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A rare presentation of neurological scrub typhus with hydrocephalus: Case report

Yarraiahgari Maheswara[1*], **Revat Meshram**[2], **Jayant Vagha**[3], **Amar Taksande**[4]

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Authors' Affiliation:
[1]Post Graduate student, Department of paediatrics, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi, Meghe, Wardha, Maharashtra, India, Pincode-442004
[2]MD Associate Professor, Department of Paediatrics, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi, Meghe, Wardha, Maharashtra, India, Pincode-442004
[3]MD Professor, Department of Paediatrics, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi, Meghe, Wardha, Maharashtra, India, Pincode-442004
[4]MD Professor, Head of Department, Department of Paediatrics, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi, Meghe, Wardha, Maharashtra, India, Pincode-442004

Contact List

Yarraiahgari Maheswara	ymahesh963@gmail.com
Revat Meshram	rjmeshram@yahoo.com
Jayant Vagha	jayantvagha@gmail.com
Amar Taksande	amar.taksande@gmail.com

[*]**Corresponding Author**
Post Graduate student, Department of Paediatrics, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi, Meghe, Wardha, Maharashtra, India
Email: yamhesh963@gmail.com

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ABSTRACT

Scrub typhus is zoonotic disease caused by *Orientia tsutsugamushi*. Scrub typhus transmits to human beings by arthropod vector of the Trombiculidae family (*Leptotrombidium deliense* and *L. akamushi*). The incidence of this disease is rising in various parts of India. Clinical manifestations could range from constitutional symptoms like fever, weakness, anorexia and headache to dermatological manifestations like eschar, lymphadenopathy and maculopapular rash. Eschar is considered pathognomic in suspecting scrub typhus. Complications of the disease include myocarditis, acute respiratory distress, jaundice, atypical meningitis and kidney failure amongst others. Here, this case report is about a 5-year-old boy who presented with rare complication of scrub typhus which is multiple cranial nerve palsies, meningitis and hydrocephalus. The presence of the characteristic eschar over the abdomen raised the suspicion of Scrub typhus. Diagnosis was confirmed by a positive serology and the patient responded well to medical management with injectable doxycycline.

Keywords: Scrub typhus, Meningitis, Eschar, Cranial nerve palsy, hydrocephalus

1. INTRODUCTION

Scrub typhus is a mite-borne infectious disease which is caused by *Orientia tsutsugamushi* (previously known to be *Rickettsia tsutsugamushi*). This disease was first described by the Chinese in the 3rd century, but the description of its classical features did not appear in the western literature until the end of the 19th century. Farmers accounted for approximately two-thirds of all reported cases with incidence rates being the highest in people aged 40 to 60 years of age. However, it was seen that young children had higher rates of infection than young adults. Around 80 percent of the cases occurred during the months of summer and autumn (July to November). *O. tsutsugamushi* is an obligate intracellular bacterium which primarily targets endothelial cells and phagocytes for replication (Rodino et al., 2019). Hence, the disease pathogenesis occurs predominantly in highly vascularized organs like the lung, liver, brain, etc (Xu et al., 2017) and may also present with nonspecific febrile illness or constitutional symptoms like fever, macular or

maculopapular rash, myalgia and headache. The appearance of eschar occurs at the site of the infecting chigger bite. Subsequent central necrosis follows, which in turn leads to the formation of a characteristic eschar with a black crust or with organ dysfunction, such as involvement of the kidney in form of acute kidney injury or lung in form of pneumonia or heart in form of myocarditis, liver in form of hepatitis or even the central nervous system in the form of meningitis (Misra et al., 2015). Micro immunofluorescence is considered as the investigation of choice. Lymphohistiocytic vasculitis on skin biopsy is a classical finding and is considered as the pathological hallmark for scrub typhus (Chung et al., 2012). Doxycycline is the drug of choice. Alternative effective drugs are macrolides.

