

## CASE REPORT

# Scrub Typhus with Multiple Cranial Nerve Palsy: A Rare Case Presentation

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### ABSTRACT

Scrub typhus, a rickettsial disease endemic in several parts of India, usually presents with acute symptoms. It is caused by small intracellular Gram-negative bacteria belonging to the Rickettsiaceae family. Optic neuritis and lateral rectus palsy may be associated with a range of autoimmune disorders, infectious diseases and raised intracranial tension. In this case, we report optic neuritis and lateral rectus palsy induced by *Orientia tsutsugamushi*. We report a case of a 23-year-old woman presenting with complaints of high-grade fever, vomiting and generalized swelling since 5 days. During this febrile period, on 4/10/2021, she complained of difficulty in vision and double vision. She was found to be positive for scrub typhus on 5/10/2021. Optic neuritis was diagnosed on the basis of ophthalmologic examination and magnetic resonance imaging (MRI) brain. Investigation was done to rule out autoimmune disorders (vasculitis and connective tissue diseases). Rickettsial optic neuritis was confirmed by detection of specific antibodies in serum and the negativity of other serologic tests. Fever, eschar, history of tick exposure and supportive diagnostic tests usually lead to the diagnosis. This case aims to raise awareness among the healthcare providers for this type of association. Scrub typhus should be included in the differential diagnosis when a patient presents with fever with or without eschar and isolated or multiple cranial nerve palsy.

**Keywords:** Eschar, *Orientia tsutsugamushi*, rickettsial disease

Scrub typhus, a rickettsial disease endemic in several parts of India, usually presents with acute symptoms. Scrub typhus is caused by small intracellular Gram-negative bacteria belonging to the Rickettsiaceae family. They are transmitted by transovarial and transstadial route in trombiculid mites.<sup>1</sup> Infected larval mites (chiggers) inoculate organism into the skin. The clinical presentation of scrub typhus infections varies from mild and self-limiting to fatal. Disseminated vasculitis is the basic pathogenic mechanism of this infection and it may subsequently lead to multiple-organ involvement.<sup>2</sup> Violations [involvement of] eye during scrub typhus infection are uncommon. We report a case of optic neuritis and lateral rectus palsy revealing *Orientia tsutsugamushi* infection in a 23-year-old woman.

### CASE REPORT

A 23-year-old woman hailing from Western Rajasthan presented with a 5 days' history of high-grade fever, vomiting and generalized swelling. She also developed yellowish discoloration of sclera. After 2 days of admission, she developed difficulty in vision. On examination, the patient was febrile; pulse rate was 98/min, regular; blood pressure (BP) was 120/70 mmHg and respiratory rate was 18/min. The patient had a dark black, pigmented, raised patch on left arm suggestive of an eschar (Fig. 1). On neurological examination, cranial nerve examination revealed left lateral rectus palsy (Fig. 2). Then, the patient underwent an ophthalmologic consultation, which showed low visual acuity. Her visual acuity was 6/10. Fundoscopy revealed that the left eye optic disc was pale and there were no retinal vessel abnormalities (Fig. 3).

There were no other significant findings on physical examination.

Other blood results indicated moderate anemia, and peripheral blood smear showed normocytic normochromic anemia with relative lymphocytosis. Malaria parasite slide and dual antigen were negative, there was increased white cell count and platelet count was normal. Aspartate aminotransferase - 424 IU/L,

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Figure 1. Eschar



Figure 2. Left lateral rectus palsy

alanine aminotransferase - 345 IU/L, total bilirubin - 2.5 mg/dL (direct bilirubin - 2.173), alkaline phosphatase - 594 IU/L, erythrocyte sedimentation rate - 20 mm/hr. Serum C-reactive protein was within normal range, serum calcium - 8.7 mg/day, serum albumin - 2 g/dL. Urine microscopy showed no cells or casts. Proteinuria was negative and renal function test revealed urea - 56 mg/dL, creatinine - 1.72 mg/dL.

