Infect Dis Trop Med 2026; 12: e1809

When a sip of water triggers fear: an imported case of human rabies in Italy

M. Ferrari[1], C. Forlini[1], L. Bianchi[1], F. Crippa[2], R. Giossi[3], G.D. Casella[1]

[1]Department of Anesthesia and Critical Care, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy
[2]Infectious Diseases Department, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy
[3]Chemical-Clinical Analyses, Poison Control Center and Clinical Pharmacology Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

M. Ferrari and C. Forlini equally contributed to the manuscript

ABSTRACT:

— ***Background:*** Rabies is an almost invariably fatal viral encephalitis, extremely rare in Europe but still endemic in parts of Africa and Asia. Imported cases can present with atypical or misleading symptoms, especially when concurrent medical conditions divert diagnostic attention.

— ***Case Report:*** We describe a 25-year-old man, born in Gambia and living in Northern Italy, admitted for a traumatic lower-limb amputation whose initial clinical picture was dominated by anxiety and dysphagia selectively for cold liquids. Hydrophobia, autonomic dysfunction, and encephalitic signs gradually developed. The suspicion of rabies was eventually raised by a nurse recalling hydrophobic behaviour from online clinical videos. Molecular testing confirmed rabies virus infection.

— ***Conclusions:*** This case highlights the diagnostic pitfalls of imported rabies in non-endemic settings and the importance of maintaining clinical suspicion even when confounding factors such as trauma or psychiatric features predominate. Early recognition is essential for appropriate infection control precautions and post-exposure prophylaxis of contacts.

— ***Keywords:*** Rabies, Imported infection, Hydrophobia, Trauma, Critical care, Encephalitis.

— ***Abbreviations:*** CSF: Cerebrospinal Fluid; ECG: Electrocardiogram (or Electrocardiography); ED: Emergency Department; EEG: Electroencephalogram; ER: Emergency Room; ICU: Intensive Care Unit; IM: Intramuscular; IVIg: Intravenous Immunoglobulin; MRI: Magnetic Resonance Imaging; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; PCR: Polymerase Chain Reaction; PEP: Post-Exposure Prophylaxis; RABV: neutralizing anti-rabies virus; RIG: Rabies Immunoglobulin; RNA: Ribonucleic Acid; CT: Computed Tomography (or CT scan); WBC: White Blood Cells; WHO: World Health Organization.

INTRODUCTION

Rabies is a neurotropic zoonosis caused by Lyssaviruses, mainly transmitted by bites from infected animals. Once clinical symptoms appear, the disease is almost universally fatal, causing up to almost 60,000 deaths per year worldwide[1]. Most cases originate from Asia and Africa, with more than 40% occurring in children below 15 years of age. Member states of the European Union are considered free of terrestrial rabies, except for Romania and Poland. Nonetheless, imported cases occur sporadically, primarily in travellers or migrants returning from endemic regions[2]. The most recent imported case was described in Spain in 2025 (Table 1). Because rabies is now rarely seen in European hospitals, its early manifestations, such as paraesthesia, dysphagia, anxiety, or hydrophobia, are easily misinterpreted.

Corresponding Author: Michele Ferrari, MD; e-mail: ferrari.michele87@gmail.com

Table 1 . List of rabies cases diagnosed in the European Union (EU)/European Economic Area (EAA), 2015-2025.

Year	Country of diagnosis (EU/EAA)	Exposure
2025	Romania	Local (dog)
2025	Spain	Ethiopia
2025	United Kingdom	Morocco
2025	France	Under investigation
2023	France	Morocco
2022	Romania	Local (cat)
2019	Italy	Tanzania
2019	Latvia	India
2019	Spain	Morocco
2019	Norway	Philippines
2019	France	France (bat)
2018	United Kingdom	Morocco
2017	France	Sri Lanka

Adapted from Hurmuzache M, Gradinaru MA, Bărbuceanu F, Moțiu R, Popescu R, Lutic A, Müller T, Freuling CM, Vuta V. Death in the EU/EEA from autochthonous human rabies, Romania, July 2025: a call for action. Euro Surveill 2025; 30: 2500794 under Creative Commons Attribution 4.0 International License.