2. CASE REPORT

A 5-year-old male child was brought to the hospital with complaints of fever for 10 days, blackish discoloration of skin over lower abdomen for 5 days, weakness on left upper limb and lower limb, left side drooping of eye lids and inward deviation of left eye for 4 days. As narrated by the mother, child developed continuous fever which was abrupt in onset, high grade in nature, not associated with chills and rigors, no diurnal and seasonal variation and associated with generalised, dull aching type of headache and body pain. Patient also had blackish discoloration of skin over lower abdomen constituting a single, painless, nonpruritic rash around 1cm in diameter. Patient initially had poor oral intake with decreased activity which progressed over two days to weakness on left side upper and lower limb. This was associated with left sided drooping of eye lids and inward deviation of left eye (Figure 1).

Figure 1 Ptosis and medial deviation of left eye

Patient was immunized as per national immunisation schedule and had a normal developmental history. There was no significant past or family history. There was no history of exposure to any toxins or ingestion of any drugs. On admission to our PICU, child was afebrile, drowsy with vital parameters of heart rate of 60/ min, respiratory rate of 22 beats per min, blood pressure-130/80 mm hg with no requirement of oxygen. Local examination of the rash revealed a crusty, necrotic lesion in lower part of abdomen below umbilicus, 1x0.5 cm in diameter associated with inguinal lymphadenopathy, most probably an eschar (Figure 2).

Central nervous system examination showed that the patient was drowsy, not oriented to time, place and person, GCS score - 12/15, with drooping of left eyelid (left oculomotor nerve palsy), medial deviation of left eyeball (left abducens nerve palsy), hypotonia, power- 3/5 in left upper and lower limb with normal tone and power on right side. Superficial and deep tendon reflex

were normal in all 4 limbs, plantar reflex- extensor on left side, flexors on right side. There were no sensory, cerebellar and meningeal signs noted. Abdominal examination revealed soft, non-tender abdomen with liver palpable 3 cm below coastal margin and no splenomegaly. All other systems were within normal limits.

Patient was kept nil per oral and started on IV fluids, inj. Ceftriaxone, inj. Pan and inj. Paracetamol. Hypertonic saline loading followed by maintenance was given in view of depressed sensorium, bradycardia and hypertension suspecting raised intracranial pressure. Laboratory investigations showed CBC- Hb-10.4 gm/dL, TLC- 15000/c.mm, platelet-3.09 lakhs, CRP-18.56 (elevated), ESR-33 (elevated), mildly elevated liver enzymes and normal renal function. MRI brain with contrast and venography was done in view of medial deviation of left eye and ptosis of left eye. Report suggestive of supratentorial ventriculomegaly with sulcal effacement (Figure 3).

Figure 2 Crusty, necrotic Eschar 1 x 0.5cm, present over lower part of abdomen

Lumbar puncture was done in view of meningitis, report suggestive of CSF glucose- 60, parallel sugar- 96 mg/dl, protein- 101, LDH-78, Ph-7.2, presence of 40 cells predominantly lymphocytes, suggestive of atypical meningitis. TB work up was done which was suggestive of Mantoux test negative and CBNAAT negative. ELISA for scrub typhus–positive, so injectable doxycycline was added.

Child responded well to injection Doxycycline. Within 24 hours, fever spikes subsided and within 48 hours of starting treatment, proper sensorium was regained with GCS of 15/15. On 5th day, improvement was noted in weakness of the left hand and leg with power increasing to 4/5. On 8th day ptosis and medial squint of the left eye started improving. Doxycycline was continued for 10 days and omitted. Child was shifted to ward and discharged after 14 days. On discharge child had regained full power of life upper and lower limb and there was complete resolution of ptosis and medial deviation of eye. Child was advised to repeat an MRI Brain after 3 weeks and discharged. Patient came for follow up MRI Brain was done and hydrocephalus regressed (Figure 5).