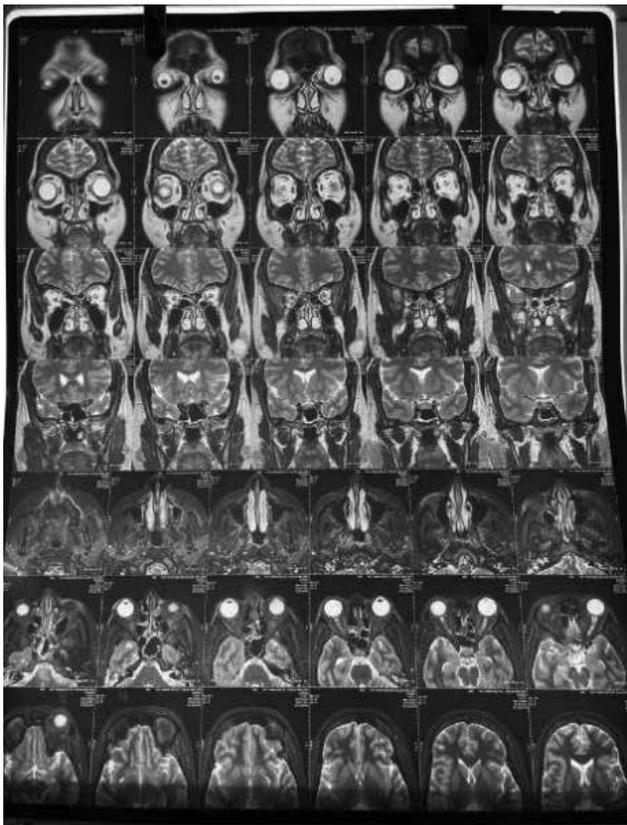


Figure 3. Pale optic disc

Immunological exams, including complement fractions C3 and C4, rheumatoid factor, antinuclear antibodies, antineutrophil cytoplasmic antibodies, antiphospholipid antibodies were negative. Cerebrospinal fluid (CSF) examination was done which was clear in color, glucose level - 75 mg/dL, protein level - 112 mg/dL, cells -130/ $\mu$ L, in which 70% were lymphocytes and 30% neutrophils; adenosine deaminase (ADA) - 8 IU/ $\mu$ L. Culture sensitivity report showed sterile sample; cartridge-based nucleic acid amplification test (CBNAAT) sample was negative for tuberculosis.

Blood for hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (HCV), venereal disease research laboratory (VDRL), human immunodeficiency virus (HIV)-1 and HIV-2 antibody, dengue NS-1 antigen and IgM, IgG anti-dengue antibody by enzyme-linked immunosorbent assay (ELISA), Widal test were negative.

Considering the patient's area of living, clinical presentation of fever and skin lesion, blood test to confirm scrub typhus (IgM) was sent which came out positive on ELISA. Chest X-ray was normal. Brain magnetic resonance imaging (MRI) with intravenous contrast showed left optic nerve appearing mildly thickened (Fig. 4) and abnormal post-contrast



**Figure 4.** MRI brain showing left optic.

enhancement; rest of white matter and grey matter interpreted as nonspecific abnormalities.

A diagnosis of left eye optic neuritis and 6th cranial nerve palsy related to rickettsial infection was made on the basis of clinical, immunological, serological and imaging findings, and the patient also had an eschar on the left arm. The patient received corticosteroid therapy - intravenous methylprednisolone pulse for 5 days followed by 1 mg/kg/day tapering dose of oral steroid for 2 weeks and doxycycline 200 mg/day for 15 days. After the initiation of treatment, the patient reported a marked improvement in vision which was confirmed by ophthalmological examination (Visual acuity 8/10 in the left eye).

## DISCUSSION

Scrub typhus is a tropical illness caused by *O. tsutsugamushi*, transmitted to human beings by an arthropod belonging to the family Trombiculidae. It is associated with multisystem involvement. *O. tsutsugamushi* is an obligate intracellular Gram-negative bacterium. It is prevalent in some parts of India including North eastern region.<sup>3</sup> Rickettsial organisms are transmitted to people by insects (ticks and mites) and cause diseases such as typhus, the

spotted fevers and scrub typhus.<sup>1</sup> Rickettsiae are small, nonflagellated, Gram-negative coccobacilli.<sup>4</sup>

Optic neuritis is closely associated with multiple sclerosis and neuromyelitis optica. However, it may also be associated with an array of autoimmune or infectious diseases. Optic neuritis due to infections is rare. Neuroretinitis is the most common ocular manifestation in eye infections.<sup>5</sup> After entering humans, these microorganisms invade the vascular endothelium and reticuloendothelial cells, causing vasculitis. This leads to skin rash, swelling, microvascular leakage, tissue hypoperfusion and end-organ ischemic injury. Thrombus formation results in tissue infarction and hemorrhagic necrosis.<sup>4</sup>

The common organ system complications seen in scrub typhus are hepatitis, acalculous cholecystitis, pancreatitis, acute renal failure, acute respiratory distress syndrome, hilar lymphadenopathy, pleural effusion, meningoencephalitis, seizures, vasculitic cerebral infarct, cardiac rhythm abnormalities, myocarditis, etc.<sup>6</sup> Fever, neurological disturbances and skin rash are the major symptoms of rickettsial infection.<sup>1</sup> Ocular involvement in rickettsial disease is uncommon and usually underdiagnosed.

