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Oropouche Fever Associated with Combined Central and Peripheral Demyelination (CCPD): A Case Report from Ceará, Brazil, 2024

Abstract

Background: Oropouche fever, caused by the *Oropouche orthobunyavirus* (OROV), is an arboviral illness transmitted by midges and mosquitoes. Although commonly regarded as a mild illness, severe neurological manifestations are increasingly being reported.

Case Summary: We report a 48-year-old female patient from Capistrano, Ceará, Brazil, who developed Combined Central and Peripheral Demyelination (CCPD) following confirmed OROV infection. Her clinical presentation included ascending flaccid tetraparesis, bilateral facial paresis, and progressive visual loss. Neurological investigation confirmed demyelinating polyneuropathy and retrobulbar optic neuritis. Despite initial corticosteroid therapy, gradual and partial clinical improvement was observed after plasmapheresis; however, visual and motor deficits persisted even after 90 days.

Conclusion: A reported case of combined central and peripheral demyelination (CCPD) associated with OROV represents an unprecedented complication, emphasizing the potential for severe outcomes linked to OROV infection. This highlights the need for increased clinical awareness and greater attention to the epidemiology of this disease. OROV infection has demonstrated the capacity to cause severe neuroinvasive complications, underscoring its critical and emerging epidemiological significance amidst the ongoing epidemic in the Americas. Driven by a novel reassortant lineage of OROV, this outbreak has been associated with previously unreported severe manifestations, including adult and fetal deaths. Enhanced surveillance systems and targeted training for the early recognition of neurological complications are essential to mitigate long-term impacts and guide public health strategies to address the growing burden of this arboviral infection.

Keywords: Oropouche virus; Combined central and peripheral demyelination; Communicable diseases, emerging; Arbovirus

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Introduction

Oropouche fever, caused by the *Oropouche orthobunyavirus* (OROV), is an emerging arboviral illness endemic to Latin America. OROV is transmitted primarily by biting midges (*Culicoides paraensis*) and occasionally by mosquitoes. Its clinical presentation often mimics other arboviral diseases such as dengue and chikungunya, complicating its diagnosis[1]. Although generally regarded as a mild, self-limiting illness, significant gaps remain in our understanding of its full clinical spectrum, particularly regarding severe manifestations. The current outbreak in the Americas is associated with a novel reassortant lineage, OROVBR_2025_2024,[2] which has been linked to severe cases and fatalities, including fetal deaths. Recent reports from Cuba describe neurological complications, particularly Guillain-Barré Syndrome (GBS), highlighting the neurotropic potential of OROV[3]. This case details a severe neurological presentation of OROV-associated Combined Central and Peripheral Demyelination (CCPD) in a previously healthy individual. The criteria for CCPD diagnosis were applied to this patient based on the framework described by Cortese et al. (2016)[4]: A) acute (within the previous month), subacute (1–2 months previously), or chronic (over 2 months previously) onset of symptoms of central nervous system (CNS) and/or peripheral nervous system (PNS) impairment; B) evidence of CNS lesions suggestive of demyelination on brain and/or spine MRI; C) presence of peripheral neuropathy confirmed by nerve conduction studies (NCS); and D) exclusion of other potential causes of combined CNS and PNS involvement as outlined in the referenced study To the best of our knowledge, this is the first reported association between CCPD and OROV, further emphasizing the need for heightened clinical vigilance and robust diagnostic capabilities in endemic areas. The significance of CCPD lies in its rare and severe nature, which highlights OROV's neurotropic potential and its capacity to impact both the central and peripheral nervous systems.

Case Report

Patient Presentation

A 48-year-old female patient from Capistrano, Ceará, presented with acute febrile illness on August 12, 2024. Her symptoms included high fever (39°C), chills, severe headache, and myalgia. RT-qPCR testing performed at the municipal health unit confirmed OROV infection on August 14, 2024[5]. Despite residing in an urban area, she frequently visited rural regions where OROV circulation had been documented, including a case of vertical transmission[6]. Laboratory investigations ruled out other arboviral infections, including dengue, chikungunya, Zika, and Mayaro viruses, through specific serological and molecular testing.[5,7] Fever persisted for two weeks and was unresponsive to antipyretics. Severe lower back pain, profuse sweating, and dry mouth were also reported.

Neurological Progression

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By the third week of illness, the patient experienced paresthesias in her lower limbs, progressing to ascending paresis affecting both upper and lower limbs. She also developed bilateral facial weakness and significant visual loss, perceiving only shadows. Due to worsening symptoms, she sought emergency care and was referred to a tertiary hospital in Fortaleza.

