

#### **Case Report**

# Unusual Canine Rabies Manifesting as Horner's Syndrome: A Call for Expanded Diagnostic and Reservoir Surveillance

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# A B S T R A C T

Rabies remains a significant zoonotic disease, with classical encephalitic and paralytic forms being the most frequently observed clinical presentations. However, emerging reports suggest atypical manifestations involving sensory and autonomic pathways, raising concerns about alternative transmission sources and viral neurotropism. This study describes an unusual case of rabies in a Doberman exhibiting Horner's syndrome and neurological deficits in the absence of a bite history. Eight additional canine cases from the same region exhibited similar atypical signs, raising concerns about region-specific rabies virus (RV) variants or alternative wildlife reservoirs. The increasing occurrence of fatal rabies from minor exposures, such as scratches without bleeding, further supports the hypothesis of evolving viral strains with enhanced infectivity. This case highlights the urgent need for molecular surveillance, advanced diagnostics, and a One Health approach integrating ecological conservation with zoonotic disease mitigation.

**Keywords:** Rabies, Horner's Syndrome, Lyssavirus

### Introduction

29

Rabies is a fatal viral disease caused by the rabies virus and related lyssaviruses, predominantly transmitted through the bite of infected mammals. Classical presentations include encephalitic (furious) and paralytic (dumb) forms, affecting motor neurons and the central nervous system.<sup>1</sup> However, recent studies have reported atypical cases involving the autonomic nervous systems, raising concerns about the potential role of alternative viral reservoirs and transmission dynamics.<sup>2,3</sup>

Horner's syndrome is characterised by miosis, ptosis, enophthalmos, and third eyelid prolapse.<sup>4</sup> It is an uncommon clinical feature in rabies,<sup>5</sup> suggesting involvement of the sympathetic nervous system. The current case report documents an unusual case of rabies in a Doberman from Tamil Nadu's delta region, presenting with Horner's syndrome. The absence of bite history, coupled with negative ante-mortem tests and delayed symptom onset, further confounded clinical suspicion.

Notably, this study also reports a cluster of eight terminalstage canine rabies cases from the same geographic region, all presenting with Horner's syndrome—distinct from the index case, which exhibited early clinical signs at the time of presentation. These unique cases are reported from Tamil Nadu's delta districts, specifically from rural villages characterised by a mosaic of wetland rice fields, fruit and coconut orchards and sacred groves-landscapes that may influence animal reservoirs and contribute to the persistence of the rabies virus in the environment. Given the diagnostic limitations of Negri body detection and the absence of molecular confirmation in field settings, such presentations underscore the urgent need for enhanced surveillance, molecular diagnostics, and ecological studies to understand potential viral evolution at the wild-domestichuman interface.

#### Study Area and Land Use

Orathanadu taluk is located in the eastern part of Thanjavur district, Tamil Nadu, within the fertile Cauvery Delta region. The landscape is mostly flat and largely rural, with agriculture being the main land use. According to Bhuvan land use/land cover (LULC) data, the area is predominantly covered by croplands, particularly paddy fields, along with coconut plantations, mango orchards, and small patches of tree cover.<sup>6</sup> Scattered throughout the taluk are village ponds and tanks that support farming and livestock needs. Some of the remaining tree-covered areas include sacred groves, which are traditionally protected and serve as roosting sites for bats and other wildlife. These groves are often located near settlements and farmland, creating a mixed-use landscape where people, domestic animals and wild animals are in close proximity.<sup>6-8</sup>

# **Materials and Methods**

#### **Case Presentation**

A two-year-old unvaccinated male Doberman was presented to the Veterinary Clinical Complex Hospital, Orathanadu, with complaints of anorexia and persistent leftward turning. The animal had been previously treated for suspected lameness by a local veterinarian.

#### **Clinical Examination**

The dog exhibited a persistent head turn towards the left (Figure 1), right forelimb lifting (Figure 2) and normal mentation. A detailed neurological examination revealed anisocoria, miosis and third eyelid prolapse in the right eye, consistent with Horner's syndrome (Figure 3). Additionally, right forelimb monoparesis and ataxia were noted.



Figure 1.Persistent head turn towards the left



Figure 2. Right forelimb lifting



Figure 3. Horner's syndrome

# **Diagnostic Investigations**

Lateral flow tests for rabies and canine distemper were negative. Blood parameters, including glucose levels, were normal. Radiographic evaluation ruled out skeletal abnormalities, while cerebrospinal fluid (CSF) analysis did not reveal any significant changes. Rabies antigen testing using the QuickVet<sup>®</sup> Kit on CSF samples was negative on the day of presentation. The animal's mentation was also normal on the day of presentation. The dog's condition deteriorated, progressing to flaccid paralysis in all four limbs with lateral recumbency, frenzied behaviour (Figure 4), salivation and eventual demise. Postmortem hippocampal impression smear analysis confirmed the presence of inclusion bodies (Negri bodies) (figure 5).



