INTRODUCTION
Scrub typhus is a mite borne infection, caused by Orientia tsutsugamushi. It is a common cause of pyrexia of unknown origin, especially in the Indian subcontinent. Although it is well known that the infection can affect various systems, and present itself in myriad ways, we present a rare finding of opsinclonus associated with scrub typhus infection. It emphasizes on how even common and well known diseases can have unusual manifestations.

Key words: Opsoclonus myoclonus syndrome, Scrub typhus

ABSTRACT
Scrub typhus is a mite borne infection, caused by Orientia tsutsugamushi. It is a common cause of pyrexia of unknown origin, especially in the Indian subcontinent. Although it is well known that the infection can affect various systems, and present itself in myriad ways, we present a rare finding of opsoclonus associated with scrub typhus infection. It emphasizes on how even common and well known diseases can have unusual manifestations.

INTRODUCTION
Scrub typhus is a rickettsial infection, caused by Orientia tsutsugamushi, and transmitted to humans by the bite of the Trombiculid mite. Classically presenting as pyrexia of unknown origin, its physical manifestations can vary from mild illness to multiorgan dysfunction. Florid central nervous system (CNS) manifestations are however, uncommon. We present the case of a patient diagnosed with scrub typhus, presenting with opsoclonus.

CASE REPORT
A 60-year-old male, who had no major illness in the past, was admitted with complaints of fever with chills for 2 weeks, associated with yellowish discoloration of eyes for 2 days. On examination, patient was deeply icteric, but had no other general examination findings. On central nervous system examination, patient was found to be drowsy but oriented to time, place and person, with a Glasgow Coma Score (GCS) of 12/15. There were no sensory, motor or cerebellar deficits, and no abnormal movements. Cranial nerve examination was normal. Eye examination showed multiaxial, involuntary, saccadic movements of both eyes, suggestive of an opsoclonus. There was no limitation of voluntary eye movements, with full range of uniocular and conjugate eye movements.

Respiratory system examination revealed bilateral diffuse crepitations, throughout both lung fields. Per abdominal examination showed no hepatosplenomegaly. Careful systemic examination revealed the presence of an eschar at the anterior border of the right axilla.

Routine investigations revealed a deranged liver function test (LFT), with a total bilirubin of 17.3 mg/dL, direct bilirubin of 15.6 mg/dL, two fold elevations of aspartate transaminase (AST) and alanine transaminase (ALT) levels, and a 10 fold elevation of alkaline phosphatase (ALP) levels (Table 1). Renal function test (RFT) was also deranged, with serum urea 132 mg/dL and creatinine 2.6 mg/dL. Total counts were 9000 cells/mm³. Platelet counts were low, at 22000 cells/mm³. Chest X-ray (CXR) showed bilateral diffuse heterogeneous opacities, suggestive of Acute Respiratory
Distress Syndrome (ARDS); arterial blood gas analysis showed type I respiratory failure; Electro-cardiogram (ECG) and Echocardiogram were normal. In view of the eschar, Scrub IgM and Immunofluorescence were sent. Scrub IgM (BacT/ALERT FA PLUS, Biomereieux Inc, Durham NC) was positive, and immunofluorescence was strongly positive (1:128). Blood cultures were sterile.

A diagnosis of Multi-Organ Dysfunction Syndrome due to Scrub typhus was made. Patient was treated with a full course of azithromycin and doxycycline. Patient recovered rapidly after initiation of treatment, with complete resolution of all signs and symptoms; patient was conscious, oriented, with normal liver and kidney function, and normal CXRs, at the time of discharge. Patient was treated with a tapering dose of steroids for the ARDS, and initially managed with non-invasive ventilation which was changed to oxygen through Venturi mask as the patient recovered; chest findings were normal at the end of 6 days of treatment (Figure 1).