Hospital Admission

Upon admission on September 17, 2024, the patient exhibited ascending flaccid tetraparesis, bilateral facial paresis, and areflexia. Visual acuity was reduced to 20/50 bilaterally, with pupillary reflex impairment. Laboratory tests, including cerebrospinal fluid (CSF) analysis, revealed elevated protein levels (156 mg/dL) with a low cell count (2 cells/µL, predominantly lymphocytes), consistent with CCPD.

Comprehensive Diagnostic Assessment

Laboratory Findings

- **Hematology and Biochemistry**: Hemoglobin: 15.3 g/dL; Leukocytes: 8500/µL; Platelets: 346,000/µL; C-reactive protein (CRP): 5 mg/L; Erythrocyte Sedimentation Rate (ESR): 27 mm/h; Calcium: 10.7 mg/dL; Creatinine: 0.72 mg/dL; ALT: 63 U/L; AST: 22 U/L.
- **Infectious Disease Markers**: HIV: Non-reactive; HBsAg: Non-reactive; HCV: Non-reactive; VDRL: Non-reactive; OROV: positive RT-qPCR.
- **Autoimmune Profile**: C3: 118 mg/dL; C4: 43.8 mg/dL; Rheumatoid Factor (RF): 20.7 IU/mL.
- **CSF Analysis**:
    - Cell Count: 2 cells/µL (86% lymphocytes, 3% neutrophils);
    - Protein: 156 mg/dL;
    - Glucose: 135 mg/dL;
    - VDRL: Non-reactive;
    - ADA: 0.72 U/L;
    - Mycobacterium tuberculosis DNA: Not detectable (Xpert MTB/RIF);
    - Arbovirus Testing:
        - Zika Virus IgM: Non-reactive (ELISA);
        - Chikungunya Virus IgM: Non-reactive (ELISA);
        - Dengue IgM: Non-reactive (Capture ELISA).

Imaging and Neurological Studies (Figure 1)

- **Magnetic Resonance Imaging (MRI)**: Edema of lumbar nerve roots and bilateral facial nerve swelling.
- **Optical Coherence Tomography (OCT)**: Bilateral loss of ganglionic cells in the papillomacular bundle.
- **Electroneuromyography (ENMG)**: Motor-predominant demyelinating polyneuropathy with prolonged latencies and reduced conduction velocities.

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Clinical Management

Initial treatment with corticosteroids (prednisone 40 mg/day for 7 days) yielded minimal improvement. Plasmapheresis, administered over five sessions, led to gradual and partial recovery. Empirical antivirals and antibiotics were initiated but discontinued after excluding infectious etiologies such as listeria and herpes. During hospitalization, the patient experienced dysautonomia post-plasmapheresis, necessitating medical intervention after severe hypotension.

Clinical Course and Follow-Up

By discharge on October 1, 2024, the patient showed partial recovery, with improved motor strength and visual acuity. Residual symptoms included moderate headache, photophobia, nausea, and floaters. The patient's gait remained impaired, requiring assistance for mobility. By November 18, at follow-up, she demonstrated stable gait with occasional support and visual acuity of 50/100 bilaterally. Mild proprioceptive and sensory deficits persisted, predominantly in the left foot.

Phylogenetic analysis

A serum sample of the patient, collected in August, underwent total nucleic acid extraction followed by RT-qPCR testing to OROV (4). We applied an amplicon-based whole-genome nucleotide sequencing protocol (5) to characterize the OROV genome. Near-to-complete sequences for all three genome segments (L, M, and S) were recovered and concatenated for phylogenetic reconstruction using maximum likelihood inference on IQ-TREE multicore version 2.1.1 [8], employing a non-redundant dataset containing sequences published in previous studies[2,6,9].

The genome generated belongs to the new OROVBR_2025_2024 lineage [2,9]. Phylogenetic analysis revealed a highly supported monophyletic clade (UltraFast Bootstrap 99.5, SH-aLRT 100) containing sequences from other severe cases, including a fatal vertical transmission case previously described in Ceará[6]. This clade is part of a broader lineage linked to cases in Santa Catarina, Paraná, Amazonas, and Pernambuco, Brazil, as well as Leticia, Colombia. These sequences belong to the previously described AM-I sublineage of the OROVBR/2023-2024 [2,6,9] (Figure 2).