We report here the first case of imported human rabies in Italy since 2019[3], and a previous case in 2011[4]. The last Italian autochthonous human case was described in Naples in 1968[5], where it was endemic at the time. Italy was declared rabies-free in 2013 by the Italian government, following a strong animal vaccination campaign. Since then, prophylactic vaccination is recommended for household pets but not mandatory, unless traveling outside of the European Union. The following case illustrates how diagnostic reasoning can be confounded by concurrent trauma and psychiatric features, delaying the recognition of an imported rabies infection.

Case Presentation

A 25-year-old man presented to a peripheral emergency department in northern Italy, reporting being assaulted with pepper spray three days earlier. He complained of dizziness, dysphagia, and difficulty swallowing cold water in the last 24 hours. Attempts to drink cold liquids provoked immediate spitting and brief tachycardia, whereas warm tea and solid foods were tolerated. He reported right shoulder pain and vague abdominal discomfort without tenderness. Medical history included tuberculous pleuritis treated two years prior. He appeared anxious but was afebrile and neurologically intact. Laboratory studies, ECG, and radiographs were unremarkable. Neurologic and psychiatric evaluations revealed no focal deficits or psychosis. Following a negative cerebral CT scan, he was discharged with nonsteroidal anti-inflammatory drugs (NSAIDs).

The following day, he presented to another emergency department with palpitations, dyspnea, and persistent difficulty swallowing cold liquids. The temperature was 37.4°C, white blood cells (WBC) 10,500/µL, and C-reactive protein (CRP) was negative. ECG and echocardiography were normal. Cold water again triggered abrupt spitting and tremors. Psychiatric consultation confirmed anxiety without psychosis. Brain CT remained normal, and toxicological screening was negative. He received oral delorazepam and was discharged.

That night, he was found on railway tracks with near-complete traumatic amputation of the distal right leg. He was sedated with ketamine and transported to a trauma center, where the amputation was completed under total intravenous anesthesia. He was found febrile preoperatively and kept reporting being poisoned by someone, showing a consistently altered mental status. Despite analgesia and hydration, he remained hypertensive (205/100 mmHg) and tachycardic (up to 135 bpm), experienced pseudo-seizure-like episodes, and exhibited copious salivation. He remained conscious between episodes and reported being in Gambia four months earlier; nonetheless, he was healthy until the week before. No fever was reported at home. Lumbar puncture revealed 32 mg/dL protein, 99 mg/dL glucose, 8 cells/µL (neutrophils), and lactate 2.2 mmol/L. Cultures were negative, and no further molecular assays were ordered. He was transferred to the intensive care unit (ICU) due to an uncertain diagnosis, unclear neurological status, and a possible suicidal attempt. He consistently reported fear of dying from an incurable illness.

In the ICU, the patient refused all oral intake for three days. Intravenous therapy (IV) was continued, and paralytic ileus developed. Hyperthermia persisted and was controlled with continuous IV diclofenac. A toxicology consult for rare psychotropics (i.e., cathinone derivatives, *Salvia Divinorum*, ayahuasca, psilocybin) was requested. With no antipsychotic history, neuroleptic malignant syndrome was considered unlikely. Tests for systemic lupus and a second lum-

bar puncture were planned to rule out autoimmune central nervous system (CNS) disease.

Attempts at minimal oral administration triggered sinus pauses of up to 6 seconds, progressing to a 14-second complete heart block and cardiac arrest; circulation returned after epinephrine. He was intubated, sedated, and received a leadless ventricular pacemaker (Micra AV2, Medtronic, minimum rate 50 bpm). Echocardiography was unremarkable. Post-ictal psychosis with temporal-lobe–related dysautonomia was suspected[6], but MRI and EEG were normal. During awakening trials, he became comatose with stereotyped neck extension; even light tactile stimulation provoked further sinus pauses, overridden by pacing.

