Introduction

After its re-emergence, scrub typhus has become an important cause of morbidity and mortality in patients presenting with febrile illness during monsoon and post-monsoon season. This zoonotic disease is caused by Orientia tsutsugamushi mainly targeting the endothelial cells. Majority of sequelae due to scrub typhus are the outcome of ‘Rickettsial vasculitis’. Clinical manifestation include fever, headache, myalgia, gastrointestinal symptoms, maculopapular rash, eschar and regional lymphadenopathy. Complications appear from second week onwards in form of multiorgan dysfunction. Central nervous system involvement is a known complication of scrub typhus and manifestations include aseptic meningitis, meningoencephalitis, acute disseminated encephalomyelitis, cerebral infarction, cerebellitis, subdural haemorrhage and isolated cranial nerve palsies. Here we are presenting a case of scrub meningitis complicated by multiple cranial palsies and cerebellitis. Hence it needs to be differentiated from acute bacterial meningitis and tubercular meningitis as delay in diagnosis and treatment will affect the morbidity and mortality.

Abstract

Meningitis or meningoencephalitis is a known complication of scrub typhus. Focal neurological deficits are rarely reported including hemiparesis, quadriparesis and isolated cranial nerve palsies. Here we are reporting a 24 years female who presented with fever, headache, ptosis, diplopia, facial deviation and unsteadiness of gait due to scrub typhus. Scrub typhus can present as acute or subacute meningitis complicated by multiple cranial palsies and cerebellitis. Hence it needs to be differentiated from acute bacterial meningitis and tubercular meningitis as delay in diagnosis and treatment will affect the morbidity and mortality.

Case History

A 24 years female was admitted with five days history of fever associated with chills followed by diffuse and severe headache on day three of illness. On the morning of day four, she noticed sudden onset drooping of left eyelid, diplopia and deviation of angle of mouth along with unsteadiness of gait with tendency to fall towards left. There was no history of vomiting, convulsions, altered consciousness, any other cranial nerve involvement or weakness of any part of the body. There was no respiratory, abdominal or urinary complaint. On examination, she was febrile with a temperature of 102.3°F and haemodynamically stable. There was an eschar over the left axilla (Figure 1 Eschar).

On neurological examination, there were infra-nuclear palsies of oculomotor nerve with pupillary sparing, glossopharyngeal nerve, vagus nerve and hypoglossal nerve and supra-nuclear paralysis of facial nerve on the left side. Cerebellar signs such as gait ataxia, dysmetria and dysdiadochokinesia were present on the left side. Examination of motor and sensory system was normal. Rest of the systemic examination was normal. On investigations she had leukocytosis (13600/mm³) with neutrophilia (90%), normal platelet count (2,50,000) and erythrocyte sedimentation rate was 40 mm in 1st hour. Her liver function tests (LFTs) showed total serum protein-7.1gm/dl, serum albumin-3.8 gm/dl, total serum bilirubin-1.66mg/dl, direct bilirubin-1.0mg/dl, aspartate aminotransferase-196 U/litre, alanine aminotransferase 98 U/litre. Renal functions were normal. Weil-Felix test was positive (OXK-1:320). Her IgM ELISA (inBios International, Inc. USA) was positive for scrub typhus. Blood and urine cultures were sterile. Chest X-ray, Widal agglutination test, peripheral blood film for malarial parasite were normal. Results of cerebrospinal fluid examination are shown in Table 1.

Non contrast cranial computed tomography on day of admission showed multiple white matter hypodensities in both the cerebellar hemispheres. Postcontrast gadolinium MRI brain done on third day of admission revealed multiple hyper-intensities in right frontoparietotemporal region, right thalamus, left temporal lobe and bilateral cerebellar hemispheres with focal meningeal enhancement on T2 and fluid attenuated inversion recovery images with evidence of restricted diffusion and corresponding low ADC values (Figure 2 MRI of patient obtained 3 days after admission showing hyper intensities in right temporal lobe).
frontotemporoparietal region and left cerebellar hemisphere on T2 weighted fluid attenuated inversion recovery and diffusion weighted images (A-C and Figure 3 T1 weighted postgadolinium MRI showing focal meningeal enhancement in left cerebellar hemisphere). Furthermore, there was swelling of gyral spaces in frontoparietotemporal region. No enhancement was evident on post gadolinium scan (Figure 3). Patient was given doxycycline 100 mg twice a day. She became afebrile on day three of therapy and her total leucocyte count and LFTs were repeated on day seven of admission and were normal. Ninth, tenth and twelfth cranial nerve palsies improved during hospital stay. Third and seventh nerve palsies resolved completely when patient was seen in follow up after one month. Follow up non-contrast cranial computed tomography done on 13th day of admission showed decrease in the size of the hypodensities.

**Discussion**

Neurological involvement in scrub typhus may be attributed to *O. tsutsugamushi* being an intracellular obligate parasite of professional and non-professional phagocytes that invade the central nervous system as a part of systemic infection. Pathologically, mononuclear cell meningitis, typhus nodule, perivascular cuffing of arteries, focal haemorrhages in parenchyma and meninges and degeneration of ganglion cells may be present. Meningitis or meningoencephalitis is the most common manifestation reported in 15%-50% patients with scrub typhus in different studies. Common symptoms include fever (100%, mean duration of fever 7.0±3.5 days to 8.4±3.5 days), headache (76-100%), meningism, altered sensorium (4-50%), Seizures, motor weakness, and cranial nerve deficit are also present. CSF findings of scrub typhus include mild lymphocytic pleocytosis (<250 cells/μL) with mononuclear predominance, raised proteins and normal sugar. Similar CSF findings may be seen in viral encephalitis, tubercular meningitis and leptospirosis. Our patient had fever, headache and CSF findings were consistent with scrub meningitis. Presence of *O. tsutsugamushi* in CSF was demonstrated by Pai et al by nested PCR and Karp and Boryong genotypes were isolated from CSF. An equal proportion of Karp (27%) and Keto (27%) genotypes has been reported from our state. Meningeal enhancement may be seen in neuroimaging studies. In our patient, clinical cerebrovascular involvement was present on the left side though in neuroimaging studies bilateral cerebellar lesions were seen. Involvement of cerebellum in scrub typhus occurs rarely. Cranial nerve involvement is seen in ~25% of patients with symptomatic involvement of abducens, facial and vestibulocochlear nerve with or without meningitis. Besides eighth nerve, ischemia of the glial part and mononuclear infiltrations of other cranial nerve including trochlear, facial, oculomotor, abducens, vago-glossopharyngeal complex and spinal nerve was documented by Noad et al. Two mechanisms have been proposed for cranial nerve involvement in scrub typhus though exact mechanism is not known. These mechanisms involve either direct invasion of central nervous system by *Orientia tsutsugamushi* leading to acute stage vasculitis or secondary immune mechanism causing vasculitis of vasa vasiorem of nerve. In our patient involvement of third, seventh, ninth, tenth and twelfth cranial nerves was seen in early part of illness and deficit improved completely during convalescent period. If the patient of scrub meningitis is presenting during first week of illness with cranial nerve involvement then it poses a diagnostic dilemma as similar clinical presentation is seen in acute bacterial meningitis.

**References**