Discussion

A reported case of combined central and peripheral demyelination (CCPD) associated with OROV represents an unprecedented complication, emphasizing the potential for severe outcomes linked to OROV infection. This case underscores the neurotropic potential of OROV, demonstrating its capacity to cause CCPD, a rare and severe condition characterized by simultaneous central and peripheral nervous system demyelination. The coexistence of retrobulbar optic neuritis and demyelinating polyneuropathy further

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highlights the severity of CCPD and its profound impact on neurological function. Pathogenesis likely involves autoimmune cross-reactivity affecting both oligodendrocytes and Schwann cells[10]. Clinicians should maintain a high index of suspicion for neurological complications in OROV-endemic regions, and public health efforts must focus on surveillance and early intervention to mitigate long-term sequelae.

Public health strategies should prioritize enhanced surveillance and early interventions to mitigate the long-term impacts of these severe manifestations. Improved diagnostic capabilities, including advanced neuroimaging and RT-qPCR testing, are critical for timely recognition and appropriate management of OROV-associated CCPD. While plasmapheresis showed partial efficacy in this case, with visual and motor deficits persisting even after 90 days, further research is necessary to clarify its therapeutic role and to develop standardized treatment protocols. Additionally, targeted surveillance efforts should focus on rural areas where *Culicoides paraensis*, the primary vector, is prevalent.

The reassortant OROV strain detected in Brazil has exhibited heightened replication in mammalian cells, possibly correlating with severe clinical outcomes[11]. The geographic expansion of OROV and the emergence of neuroinvasive complications necessitate increased public health awareness. The first confirmed case of OROV in Ceará occurred in June 2024, with a total of 243 cases reported by Epidemiological Week 45[6]. Although the majority of cases were mild, the complications and deaths observed during the ongoing expansion of transmission of the Oropouche virus genotype OROVBR-2025-2024 to multiple countries underscore the urgent need for a more comprehensive understanding of the clinical spectrum of Oropouche fever.

Authorship, Ethical Aspects, and Conflicts of Interest

All authors contributed significantly to the conception, design, and writing of this manuscript and take full responsibility for its content. Each author has reviewed and approved the final version of the manuscript, ensuring its accuracy and compliance with scientific and ethical standards.

The patient involved in this study was fully informed about the nature and purpose of this report. She reviewed the content, provided her consent for publication, and signed an Informed Consent Form (TCLE) in accordance with ethical guidelines.

The study was approved by the Research Ethics Committee in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval ensures that the investigation adhered to the highest standards of research ethics and the protection of patient rights.

The authors declare no conflicts of interest in relation to this manuscript.

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FIGURES

Figure 1. A - The T2-weighted MRI of the lumbar spinal cord. Arrow show nerve root edema. **B -** MRI brain T1-weighted image with contrast. Arrows indicate enhancement of right facial nerve. **C -** Optical coherence tomography revealed bilateral loss of ganglionic cells in the papillomacular bundle shown in white on the circle graphic. RE: right eye. LE: left eye.

