

Abducens Nerve Palsy in a Patient with Scrub Typhus: A Case Report

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Abstract. Abducens nerve palsy is a known but rare complication of a few bacterial and viral infections like *Mycoplasma pneumoniae*, cytomegalovirus, Epstein-Barr virus, Hanta virus, herpes zoster, and measles. Abducens nerve palsy due to scrub typhus is extremely rare and so far only one case has been reported in the literature. Scrub typhus is a febrile illness caused by rickettsia, *Orientia tsutsugamushi*, a gram negative intracellular obligate parasite which is endemic in Asia. This disease can present with wide range of clinical manifestations with involvement of any organ system, alone or in combination. Central nervous system involvement is very common and includes meningism, altered sensorium to focal neurological deficits. We present a rare manifestation of Scrub typhus in the form of sixth cranial nerve involvement which responded to the treatment with doxycycline.

INTRODUCTION

Scrub typhus is a tropical acute febrile rickettsial disease caused by *Orientia tsutsugamushi* which proliferates within the endothelial cells of small vessels in humans. It is transmitted to vertebral hosts (rodents and humans) by the bite of larval mites (chiggers) of the genus *Leptotrombidium*. This disease occurs throughout Asia and Australia. The geographic range stretches from Far East to Middle East (Koh *et al.*, 2010). There are approximately 1 million new cases each year worldwide and over 1 billion people at risk. The clinical manifestations are diverse and vary from a simple febrile illness to widespread potentially fatal multi-organ dysfunction. Typical systemic clinical features of this infection include fever, headache, myalgias

and gastrointestinal disturbances. A maculopapular rash spreading to extremities from trunk, eschar at the bite site of the mite and regional lymphadenopathy are also commonly seen. Besides these common clinical manifestations, if untreated, this infection is known to cause widespread organ system dysfunction. Involvement of central nervous system manifests as aseptic meningitis, diffuse encephalomyelitis, deafness due to involvement of eighth cranial nerve and rarely peripheral neuropathy. Abducens nerve palsy secondary to scrub typhus is very unusual and rare and so far only one case has been reported in the medical literature (Lee *et al.*, 2010). We present another case of abducens cranial nerve palsy secondary to scrub typhus which resolved following successful antibiotic treatment.

Case Report

A 23 year old female presented to the hospital with complaints of high grade fever, headache and myalgia for 5 days and altered mental status for past 1 day. Her neurological examination revealed some disorientation to time, place and person but initial cranial nerves, motor and sensory system examination was normal. No neck rigidity was demonstrated. Both Kernig's and Brudzinski signs were absent too. Dermatologic examination revealed an eschar (Figure 1) at right lower back and no other rashes were seen. Other organ systems examination including respiratory, cardiovascular and gastrointestinal system was in normal limits. A lumbar puncture was performed due to the history of high grade fever and altered sensorium which revealed mononuclear pleocytosis (lymphocyte count: 15), normal glucose (60mg/dL) and normal proteins levels (40mg/dL). CSF Gram stain and culture were noncontributory. Serum reverse transcriptase polymerase chain reaction for dengue virus was negative. However, polymerase chain reaction analysis (PCR) of the CSF targeting the 56 kDa protein antigen specific to *O. tsusugumashi* was positive. Patient was started on oral doxycycline therapy.

On second day she developed sudden diplopia with right esotropia (Figure 2A). Visual acuity was normal, pupils were isochoric and fundus examination was normal too. Ocular muscle examination showed profound weakness of the right lateral rectus muscle. On the basis of these findings, a diagnosis of right abducens nerve palsy was made.

A cranial magnetic resonance examination was normal. Her right abducens nerve palsy completely resolved with doxycycline (Figure 2B).