The opsoclonus observed at presentation decreased 2 days after initiation of therapy for Scrub typhus, and was absent 3 days after treatment with doxycycline and azithromycin. That the opsoclonus was a part of the

<table>
<thead>
<tr>
<th>Laboratory investigation</th>
<th>Day 1*</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 7</th>
<th>Day 9</th>
<th>Day 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Bilirubin (mg/dL)</td>
<td>17.3</td>
<td>14.6</td>
<td>5.7</td>
<td>-</td>
<td>3.6</td>
<td>2.1</td>
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<tr>
<td>Direct bilirubin (mg/dL)</td>
<td>15.6</td>
<td>12.5</td>
<td>5.0</td>
<td>-</td>
<td>2.3</td>
<td>1.5</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>103</td>
<td>108</td>
<td>84</td>
<td>-</td>
<td>55</td>
<td>49</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>49</td>
<td>45</td>
<td>64</td>
<td>-</td>
<td>89</td>
<td>80</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>459</td>
<td>390</td>
<td>500</td>
<td>-</td>
<td>336</td>
<td>214</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>2.6</td>
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<td>1.2</td>
<td>1.0</td>
<td>0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Urea(mg/dL)</td>
<td>132</td>
<td>167</td>
<td>119</td>
<td>-</td>
<td>88</td>
<td>48</td>
</tr>
</tbody>
</table>

AST = aspartate transaminase; ALT = alanine transaminase; ALP = alkaline phosphatase
*treatment initiated

Figure 1: Chest X-ray showing the presence of bilateral fluffy opacities, suggestive of ARDS (left) and showing complete resolution, 8 days after initiation of treatment (right).
underlying infection was proven by the fact that it disappeared rapidly on treatment.

DISCUSSION

CNS involvement in scrub typhus occurs in a sizeable number of patients, with an estimated prevalence of 12.5%-26%. Proposed mechanisms for entry of the causative agent into the CNS include infecting the circulating monocytes during a meningeal inflammation or by directly invading the endothelium through the luminal membrane and then being released, through the basal cell membrane, into the perivascular space.

Scrub typhus most commonly presents as either meningitis or meningo-encephalitis. However, myriad manifestations have been described in literature. Cranial nerve deficits have been reported in up to 25% of patients, with the abducens nerve being the most commonly involved nerve. Trigeminal neuralgia, acute sensorineural hearing loss and facial nerve palsy have also been reported. Chiou YH et al described a case of a patient developing transient Parkinsonism with myoclonus after a scrub typhus infection. Chen et al reported a case of Scrub typhus presenting as Acute Disseminated Encephalomyelitis. Various case reports have been published describing peripheral nervous system involvement in scrub typhus in the form of Guillain Barre Syndrome or Polyneuropathy. However, scrub typhus presenting with opsoclonus is an entity rarely reported.

Opsoclonus can be broadly classified as having paraneoplastic, parainfectious and miscellaneous causes. It is seen more often in children, in whom paraneoplastic conditions take precedence over parainfectious causes, with the most common malignancy being a neuroblastoma. Descriptions of opsoclonus in adults are largely confined to case reports and small case series, wherein parainfectious causes are more or equally likely as paraneoplastic conditions; paraneoplastic conditions may need to be excluded based on clinical context. Infections described in association with opsoclonus include Lyme’s disease, post streptococcal, varicella zoster virus (VZV), Epstein barr virus (EBV), Coxsackie b virus, enterovirus and West Nile encephalitis virus. Opsoclonus-myoclonus syndrome may develop during the human immunodeficiency virus (HIV) seroconversion illness. Malignancies described with opsoclonus in adults most commonly include small cell cancer of the lung, followed by breast, gastric, ovarian malignancies and malignant melanomas.

Rare non-paraneoplastic, non-parainfectious autoimmune cases have been reported. One case report mentions opsoclonus in a patient with glutamic acid decarboxylase-65 (GAD65) antibody. Another unusual reported entity is OMS developing during pregnancy, which is assumed to have an autoimmune cause. Opsoclonus has also rarely described following exposure to cocaine and phenytoin.

D’sa S et al,1 and TS Nam, et al,2 have described patients, who presented with fever and jaundice, having an opsoclonus on examination, along with an eschar. The patient was treated with Doxycycline, with rapid resolution of symptoms.1,2

Our patient was well premorbid, and had no signs or symptoms suggestive of malignancy. Clinical examination showed an eschar, and
rapid resolution of the opsoclonus occurred with the initiation of treatment for Scrub typhus, hence no further evaluation was done. To the best of our knowledge, this is only one of the few reports published regarding this peculiar manifestation of scrub typhus. It underlines how even common and well known diseases can have unusual manifestations.

REFERENCES