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PEDIATRIC HUMAN RABIES IN FEZ, MOROCCO: EPIDEMIOLOGICAL, CLINICAL, DIAGNOSTIC AND INTENSIVE CARE FEATURES OF FOUR FATAL CASES

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ABSTRACT

Background: Human rabies is a vaccine-preventable zoonosis that is almost invariably fatal once neurological symptoms appear. Children remain vulnerable where dog-mediated transmission persists. This study describes the epidemiological circumstances, clinical presentation, diagnostic findings, intensive care management and outcomes of pediatric rabies cases admitted to a tertiary hospital in Fez, Morocco.

Methods: We conducted a retrospective descriptive case series of patients aged 15 years or younger admitted to the Mother-and-Child Intensive Care Unit of Hassan II University Hospital, Fez, from 1 January 2018 to 31 December 2025. Data were extracted anonymously from medical records.

Results: Four male patients aged 11–15 years (mean, 13.3 years) were included. Three exposures (75%) occurred in rural areas. All were category III exposures caused by non-domestic dogs of undocumented vaccination status; three patients had transdermal bites and one had ocular/nasal mucosal exposure. Furious rabies occurred in three patients and paralytic rabies in one. Hydrophobia was present in three patients and autonomic manifestations in all four. Saliva and nuchal skin biopsy PCR were positive in all three patients tested. No patient had documented wound cleansing or appropriate post-exposure prophylaxis (PEP). All required mechanical ventilation and all died, after intensive care stays of 3 to 10 days.

Conclusion: This small series highlights missed opportunities for prevention after severe exposures. Immediate wound cleansing, prompt and complete PEP, access to rabies immunoglobulin, community education and sustained dog vaccination are essential to prevent pediatric rabies deaths.

Keywords: Human rabies; Child; Post-exposure prophylaxis; Intensive care; Morocco; Dog-mediated rabies.

1 INTRODUCTION

Rabies is a viral zoonosis caused by lyssaviruses and transmitted to humans mainly through the saliva of infected mammals, most commonly dogs. Infection can follow a bite, a scratch or contamination of broken skin or mucous membranes. Once clinical neurological disease develops, rabies is almost invariably fatal; however, timely and complete post-exposure prophylaxis (PEP) can prevent the disease [1–3].

The burden of dog-mediated human rabies remains concentrated in Africa and Asia. Children are particularly vulnerable because of their frequent contact with dogs, their difficulty in reporting exposures and their dependence on adults to obtain timely care [2,4]. In Morocco, rabies remains a public-health concern, and a regional study has described the challenges of PEP delivery, particularly among the rural population [5].

Clinical disease may present as furious encephalitis or as a paralytic syndrome. Hydrophobia, aerophobia, behavioural changes, dysautonomia, respiratory failure and cardiovascular complications may occur. Ante-mortem diagnosis requires an appropriate combination of clinical and exposure history with laboratory testing; repeated saliva sampling and nuchal skin biopsy can support virological confirmation [6–8].

The objective of this study was to describe the epidemiological circumstances, clinical and diagnostic features, intensive care management and outcomes of pediatric human rabies cases admitted to the Mother-and-Child Intensive Care Unit of Hassan II University Hospital, Fez, Morocco, between 2018 and 2025.

2 MATERIAL AND METHODS

2.1 Study design and setting

This retrospective descriptive case series was conducted in the Mother-and-Child Intensive Care Unit of Hassan II University Hospital, Fez, Morocco. The study covered the period from 1 January 2018 to 31 December 2025 (eight calendar years).

2.2 Study population

All patients aged 15 years or younger who were hospitalized in the unit during the study period with human rabies and an available medical record were eligible. Patients older than 15 years and patients in whom another diagnosis was definitively established were excluded. Four patients met the study criteria.