DISCUSSION

Scrub typhus presents with wide array of manifestations. The disease begins with the inoculation of the pathogen in the skin following the bite of the mite. Multiplication of the organism at the bite site frequently results in eschar (Figure 1) formation which is a pathognomic clinical finding seen in 7%-80% patients. The incubation period in human hosts range between 6-21 days. Pathologically, this disease is characterized by focal or disseminated vasculitis and perivasculitis. The diagnosis of scrub typhus is based on the patient's history of exposure,



Figure 1. Eschar from the bite of a *Leptotrombidium* mite

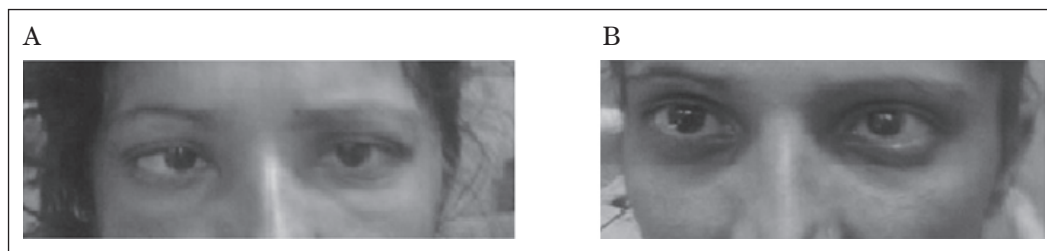


Figure 2. A: Right esotropia of in primary position limited abduction in the right eye. B: Resolved right esotropia with limitation in abduction in the right eye following antibiotic treatment

Table 1. Common organ system complications seen in scrub typhus

Central Nervous System	Aseptic Meningitis Meningoencephalitis Sensorineural Hearing Loss (8 th nerve) Seizures Vasculitic Cerebral Infarct
Respiratory System	Interstitial Pneumonia Consolidation Pleural Effusion Hilar Lymphadenopathy Acute Respiratory Distress Syndrome (ARDS)
Cardiovascular System	Cardiac Rhythm Abnormalities Myocarditis Cardiomegaly Congestive Heart Failure
Gastrointestinal System	Hepatitis Acalculus Cholecystitis Splenic Vasculitic Infarcts Ascites Pancreatitis
Renal System	Acute Renal Failure

the clinical features, and the results of serologic testing. Demonstration of eschar (Figure 1) on physical examination although pathognomic is seen in variable frequency. The mainstay of laboratory diagnosis remains serologic testing. CSF examination in these patients is consistent with aseptic meningitis. Focal neurological deficits in the form of monoparesis, hemiparesis have been described with scrub typhus infection. Lee *et al.* (2007) reported a case of scrub typhus associated with Guillain Barre Syndrome. Cranial nerve involvements are rarely seen in patients with scrub typhus with most

notable involvement of eight cranial nerve presenting as sensorineural hearing loss (Kang *et al.*, 2009). Lin *et al.* (2011) described a patient of scrub typhus presenting with bilateral facial nerve paralysis. Involvement of abducens nerve alone in scrub typhus is very rare and besides our case, only other case reported was by Lee *et al.* (2010). The exact mechanisms behind the development of different cranial nerve involvement including the palsy of abducens nerve is still unclear. One of the proposed hypothesis includes microinfarction of the abducens nerve due to vasculitic involvement of vasa

vasorum of the nerve and stretching of the vessels due to dilated ventricles (Kang *et al.*, 2009; Lee *et al.*, 2010). Isolated abducens nerve palsy due to some viral and bacterial infections have been reported to cause abducens nerve palsy either unilaterally or bilaterally. Most notably *Mycoplasma pneumoniae*, West Nile fever, dengue fever, brucellosis, tuberculosis and cytomegalovirus have been associated with abducens nerve palsy. (Neuberger *et al.*, 1979; Cunha *et al.*, 2006; Greco *et al.*, 2006; Daniel *et al.*, 2009; Shivnathan *et al.*, 2012). Some reports also describe nerve palsies secondary to immunizations for measles, measles-mumps-rubella, diphtheria-tetanus-pertussis vaccines (Werner *et al.*, 1983; Lee *et al.*, 2007; Kang *et al.*, 2009). Scrub typhus is known to involve the central nervous system frequently but involvement of only the abducens nerve is very rare with only one such case being reported in medical literature (Lee *et al.*, 2010).

In our patient, given the development of abducens nerve palsy at the peak of symptoms of scrub typhus and more importantly, complete resolution of the deficit with antibiotic therapy, we conclude that this event was most likely secondary to scrub typhus infection. In endemic areas, isolated abducens nerve palsy especially with other associated classic clinical features like headaches, high grade fever, eschar and maculopapular rash should alert physicians to the possibility of scrub typhus. It is also important to note that, central nervous system involvement with scrub typhus including cranial nerve deficits are easily reversible without any permanent sequelae with timely diagnosis and with appropriate antibiotics such as doxycycline, chloramphenicol and fluroquinolones.

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