The rickettsial infection may involve any part of the eye. Retinitis with or without mild or moderate vitreitis is a common clinical finding. It presents as white retinal lesions adjacent to retinal vessels and are variable in number, size and location.<sup>7</sup> Cystoid macular edema, serous retinal detachment, hypofluorescent choroidal spots, conjunctival hemorrhage and uveitis have also been noted.

Optic nerve involvement has been noted, including optic disc edema, optic disc staining on fluorescein angiography and optic neuritis with or without visual loss.<sup>8</sup>

Diagnosis of rickettsial infection is usually based on serology along with the clinical presentation and history of exposure to ticks, travel in endemic area, symptoms during summer months, etc. Doxycycline is the antibiotic of choice in rickettsial diseases.<sup>8</sup> Along with doxycycline, systemic steroids should be prescribed in case of ocular involvement, including severe retinitis, vitreitis, retinal vascular occlusion or optic nerve involvement.<sup>7</sup>

Our case report illustrates the difficulties in diagnosing the exact cause of optic neuritis and left rectus palsy when it is associated with multiple clinical and immunological disorders.

**CONCLUSION**

Rickettsial fever is endemic in some states of India and its diagnosis requires a high index of suspicion as its initial clinical features resemble many diseases. However, focal neurologic signs with classic clinical features, like fever, maculopapular rash, eschar, in an endemic area, should alert the physician to consider scrub typhus as one of the possible differentials. The positive rickettsial serology, CSF finding, and the epidemiologic context and the negativity of all other investigations established the diagnosis of rickettsial infection in this case. Corticosteroids and doxycycline were prescribed with a partial improvement of visual acuity.

Rickettsioses should be considered in the differential diagnosis of acute optic neuritis with 6th cranial nerve palsy in areas where scrub typhus fever is endemic. Diagnosis must be early in order to have a better response to treatment, combining doxycycline and corticosteroids.

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**Antibodies Weak Against Omicron Variant, Suggests More Evidence**

Additional evidence from laboratory experiments points to the weaknesses of COVID-19 vaccines and antibody drugs against the Omicron variant.

A study posted on bioRxiv, conducted by researchers at Columbia University, noted that Omicron variant was considerably resistant to neutralization by antibodies in blood from individuals who had received Pfizer/BioNTech, Moderna, J&J or Oxford/AstraZeneca COVID-19 vaccines, or from COVID survivors.

The researchers also tested 9 approved monoclonal antibodies and 10 that are still in the experimental stage. Neutralizing potential of 18 out of the 19 antibodies was either nullified or impaired.

In a separate study, posted on bioRxiv, researchers from Europe also stated that Omicron variant was either completely or partially resistant to neutralization by 9 monoclonal antibodies that were tested in the study, and also by antibodies in blood samples obtained from vaccine recipients and COVID survivors.

The European researchers stated that neutralizing antibody levels were 5- to 31-fold lower against Omicron compared to the Delta variant... (Source: Reuters)

**No Major Side Effect with India's First mRNA Vaccine, Say Experts**

Investigators involved in Phase 3 trials for HGCO19, India's first mRNA vaccine, being developed by Genovva Biopharmaceuticals Limited, have stated that nearly 90% of trial volunteers have not experienced any side effect after receiving either one or two doses of the vaccine thus far.

Dr Ashish Bavdekar, one of the principal investigators, who is leading the trials at Pune's KEM Hospital Research Center, said that the data from the Phase 1 trial on vaccine immunogenicity was also encouraging, adding that the side effects, reported in a minority of participants, were very mild and not significant. He stated that some volunteers did not report any side effects. Dr Bavdekar said that the minor side effects included mild fever or headache. He added that the picture will be clear after the Phase 3 trials as the sample size was much larger for this phase... (Source: ET Healthworld – TNN)