2.3 Case definition and data collection

A suspected case was defined as an acute neurological disorder (including agitation, confusion, hydrophobia, aerophobia, hypersalivation or flaccid paralysis) in a patient with a preceding history of contact with a dog, particularly a bite, a scratch or saliva exposure to broken skin or mucosa. Data were extracted anonymously from medical records. Variables included demographic characteristics, residence, exposure circumstances, animal characteristics, incubation and consultation intervals, clinical manifestations, laboratory and imaging findings, virological tests, PEP and wound care, intensive care interventions, complications, length of stay and outcome.

2.4 Exposure classification and diagnostic investigations

Exposure categories were recorded according to the World Health Organization classification [11]. All four exposures were classified as category III. In three patients, saliva samples were collected at three time points (H0, H3 and H6) and nuchal skin biopsy specimens were tested for rabies viral RNA by polymerase chain reaction (PCR). Cerebrospinal fluid (CSF) PCR was performed in two patients.

2.5 Statistical analysis

Because of the small sample size, data are presented descriptively as numbers and percentages. Percentages use the four included patients as the denominator unless otherwise stated. No inferential statistical testing was undertaken.

2.6 Ethical considerations

Information was collected anonymously and the study involved no additional intervention or risk to patients. Institutional ethical approval was obtained.

3 RESULTS

3.1 Demographic and geographical characteristics

Four patients were included. All were male (4/4, 100%). Their ages ranged from 11 to 15 years, with a mean age of 13.3 years. Three patients (75%) were exposed in rural areas and one (25%) in an urban area. Two patients (50%) came from Taounate Province, one (25%) from Fez and one (25%) from Taza (Table 1).

Table 1: Demographic and geographical characteristics of the four patients

Characteristic	n/N	%
Male sex	4/4	100
Age range	11–15 years	–
Mean age	13.3 years	–
Rural exposure	3/4	75
Urban exposure	1/4	25
Taounate Province	2/4	50
Fez	1/4	25
Taza	1/4	25

3.2 Exposure circumstances

The biting animal was a non-domestic dog in all four cases. No dog had a documented rabies vaccination status. The dog was found dead in one case; its fate was unknown in the other three. Three patients (75%) sustained transdermal bites and one (25%) had saliva exposure to the ocular and nasal mucosa. The lower limb was involved in three patients (75%) and the upper limb in one (25%). Three patients (75%) had a single visible lesion; the patient with mucosal exposure had no visible skin lesion. All exposures were classified as category III (Table 2).

Table 2: Exposure characteristics

Exposure variable	n/N	%
Category III exposure	4/4	100
Transdermal bite	3/4	75
Ocular/nasal mucosal exposure	1/4	25
Lower-limb site	3/4	75
Upper-limb site	1/4	25
Single visible lesion	3/4	75
No visible skin lesion	1/4	25
Dog vaccination status undocumented	4/4	100

3.3 Incubation and clinical presentation

The incubation period was estimated at approximately 45 days in all four patients. The interval between symptom onset and consultation ranged from 1 to 7 days: one patient consulted within one day, two after approximately four days and one after seven days. All patients had non-specific prodromal symptoms, principally fever, headache and progressive fatigue. Local symptoms at the inoculation site, including pain, pruritus, dysesthesia and paraesthesia, were reported in all four patients.

Furious rabies was observed in three patients (75%) and paralytic rabies in one (25%). Fever and tachycardia with preserved blood pressure were reported in all patients at admission. Hydrophobia was present in three patients (75%), aerophobia in one (25%) and visual hallucinations in two (50%). Hypersalivation, hyperhidrosis and cardiac rhythm disturbances were reported in all four patients. One patient (25%) had sphincter dysfunction. One patient (25%)

developed myocarditis, with septal hypokinesia and a troponin concentration of 9,000 ng/L. Acute respiratory failure occurred in one patient (25%), associated with subcutaneous emphysema, pneumomediastinum and bilateral pneumothorax (Table 3).