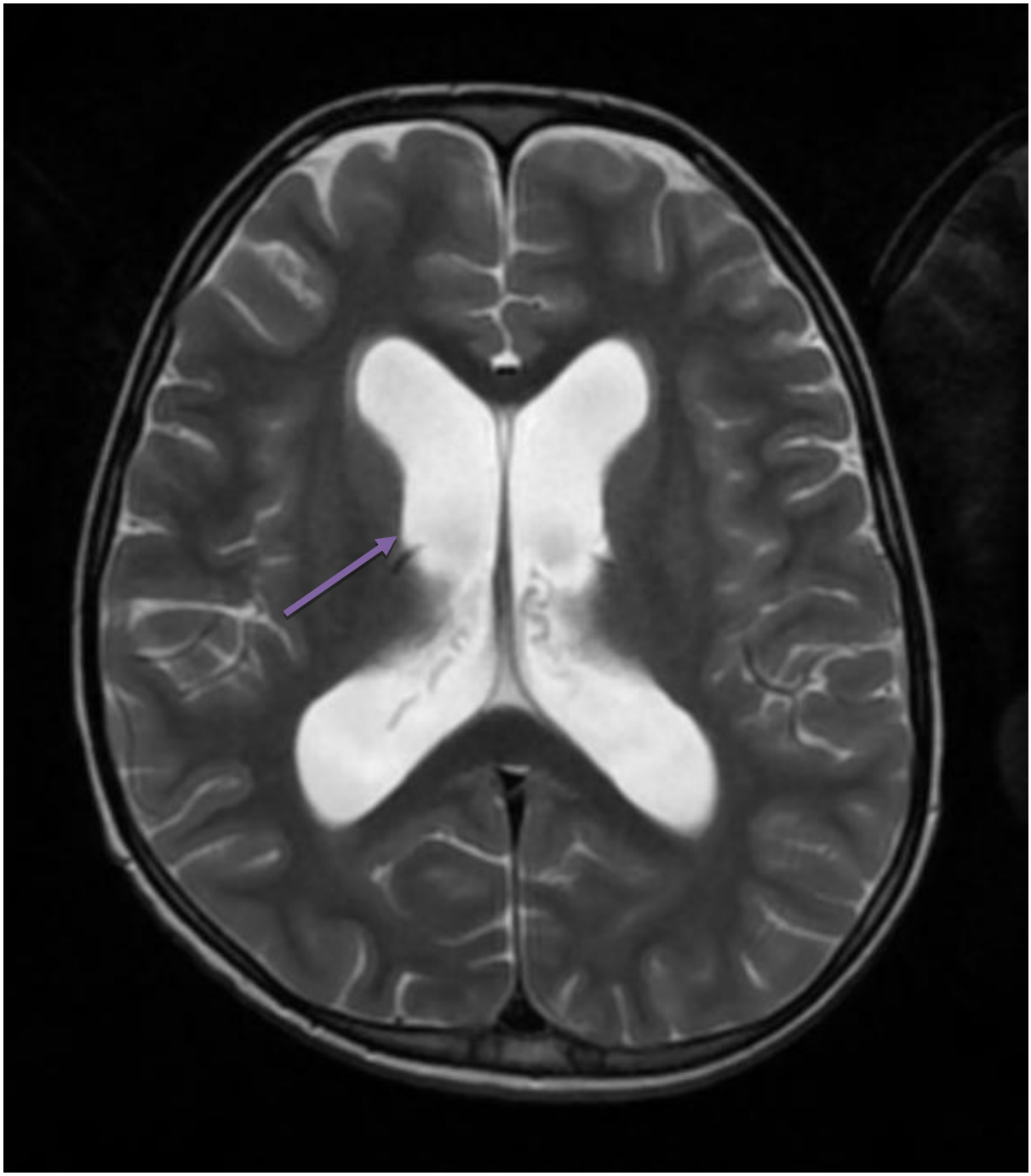

Figure 3 T2 axial MRI image showing dilation of bilateral lateral ventricles and mildly dilated fourth ventricle (Figure 4) which could be secondary to meningitis