Figure 4.Lateral recumbency and frenzy behaviour



Figure 5.Postmortem hippocampal impression smear showed presence of inclusion bodies (Negri bodies)

# **Results and Discussion**

The atypical presentation of rabies in this case characterised by Horner's syndrome and sensory-autonomic dysfunction—aligns with prior reports of non-classical manifestations in both humans and dogs.<sup>2,3</sup> However, to the best of our knowledge, Horner's syndrome has rarely been reported in veterinary rabies, making this an unusual clinical observation. The absence of visible bite wounds, the animal's normal mentation at the time of presentation and negative ante-mortem diagnostic tests further complicated early diagnosis. These findings highlight the diagnostic challenges posed by rabies cases in which the classical motor pathway involvement is minimal or delayed.

Interestingly, several additional canine cases (n = 8) brought in at the terminal stage of illness exhibiting clinical signs consistent with Horner's syndrome were documented in the same geographical region (figure 6). All were subsequently confirmed as rabies based on the presence of Negri bodies in hippocampal impression smears. In the index case reported here, confirmatory diagnostic techniques such as the fluorescent antibody test (FAT) and reverse transcription polymerase chain reaction (RT-PCR), as recommended by the World Health Organisation (WHO) for definitive rabies diagnosis and viral characterisation, were not employed. Instead, diagnosis was established through the identification of intracytoplasmic Negri bodies using William's modified Van Gieson staining method, which remains a valuable tool in field-based diagnostics.9 Although histopathological detection of Negri bodies is a classical and specific technique, it lacks the sensitivity and discriminatory power of molecular methods for strain typing or identifying emerging lyssaviruses. Future investigations should incorporate advanced diagnostic tools, including molecular assays and phylogenetic analysis, to better characterise circulating lyssaviruses and assess the potential role of wildlife reservoirs in the transmission dynamics of rabies.

Although no veterinary reports exist documenting rabies presenting with Horner's syndrome, similar manifestations have been observed in human cases. For instance, Mader et al.,<sup>2</sup> described a human rabies infection that initially mimicked acute brachial neuritis, Horner's syndrome, and Guillain–Barré syndrome, with a definitive diagnosis of rabies confirmed only postmortem. This type of diagnostic ambiguity is especially concerning in India, where paralytic rabies cases presenting with overlapping features of Guillain-Barré syndrome and other atypical neurological signs are being increasingly reported in humans.<sup>10-12</sup> Such atypical presentations raise the suspicion that region-specific rabies virus (RV) variants may be influencing the pathogenesis, potentially altering neurotropism or preferentially affecting specific neural pathways. This possibility underscores the urgent need for molecular and phylogenetic studies to investigate whether unique or evolving RV strains in India, particularly in ecologically distinct regions, are contributing to these uncommon clinical manifestations.

The increased occurrence of Horner's syndrome in rabies cases from Tamil Nadu's delta districts suggests the possibility of a region-specific rabies virus variant, potentially maintained by an unidentified reservoir host and affecting sympathetic nervous pathways during the ascending phase of the disease.<sup>3</sup> While Nagarajan et al.,<sup>13</sup> identified distinct Indian RV isolates and a separate Kerala lineage, their study did not include samples from the delta region—an ecologically unique area with intensive agriculture, semi-domesticated dog populations and complex human–wildlife interfaces—where localised viral evolution could similarly occur.





Reddy et al.,<sup>14</sup> reported that phylogroup I RV strains circulate among both wild and domestic animals in India, emphasising the role of wildlife reservoirs and the need for whole-genome surveillance at the wild-domestic-human interface. However, their analysis excluded Tamil Nadu, leaving a critical epidemiological gap. Potential reservoir species such as mongooses in this region warrants closer examination. Soler-Rangel<sup>15</sup> documented a rare case of human rabies following a cat bite, in which the patient presented with Horner's syndrome-highlighting the potential for atypical neurological manifestations in rabies infections. Cats, with their ability to move through confined spaces, may occasionally engage in aggressive encounters with dogs, presenting a plausible, though often overlooked, transmission route. While cats are known to be susceptible to rabies, there is currently no evidence supporting the existence of cat-adapted rabies virus variants.<sup>16</sup>

Ugolini<sup>17</sup> noted that classical dog rabies typically spreads via motor pathways, whereas bat-associated variants may enter through superficial wounds, exploiting sensory nerves-potentially explaining neuropathic pain and monoparesis in affected cases. In the present case, the observation of Horner's syndrome with normal mentation suggests possible early involvement of sympathetic nerves before the virus reached the brain. The observation of Horner's syndrome in human rabies cases associated with bat lyssaviruses raises the possibility that certain rabies virus variants may preferentially involve the sympathetic nervous system.<sup>18-20</sup> This neurological tropism could explain the atypical presentation observed in the present canine case. And the present case also used to reside in a car garage, where bat activities are seen, as reported by the owner of the dog.