Table 3: Clinical features at presentation and during hospitalization

Clinical feature	n/N	%
Furious clinical form	3/4	75
Paralytic clinical form	1/4	25
Fever	4/4	100
Hydrophobia	3/4	75
Aerophobia	1/4	25
Visual hallucinations	2/4	50
Hypersalivation	4/4	100
Hyperhidrosis	4/4	100
Cardiac rhythm disturbances	4/4	100
Acute respiratory failure	1/4	25
Myocarditis	1/4	25
Sphincter dysfunction	1/4	25

3.4 Laboratory, CSF and imaging findings

Haemoglobin and platelet counts were within normal limits in all patients. Leukocytosis (15,000–16,000 cells/mm^3) was observed in three patients (75%), while C-reactive protein was negative in all four. Potassium and renal function were normal in all cases. One patient had hyponatraemia, with a nadir of 118 mmol/L.

Lumbar puncture was performed in three patients. CSF protein was elevated in two. CSF white-cell counts were 5, 25 and 8 cells/mm^3, with lymphocytic predominance; CSF glucose was normal. CSF PCR was negative in the two patients tested.

Brain computed tomography (CT) was performed in two patients: one examination was normal, while the other showed three subcortical hypodense areas without contrast enhancement. Brain magnetic resonance imaging (MRI) was performed in one patient and showed multifocal T2/FLAIR and diffusion hyperintensities involving the frontoparietal, temporal and occipital parasagittal regions and both thalami. In three patients, serial saliva samples collected at H0, H3 and H6 and nuchal skin biopsy specimens were PCR-positive for rabies viral RNA.

3.5 Post-exposure management and intensive care

None of the four patients had received appropriate PEP, including rabies vaccination or rabies immunoglobulin. None had received immediate wound washing or disinfection according to the medical records. All patients were managed in a low-stimulation environment and required orotracheal intubation and mechanical ventilation. Midazolam combined with fentanyl was used in three patients (75%) and propofol in two (50%); ketamine was not used. All patients received acyclovir, whereas none received ribavirin. Two patients (50%) initially received ceftriaxone at meningeal doses, one (25%) received amoxicillin/clavulanate and one (25%) received no antibiotic. All received supportive care, including enteral nutrition, secretion management, thromboembolism prophylaxis, pressure-injury prevention and correction of fluid and electrolyte disturbances. Thoracic drainage was performed in the patient with bilateral pneumothorax (Table 4).

Table 4: Post-exposure management and intensive care interventions

Intervention	n/N	%
Documented immediate wound cleansing	0/4	0
Appropriate rabies PEP	0/4	0
Intubation and mechanical ventilation	4/4	100
Low-stimulation environment	4/4	100
Midazolam plus fentanyl	3/4	75
Propofol	2/4	50
Acyclovir	4/4	100
Ribavirin	0/4	0
Ceftriaxone	2/4	50
Amoxicillin/clavulanate	1/4	25
Complete supportive care	4/4	100

3.6 Complications and outcomes

All four patients developed haemodynamic instability described as vasoplegia and required norepinephrine. One patient (25%) developed cardiogenic shock secondary to myocarditis and required dobutamine. One patient (25%) developed ventilator-associated pneumonia. Two patients (50%) progressed to brain death, documented by clinical findings and transcranial Doppler. Intensive care length of stay ranged from 3 to 10 days (individual stays: 3, 7, 7 and 10 days). All four patients died (case-fatality proportion, 100%) (Table 5).

Table 5: Complications and outcomes

Outcome/complication	n/N	%
Vasoplegia requiring norepinephrine	4/4	100
Myocarditis with cardiogenic shock	1/4	25
Ventilator-associated pneumonia	1/4	25
Brain death	2/4	50
Death	4/4	100
ICU length of stay	3–10 days	–

4 DISCUSSION

This retrospective case series describes four pediatric patients admitted with human rabies to a tertiary intensive care unit in Fez over eight calendar years. The principal findings are the occurrence of severe category III exposures involving non-domestic dogs, the absence of documented wound cleansing and PEP in every case, heterogeneous neurological presentations, frequent autonomic manifestations and uniformly fatal outcomes once clinical disease had developed.