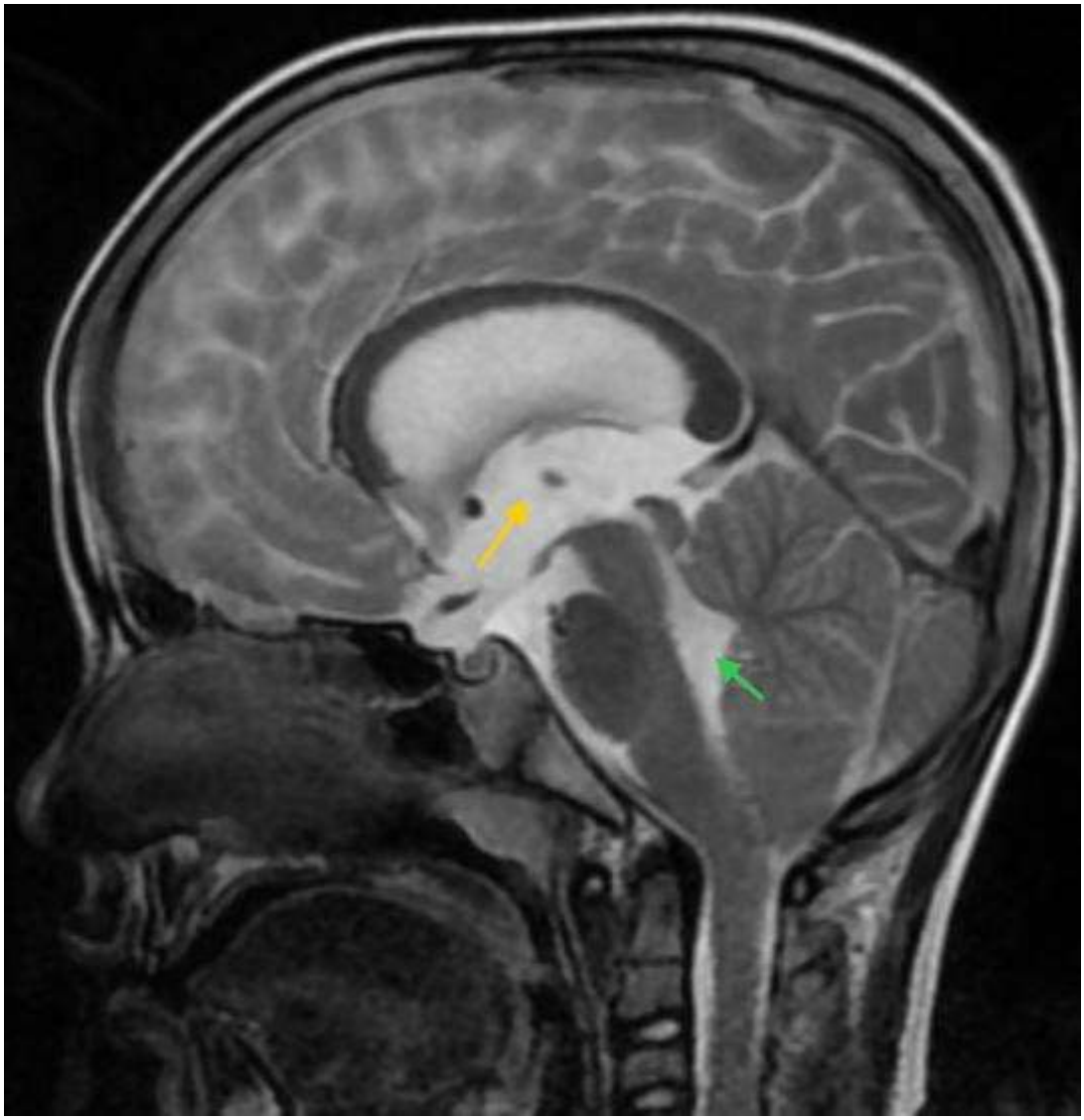

Figure 4 T2 Sagittal MRI showing dilated third (yellow) and fourth (green) ventricles