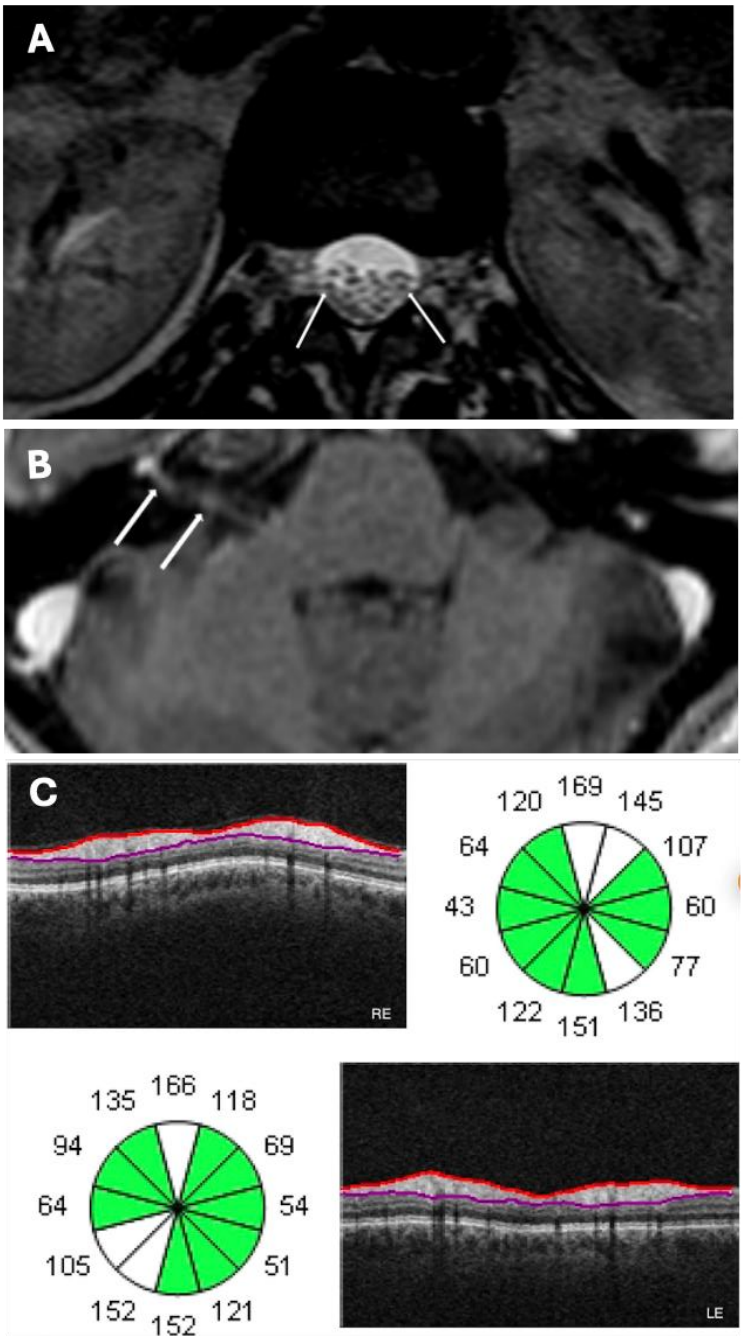

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Figure 2. Maximum likelihood tree of Oropouche virus concatenated segments. A reference dataset containing concatenated segments (L, M, and S) of the current Oropouche virus outbreak (2022-2024) representing different Brazilian regions and sequences obtained from Peru and Colombia were aligned using MAFFT v7.490 embedded in Geneios Prime 2025.0.3. Subsequently, this alignment was used for phylogenomic reconstruction by Maximum Likelihood (ML) using IQ-TREE multicore version 2.1.1 COVID-edition for Mac OS X 64-bit. MODEL-FINDER was used for evolutionary model choice, and 2000 Ultra-fast Bootstraps and 2000 SH-aLRT replicates were run to access the branches' support (the support for the CE clade is shown). The ML tree was edited with FigTree v1.4.4.

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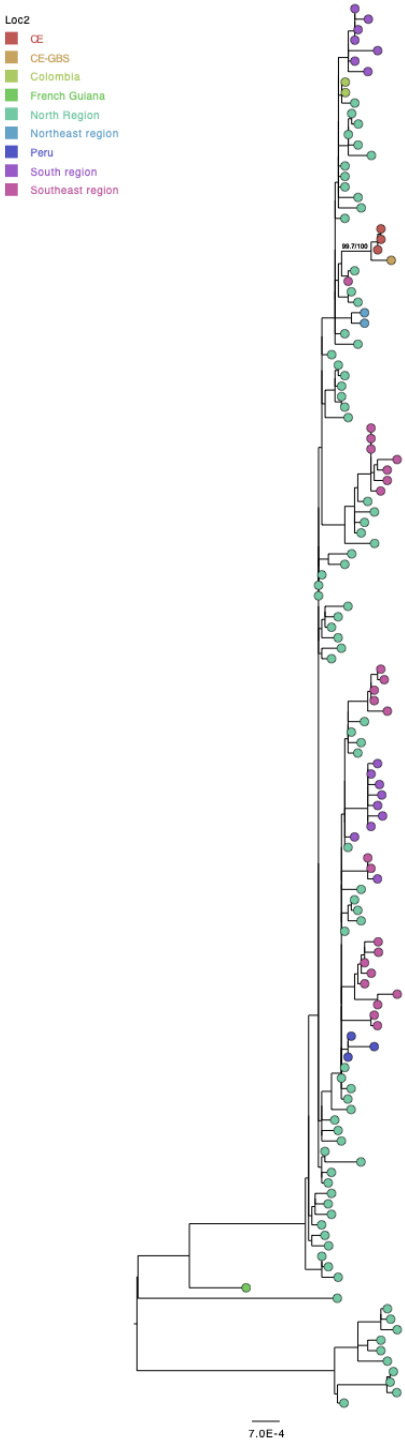

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