Udow et al.,<sup>21</sup> also found local symptoms more common in bat-transmitted rabies, even without visible bites. Banyard et al.,<sup>22</sup> emphasised the growing detection of lyssaviruses in bat populations across Asia, including anecdotal evidence of the classical rabies virus in frugivorous bats, particularly in India. In India, the emergence of fatal rabies cases from minor exposures—such as scratches or abrasions without bleeding—classified as WHO Category II, is particularly concerning. Bharti et al.,<sup>23</sup> documented such instances, raising the possibility of viral variants with enhanced infectivity through minimal skin breaches.

Importantly, of the eight canine rabies cases presenting with Horner's syndrome documented in this study, three occurred in dogs housed on isolated, fenced farms with no known history of contact with stray or domestic dogs. This raises the likelihood of transmission from unidentified reservoirs—most notably cats, mongooses, and bats.

The delta districts of Tamil Nadu, including the present study area, represent a unique ecological mosaic where rural settlements are interwoven with rice field wetlands, fruit orchards, and sacred groves or temple forests (Figure 7). These diverse landscape elements with sacred groves serve as critical habitats for a wide range of wildlife, including several bat species.<sup>7,8,24</sup> Significantly, four cases of rabies in animals presenting with Horner's syndrome were reported from areas adjacent to such ecologically sensitive habitats.

In recent years, there has been a rising trend of rabies cases in the study area, prompting a GIS-based assessment of landscape changes. False colour composite (FCC) satellite imagery from Landsat 5 (1996, 2005) and Landsat 8 (2019), analysed using the ESRI Landsat Explorer platform (ESRI, 2025), revealed progressive degradation and fragmentation of vegetation. Once characterised by dense, continuous cover, the landscape now shows increased exposure of soil, fallow fields, and built-up areas—particularly along roads and field margins (Figure 8) indicates habitat change (1996-2005-2019) visualised through Landsat false colour composites and a change detection map).<sup>25</sup> Yellow circles highlight areas of continued loss of thick vegetation. (The imagery utilised a near-infrared (NIR)-red-green band combination, where dense vegetation appears in red, while fallow land, exposed soil, or built-up areas show up as blue, white, or grey). This microhabitat loss, affecting species such as bats and mongooses, coincides with the zones where unusual rabies cases with Horner's syndrome were reported.



Figure 7-A typical landscape in delta district of Tamil Nadu (Image courtesy – Google earth)



Figure 8.Habitat change (1996-2005-2019) visualized through Landsat false color composites and a change detection map. Yellow circles highlight areas of continued loss of thick vegetation. (The imagery utilized a near-infrared (NIR)-red-green band combination, where dense vegetation appears in red, while fallow land, exposed soil, or built-up areas show up as blue, white or gray)

Potential reservoir hosts such as mongooses, bats, and feral cats are suspected due to ongoing habitat loss, with particular concern focused on bats based on the evidence presented above. Although the rabies virus has not yet been isolated from bats in Tamil Nadu, rabies-neutralising antibodies have been detected in bat sera from Nagaland,<sup>26</sup> and a rabies-like illness following a bat bite was reported in Tamil Nadu as early as 1954.<sup>27</sup> Additionally, structures resembling Negri bodies have been identified in the brain and salivary glands of dead bats in India,<sup>28</sup> suggesting potential viral involvement. A novel lyssavirus—Gannoruwa bat lyssavirus—was isolated from Pteropus medius in Sri Lanka,<sup>29</sup> a bat species also prevalent in southern India. The possibility of cross-border rabies virus variant spillover into South India is supported by Aravindh Babu et al.,<sup>30</sup> who identified Sri Lankan rabies virus variant infecting cattle in Tamil Nadu based on partial nucleoprotein gene sequencing. The Indian isolates showed 96–99% amino acid sequence identity to the Sri Lankan isolates, reaffirming that this variant may still be actively transmitted by animals in India. Additionally, the geographical proximity of Tamil Nadu's delta districts to Sri Lanka increases the likelihood of such spillover events.

Though the above evidence suggests that the unusual findings may indicate rabies caused by a different variant spreading through atypical hosts in this area, reliance on Negri body detection alone is inadequate due to its limited sensitivity and specificity. Without molecular confirmation, other neurological disorders—such as autoimmune or toxic encephalopathies—may be misdiagnosed as rabies. This diagnostic uncertainty, particularly in atypical cases presenting signs like Horner's syndrome, underscores the urgent need for molecular diagnostics such as RT-PCR and immunofluorescence assays.

# Conclusion

This article highlights the unusual presentations of rabies reported in the ecologically fragile delta districts of Tamil Nadu, India. These findings underscore the urgent need for molecular investigations to confirm the atypical disease patterns and to elucidate potential reservoir dynamics in these vulnerable ecosystems.

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