On ICU day 5, a bedside nurse, recalling clinical videos encountered on social media, suggested the possibility of diagnosing rabies. A thorough review of the patient's course revealed several features consistent with the disease: dysphagia triggered by attempts to drink, triggered by cold liquids; copious salivation; paroxysmal autonomic instability; intense fear of dying; fluctuating mental status; intermittent fever and confirmed travel to Gambia four months earlier. A phone call to the patient's sister in his home country revealed a dog bite six months earlier. The dog had died two days later. A second lumbar puncture was performed and indicated progression toward inflammatory cerebrospinal fluid (CSF) findings: protein 145 mg/dL, glucose 77 mg/dL, and 21 cells/µL (neutrophils). Samples were collected and sent for analysis: saliva and nuchal skin biopsy samples were submitted for rabies RNA PCR detection, along with CSF and serum for anti-rabies antibody titration (IZSVe, Istituto Zooprofilattico Sperimentale delle Venezie, Padova, Italia). Given the strong clinical suspicion, the patient immediately commenced rabies-specific vaccination, scheduled according to the latest WHO recommendations. Concurrently, Human Rabies Immunoglobulin (1,800 UI RIG) was administered intramuscular (IM), and intravenous immunoglobulin (IVIg) at a dose of 0.5 g/kg was administered daily for five days. Although this treatment represents a post-diagnosis rather than a standard prophylactic protocol (Figure 1), its off-label use was justified and agreed upon as a compassionate treatment. Despite anecdotal reports of the so-called "Milwaukee protocol"'s efficacy, no experimental evidence has been published. Moreover, the antiviral activity of both ribavirin and amantadine has been observed *in vitro* but not *in vivo*, either in animal models or in humans[7]. Similarly, the administration of rabies immunoglobulin (RIG) in advanced disease did not demonstrate efficacy[8], though it appears effective in early post-exposure prophylaxis[9]. On ICU day 6, the diagnosis was confirmed by positive rabies RNA in both saliva and skin biopsy samples. The antibody titration on CSF and serum samples was below detectable limits (<0.5 U/ml). Finally, even though person-to-person transmission has only been reported following organ transplantation[10], post-exposure prophylaxis (PEP) was administered to close family members and healthcare personnel with internal *ad hoc* criteria (i.e., based on performed invasive procedures). On ICU day 11, the patient exhibited the absence of all brainstem reflexes, and brain death was declared.

DISCUSSION

When the patient was admitted to the emergency department (ED) following limb trauma, the focus was on damage control. Once vital parameters were stabilized, the presenting fever and altered mental status became a major concern. Causes of hyperthermia, such as drug abuse, hyperthyroidism, antipsychotic drugs, and malignant hyperthermia, were easily ruled out. An early negative lumbar puncture ruled out meningoencephalitis. Early MRI and EEG were normal, providing false reassurance[11,12]. A zoonosis was considered extremely unlikely given that the patient had returned from Gambia more than 10 weeks before, and laboratory signs of infection were

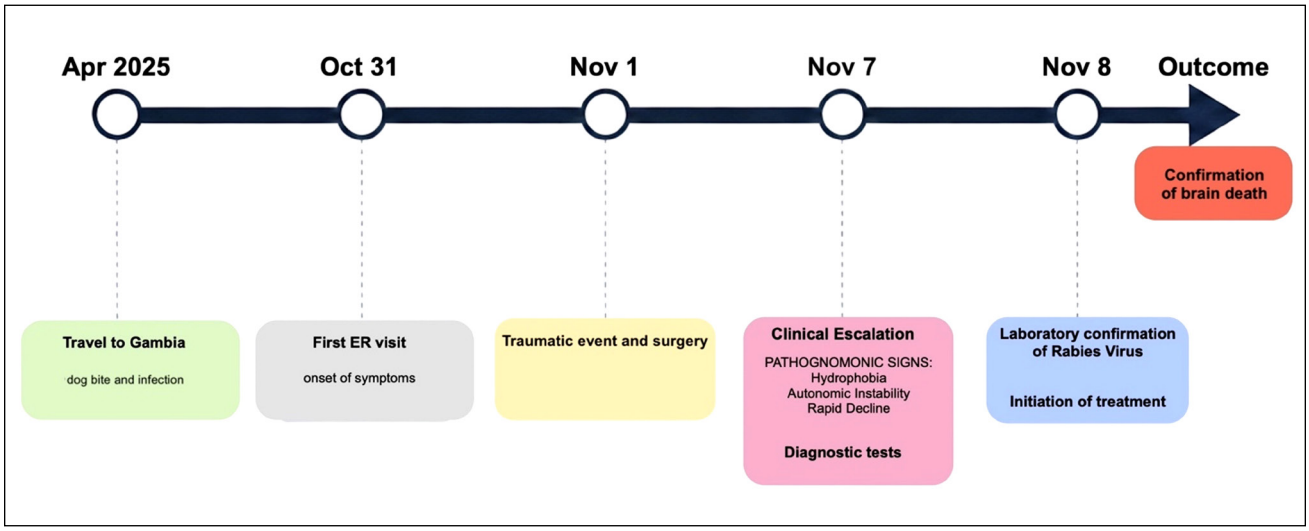

Figure 1. Clinical timeline.