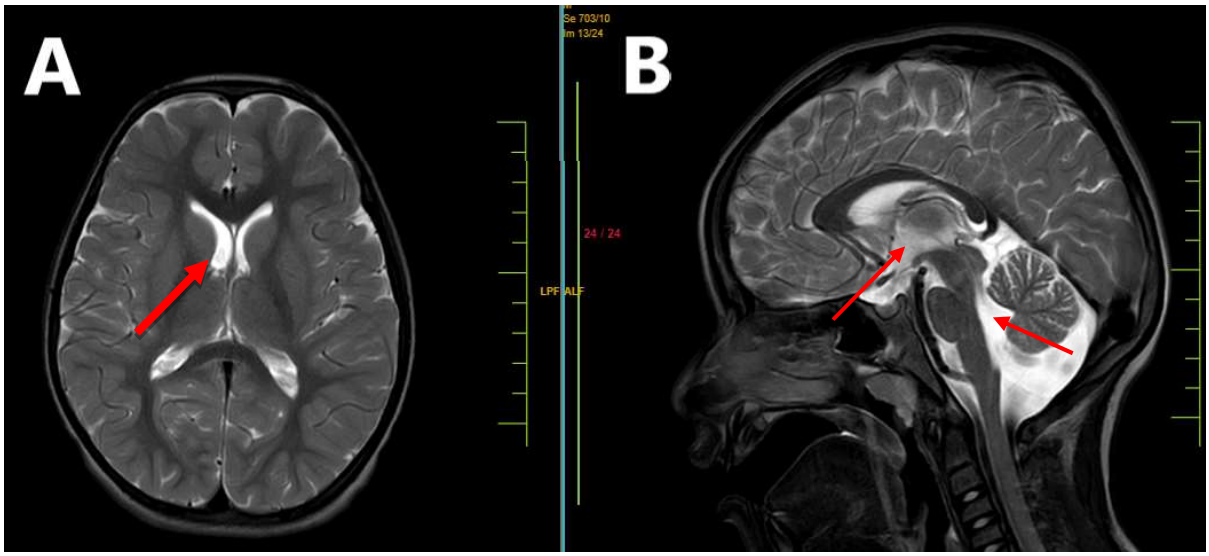

Figure 5 MRI T2WI axial (A) and sagittal (B) images at the level of gangliocapsular region show no obvious abnormality with the normal ventricular system

Our patient hence presented as a rare form of neurological scrub typhus with hydrocephalus which completely regressed with oral doxycycline.

3. DISCUSSION

The differentiating features between scrub typhus and bacterial meningitis are that the former has longer duration of fever prior to the presentation than later. Similarly, the differentiating features between scrub typhus and TB meningitis is that scrub typhus meningitis has lesser duration of symptoms and lesser CSF pleocytosis, protein, adenosine deaminase (ADA). One of those diseases is becoming more prevalent in India and other south-east Asian nations. The 56-kDa protein, which is unique and only expressed by *O. tsutsugamushi*, is a type-specific protein that neither Rickettsia nor other bacteria produce. *O. tsutsugamushi's* genetic diversity is the result of variations in this protein sequence, which is special and contains cross-reacting epitopes. Additionally, this protein has been researched for use in vaccine development (Paris et al., 2011).