All patients were male and three exposures occurred in rural settings. The canine source is consistent with reports from other rabies-endemic settings [9,10], and the need for better rabies awareness and PEP management among the rural population has been highlighted in Morocco [5]. However, this small hospital-based series cannot establish sex- or residence-specific risks. It describes only patients who reached this intensive care unit and should not be interpreted as a population-based estimate.

Three patients sustained transdermal bites, while one had ocular/nasal mucosal exposure. This latter case underscores that a visible bite wound is not required for a potentially infectious exposure when saliva contacts mucous membranes. The absence of recorded wound washing, rabies vaccination and rabies immunoglobulin represents a major missed

prevention opportunity. PEP is intended to prevent viral neuroinvasion and must be initiated promptly after a qualifying exposure, before clinical symptoms develop [3,11].

The estimated incubation period was approximately 45 days in all four cases. Although this estimate is compatible with the commonly reported interval, incubation varies according to inoculum, wound severity, anatomical site and proximity to the central nervous system [1,12]. Local pain, pruritus and paraesthesia at the inoculation site were reported in all patients and may provide a useful diagnostic clue when evaluating an encephalitic syndrome in a patient with a relevant animal exposure.

The clinical spectrum included both furious and paralytic forms. Hydrophobia was common but not universal. The paralytic presentation is particularly important because it may be mistaken for other causes of acute flaccid paralysis, including Guillain–Barré syndrome [13]. Behavioural changes, seizures and respiratory complications may also dominate the initial presentation [14,15].

Ante-mortem virological confirmation was obtained in the three patients who underwent serial saliva sampling and nuchal skin biopsy, whereas CSF PCR was negative in the two patients tested. These findings illustrate the importance of selecting appropriate specimens and, where indicated, repeating saliva sampling; a negative result from a single specimen should not be considered sufficient to exclude rabies [6–8]. The imaging abnormalities in this series were heterogeneous and are supportive rather than specific.

All patients required invasive ventilation and developed haemodynamic instability. Myocarditis and autonomic dysfunction are recognised complications of rabies, and cardiac involvement has been reported in clinical and pathological studies [16,17]. Pneumomediastinum and pneumothorax have also been described in paralytic rabies [18]. Acyclovir was administered empirically in all four cases, but it is not an established curative therapy for rabies. Once neurological disease is established, management is predominantly supportive, with attention to symptom control, organ support, communication with families and appropriate palliative care [19,20].

The most important public-health message from this series is that prevention before symptom onset is decisive. Community education should emphasise immediate, thorough wound washing and prompt presentation to a health facility after any potentially risky exposure. First-contact healthcare workers need practical training in exposure classification, wound management, vaccine schedules and the appropriate use of rabies immunoglobulin. At population level, sustained dog vaccination and coordinated human and veterinary surveillance should be pursued through a One Health approach [2,4].

4.1 Limitations

This study has several limitations. It is a retrospective, single-centre series with only four patients, which limits generalisability and precludes statistical inference. Data quality depended on the completeness of medical records, and the incubation period was an estimate rather than a measured interval. Only patients admitted to the intensive care unit were included, so cases managed elsewhere were not captured.

5 CONCLUSION

In this four-patient pediatric series from Fez, human rabies followed severe exposures involving non-domestic dogs, and no patient had received documented immediate wound care or appropriate PEP. Clinical manifestations varied, all patients required invasive ventilation and intensive care, and all died. These observations reinforce that prevention before symptom onset is the critical intervention. Immediate wound cleansing, prompt and complete PEP, access to rabies immunoglobulin for eligible category III exposures, community education and sustained dog vaccination are essential to reduce preventable pediatric deaths.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Disclosure of conflict of interest

The authors declare that they have no competing financial or non-financial interests.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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