missing. Malaria typically has shorter incubation periods (i.e., 7 to 30 days). This was one of the first diagnostic opportunities that were missed during our evaluation, possibly for two reasons: i) rabies is a significant cause of death in Gambia, and ii) rabid symptoms generally manifest from one month to one year following inoculation, even though cases up to 25 years have been hypothesized[13]. Animal bites are often not reported by patients, as was the case in our study, probably due to cultural factors in endemic areas where awareness is low. Furthermore, palpitations and dysrhythmias should have pointed to autonomic nervous system failure, another key feature of rabies, which in our case was very subtle and overlooked. Prodromal signs such as agitation, fear of impending death, and fluctuating behavioral changes can mimic psychiatric disorders in non-endemic settings. Upon psychiatric evaluation, the patient declared suffering from an untreatable disease. He reported witnessing the failure of Western medicine in his home country. Of note, when the diagnosis was made, his close relatives from Gambia were also unaware of the viral origin of rabies and the relevance of exposure to potentially rabid animals. Finally, an accurate revision of the previous two ED admissions reported diffuse, transient tremors while trying to drink water, which disappeared when drinking hot tea. The unusual presentation of temperature-sensitive hydrophobia was erroneously labelled as dysphagia for cold liquids. The term hydrophobia never appeared in charts until diagnosis was made. Hydrophobia is pathognomonic of rabies, making its correct identification a clinical cornerstone for diagnosis.

Overall, this case illustrates the profound diagnostic challenges posed by imported rabies in regions where clinicians seldom encounter the disease. The final diagnosis was made when a bedside nurse recalled social media content reporting cases of hydrophobia.

Even though no curative therapies exist once neurological symptoms emerge, early recognition remains essential for guiding supportive care, implementing infection control measures, and initiating contact tracing[9]. Although human-to-human transmission outside organ transplantation is unproven, concerns among healthcare workers persisted until systematic post-exposure prophylaxis was administered.

Diagnostic confirmation includes detection of neutralizing anti-rabies virus antibodies in serum (in previously non-immunized patients) and CSF, viral antigens in tissue (typically nuchal skin biopsy), and viral RNA (RABV) in saliva, skin, or CSF. Because rabies is not routinely included in organ-donor screening and might progress to brain death, timely suspicion is crucial to prevent potential transmission to transplant recipients[10,14].

CONCLUSIONS

In Europe, human rabies is exceedingly rare and generally imported from endemic regions of either Africa or Asia. The absence of exposure history, a long incubation period and possible psychiatric symptoms may delay diagnosis. Our recent case, the first since 2019 in Italy, reinforces that careful identification of hydrophobia, dysautonomia and hypersalivation should raise suspicion even in non-endemic areas.

Informed Consent:
Informed consent for the publication of this case report was provided by the closest relative of the patient.

Ethics Approval:
Not applicable due to the design of the study.

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

Funding:
None.

ORCID ID:
Michele Ferrari: 0000-0002-7388-5327
Clarissa Forlini: 0000-0002-1858-1080
Fulvio Crippa: 0009-0006-6291-1776
Riccardo Giossi: 0000-0002-7352-9445

Authors' Contributions:
M. Ferrari and C. Forlini contributed equally to the preparation of the manuscript. L. Bianchi, F. Crippa, R. Giossi, and G.D. Casella contributed to the revision of the manuscript.

Acknowledgements:
We are sincerely grateful to our colleagues M. Merli, V. Punzi, V. Terzi, P. Previtali, C. Borromeo, as well as to nurse L. Gardoni, for their invaluable clinical contribution and support to this work.

AI Disclosure:
Artificial intelligence tools were used exclusively for grammar checking and reference organization. No AI tool was used to generate scientific content or to interpret data.