The CNS involvement is very common in scrub typhus and it can manifest in various forms. Up to one-fifth of patients can have prominent nervous system involvement. Clinical presentation is Meningoencephalitis followed by Aseptic meningitis. Cerebrospinal fluid (CSF) analysis results, however, either show low number of monocytes or are normal. But in our patient the cerebrospinal fluid (CSF) analysis had lymphocytic predominance which was suggestive of atypical meningitis, which was uncommon. Cranial nerve deficits are seen in 25% patients. The involvement of 2nd, 3rd, 6th, 7th and 8th cranial nerves has been documented in patients with scrub typhus (Bhardwaj et al., 2013). Most commonly sixth cranial nerve involvement is seen, which can be either unilateral or bilateral. In our patient unilateral 3rd and 6th cranial nerve involvement was present. Development of sixth nerve palsy occurs at peak of symptoms of scrub typhus and more importantly, complete resolution of the deficit with antibiotic therapy (Bhardwaj et al., 2013). Facial palsy may occur in isolation or association with Guillain Barre Syndrome (Raghunathan et al., 2022). About 19% of patients showed cochlear nerve involvement, which results in sensorineural hearing loss, otalgia and tinnitus. This might be as a result of the pathogen directly invading or as a result of a secondary immune-mediated effect. Other neurological manifestations include seizures, vasculitic cerebral infarct, cerebellitis (Karanth et al., 2013), plexopathy, transverse myelitis, neuroleptic malignant syndrome and Guillain-Barre syndrome. Though many neurological complications of scrub typhus have been mentioned in literature, presentation of scrub typhus with hydrocephalus is a unique entity and has not been discussed in previous case reports. Hence our case report explores this rare complication of scrub typhus.

During the second week of the illness, some patients may also develop tremors, anxiety, slurred speech, nuchal rigidity or deafness. Extreme CNS involvement, such as seizures or brain death, is uncommon. Acute hearing loss if present, strongly suggests scrub typhus, which may be the case in up to one-third of patients, according to some reports (Phimda et al., 2007). Neurological manifestations in scrub typhus does not occur in isolation but are accompanied by multisystem involvement. Pulmonary complications are like pleural effusion, acute respiratory distress syndrome, consolidation and hilar lymphadenopathy are known in literature. Acute respiratory distress syndrome (ARDS) is considered to be one of the grave complications of scrub typhus infection and manifestations may vary from bronchitis, interstitial pneumonitis progress to ARDS in the lungs (Im et al., 2014). Cardiovascular complications like myocarditis (Chayakul et al., 1988), congestive heart failure, cardiomegaly and cardiac rhythm abnormalities have also been reported. Acute renal failure (Sittiwangkul et al., 2008), DIC (Tsai et al., 2010) is also seen. Gastrointestinal complications like ascites, hepatitis, pancreatitis (Vikrant et al., 2013), splenic infarcts are seen, but are rare.

Scrub typhus treatment must begin early in the course of the illness, based on a presumptive diagnosis, in order to reduce morbidity and mortality. The treatment of choice is tetracycline (most preferably Doxycycline). Early initiation of doxycycline leads to early control of symptoms. Constitutional symptoms like fever will subside within 1-2 days of starting treatment (Fang et al., 2012). Doxycycline should be continued for minimum of 7 days. Noncompliance of treatment leads to recurrent relapses. Newer macrolides like azithromycin which are equally effective and appropriate in children (Rajapakse et al., 2011; Phimda et al., 2007). Rifampin and azithromycin can be used as an alternative therapy in cases where there is resistance to Doxycycline (Corwin et al., 1999). The majority of scrub typhus' neurological symptoms, such as meningitis, encephalitis, myositis and cerebellar dysfunction, were successfully treated with these antibiotics. Transverse myelitis, Guillain-Barre syndrome and optic neuritis were indications of conditions with an immune pathogenesis that required treatment with steroid therapy or intravenous immunoglobulins.

4. CONCLUSION

The importance of this case report is to draw attention to the need for detailed clinical history, physical examination and knowledge on clinical presentation of scrub typhus like atypical meningitis, cranial nerve palsies and hydrocephalus. As the incidence of Scrub Typhus is increasing, an early suspicion of scrub typhus always helps in faster diagnosis and initiation of treatment. This in turn

will reduce the incidence of complications. Our patient responded well to medical management and required no surgical intervention in spite of having serious CNS complications like hydrocephalus.

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Author contribution

Yarraiahgari Maheshwara has collected information and prepared the manuscript, which has been thoroughly reviewd by Dr Revat meshram, Dr Jayant vagha and Dr Amar taksande. All the authors have read and agreed to the final manuscript.

Informed consent

Written and oral consent was obtained from patient relatives.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data collected during this study are available upon reasonable request from the corresponding author.

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