia, respiratory failure), gastrointestinal

(hemorrhage), and endocrinal complications.⁵ During the short hospitalization of our two cases until death, complications were not observed.

There is no effective treatment for rabies. In the literature, it has been reported that few patients survived after intensive care,^{5,14} but rabies is almost always fatal after the onset of symptoms. Despite the poor prognosis, immediate treatment that should ideally be administered before the onset of symptoms includes wound care, post-exposure vaccination and, if available, anti-rabies immunoglobulin injected around the site of the bite, in addition to symptomatic and supportive therapy.^{5,14-16} In our two patients, bite wound had healed by the time they were admitted to our hospital. Symptomatic treatment was immediately administered to our patients but had no obvious beneficial effect. In our two patients, the post-exposure vaccination was not administered due to ignorance of the risk of rabies and because anti-rabies vaccination is generally not accessible in the country. Moreover, anti-rabies immunoglobulin is not available in the country.

Inadequate knowledge about the risk of dog bites in the general population and medical personnel, unavailability or difficulty in accessing anti-rabies vaccine and immunoglobulins for pre- and post-exposure prophylaxis, the absence of vaccination program for animals that come in close contact with humans, lack of population control measures for stray dogs, the absence of advanced diagnostic capacity, and lack of well-defined national guidelines and policy concerning rabies have been pointed out as major challenges ahead to control rabies in Mauritania and elsewhere in the world.^{2,4,11,17-20} Although there is no specific treatment for rabies at present, effective tools and preventive measures are available.²¹ Coordinated efforts and policies are required to control and considerably reduce the prevalence of this neglected zoonosis, at least the dog-to-human rabies transmission. Our case series suggests that prompt management and increased knowledge about the risks of dog bites are the key to prevent the progression of rabies infection.

AUTHOR CONTRIBUTIONS

Boushab Mohamed Boushab drafted the manuscript and made substantial contributions to study conception and design and clinical data verification. Hacen Ahmed Benane, Sidi El-Wafi Baba, and Leonardo Basco contributed to writing and editing the manuscript. All authors have read and approved the final manuscript.

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None.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

None.

CONSENT

Written informed consent was obtained from the immediate family members of the deceased patients (the spouse as well as the brother of Case 1 and the parents of Case 2) to publish this report.

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