References

1. World Health Organization. Rabies, fact sheet. Available at: https://www.who.int/news-room/fact-sheets/detail/rabies
2. Riccardi N, Giacomelli A, Antonello RM, Gobbi F, Angheben A. Rabies in Europe: An epidemiological and clinical update. Eur J Intern Med 2021; 88: 15-20.
3. Gautret P, Diaz-Menendez M, Goorhuis A, Wallace RM, Msimang V, Blanton J, Dacheux L, Parize P, Blumberg L, Bourhy H, Grobusch MP. Epidemiology of rabies cases among international travellers, 2013–2019: A retrospective analysis of published reports. Travel Med Infect Dis 2020; 36: 101766.
4. De Benedictis P, Perboni G, Gentili C, Gaetti L, Zaffanella F, Mutinelli F, Capua I, Cattoli G. Fatal case of human rabies imported to Italy from India highlights the importance of adequate post-exposure prophylaxis, October 2011. Euro Surveill 2012; 17: 20168.
5. Filipe J, Lauzi S, Marinoni V, Servida F, Dall'Ara P. Zoonoses and pet owners: A survey on risk perception in Northern Italy. Comp Immunol Microbiol Infect Dis 2024; 112: 1-6.
6. Schuele SU, Bermeo AC, Alexopoulos AV, Locatelli ER, Burgess RC, Dinner DS, Foldvary-Schaefer N. Video-electrographic and clinical features in patients with ictal asystole. Neurology 2007; 69: 434-441.
7. Warrell MJ, White NJ, Looareesuwan S, Phillips RE, Suntharasamai P, Chanthavanich P, Riganti M, Fisher-Hoch SP, Nicholson KG, Manatsathit S. Failure of interferon alfa and tribavirin in rabies encephalitis. BMJ 1989; 299: 830-833.
8. De Pijper CA, van Thiel PPAM, van de Beek D, Brouwer MC, Aronica E, Juffermans NP, Mathôt RAA, Geurts van Kessel CH, Schinkel J, de Jong MD, Grobusch MP, Goorhuis A. Rabies in humans: A treatment approach. Travel Med Infect Dis 2025; 64: 102813.
9. Damanet B, Costescu Strachinaru DI, Levêque A. Single visit rabies pre-exposure prophylaxis: A literature review. Travel Med Infect Dis 2023; 54: 102612.
10. Srinivasan A, Burton EC, Kuehnert MJ, Rupprecht C, Sutker WL, Ksiazek TG, Paddock CD, Guarner J, Shieh WJ, Goldsmith C, Hanlon CA, Zoretic J, Fischbach B, Niezgoda M, El-Feky WH, Orciari L, Sanchez EQ, Likos A, Klintmalm GB, Cardo D, LeDuc J, Chamberland ME, Jernigan DB, Zaki SR, Rabies in Transplant Recipients Investigation Team. Transmission of rabies virus from an organ donor to four transplant recipients. N Engl J Med 2005; 352: 1103-1111.
11. Warrell MJ, Warrell DA. Rabies and other lyssavirus diseases. Lancet 2004; 363: 959-969.
12. Hemachudha T, Ugolini G, Wacharapluesadee S, Sungkarat W, Shuangshoti S, Laothamatas J. Human rabies: neuropathogenesis, diagnosis, and management. Lancet Neurol 2013; 12: 498-513.
13. Shankar SK, Mahadevan A, Sapico SD, Ghodkirekar MSG, Pinto RGW, Madhusudana SN. Rabies viral encephalitis with probable 25 year incubation period! Ann Indian Acad Neurol 2012; 15: 221-223.
14. Maier T, Schwarting A, Mauer D, Ross RS, Martens A, Kliem V, Wahl J, Panning M, Baumgarte S, Müller T, Pfefferle S, Ebel H, Schmidt J, Tenner-Racz K, Racz P, Schmid M, Strüber M, Wolters B, Gotthardt D, Bitz F, Frisch L, Pfeiffer N, Fickenscher H, Sauer P, Rupprecht CE, Roggendorf M, Haverich A, Galle P, Hoyer J, Drosten C. Management and outcomes after multiple corneal and solid organ transplantations from a donor infected with rabies virus. Clin Infect Dis 2010; 50: 1112-1119.