

Varied presentation of rickettsial meningoencephalitis in children: A case series

*Sarika Bhimrao Gaikwad¹, Punam Uke¹, Ashwini Kundalwal², Lavanya Ramakrishnan¹, Sai Samhita Chundi¹

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Introduction

Rickettsial fever is seen in the Himalayan region, Maharashtra, Karnataka, Kerala, Tamil Nadu, and many other regions in India mainly in adults¹. Clinically, rickettsial disease ranges from a mild illness to a very severe illness involving the central nervous system (CNS), with a mortality rate of 2-30%². Common neurological presenting features of rickettsial fever include meningitis, encephalitis, meningoencephalitis and acute disseminated encephalomyelitis³. Weil-Felix test, though routinely available, does not confirm the diagnosis. Immunofluorescence assay is the gold standard for diagnosing rickettsial fever but due to non-availability and high cost is not commonly used in developing countries⁴. We report 3 cases of rickettsial meningoencephalitis with varied clinical features.

Case 1

A 1-year-old girl presented with fever, 2 episodes of generalised tonic clonic convulsions (GTCS) and depressed sensorium. Seven days back she developed high grade, intermittent fever without chills and rigors and relieved on taking medication. There was no history of a rash. On admission, she was drowsy, febrile (103°F) and pale with a pulse rate of 130 bpm, regular and well felt. Respiratory rate was 40 per minute and blood pressure (BP) was 90/70 mmHg. She had a hyperpigmented rash over the trunk, not noticed by the parents. On CNS examination, Glasgow Coma Scale (GCS) score was E2, V1, M3. Tone was normal in all 4 limbs, reflexes were normal (2 +), plantar reflexes were flexor,

meningeal signs were absent and there was no cranial nerve involvement. On abdominal examination, liver was palpable 3cm below the costal margin. and firm. Bilateral conducted sounds were heard on respiratory examination.

After admission, child had multiple episodes of convulsions and was started on antiepileptic drugs and injectable 3% sodium chloride, considering increased intracranial tension. Injectable antibiotics were started. The haemoglobin (Hb) level was 7g/dL, the total leucocyte count (TLC) was 26,400/cu mm and the platelet count was 53,000/cu mm. Lumbar puncture was done and the cerebrospinal fluid (CSF) showed pleocytosis (leucocytes 247, predominantly lymphocytes), raised protein (101 mg/dL) and sugar 50 mg; gram stain and acid-fast bacilli (AFB) were negative. Dengue NS1 and Widal tests were negative. Blood and CSF culture were negative. Paracheck for malarial parasite was negative. Liver and renal function tests were negative. Fundoscopy and magnetic resonance imaging (MRI) of the brain were normal. In view of the rash, fever and altered sensorium, scrub typhus IgM was sent and this was positive. Hence tab doxycycline was started and continued for 10 days. Packed red cells (PRC) was transfused in view of the severe anaemia. Patient responded well within 48 hours of starting doxycycline and she became afebrile and regained consciousness. Diagnosis of Rickettsial meningoencephalitis was confirmed as the repeat complete blood count (CBC) showed an increase of the platelet count. Patient was allowed to feed orally and injectable antiepileptics were changed to oral antiepileptics. As child was asymptomatic and haemodynamically stable, she was discharged from hospital.

Case 2

A 5-year-old boy was admitted with fever of 15 days duration and drowsiness during fever spikes. Fever was high grade, intermittent without chills and rigors. There was a history of a macular rash on face and palms on day 3 of illness. There was no history of tick bite but there was a history of an animal shed near his house. On admission, he was shifted to the paediatric intensive care unit (PICU) because of meningoencephalitis.

¹Jawaharlal Nehru Medical College, Wardha, India,

²SMBT, India,

*Correspondence: drsarika.gaikwad@gmail.com



<https://orcid.org/0000-0003-3145-6628>

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On examination, child was febrile and had tachycardia with pulses well felt, Respiratory rate (RR) was 28 per minute and respiratory sounds were vesicular. Abdomen was soft, non-tender with no organomegaly and bowel sounds were present. Cardiac sounds were normal with no murmurs. CNS examination revealed exaggerated deep tendon reflexes, extensor plantar reflexes, absence of neck rigidity, normal cranial nerves and papilloedema on fundoscopy. A provisional diagnosis of meningoencephalitis was made.

CBC was normal. Serum calcium was low (6.9 mg/dL). CSF revealed 50 cells/cu mm mainly lymphocytes, hypoglycorrhachia (50 mg/dL), and high protein (101 mg/dL). On Gram stain, no organisms were found and on Ziehl Neelsen staining no AFB were found, CSF GeneXpert test to rule out TB meningitis was negative. Cerebral malaria and dengue encephalitis were ruled out with negative paracheck and dengue NS1.

Patient was started on injectable antibiotics, antiepileptics and Inj. mannitol in view of clinically raised intracranial tension. Later Inj. doxycycline was added as scrub typhus IGM was positive and continued for 10 days. T2 axial MRI image of brain showed dilatation of both lateral ventricles (Figures 1 and 2). T2 sagittal MRI showing dilated third (yellow arrow) and fourth ventricle (green arrow). Neurosurgical opinion was sought in view of ventricular dilatation. No active surgical management was advised and mother was asked to do repeat MRI of brain after 3 months. It can be considered as post-rickettsial meningitis sequel as other causes of meningitis and encephalitis were ruled out. Child's fever spikes decreased and sensorium improved and he was discharged.

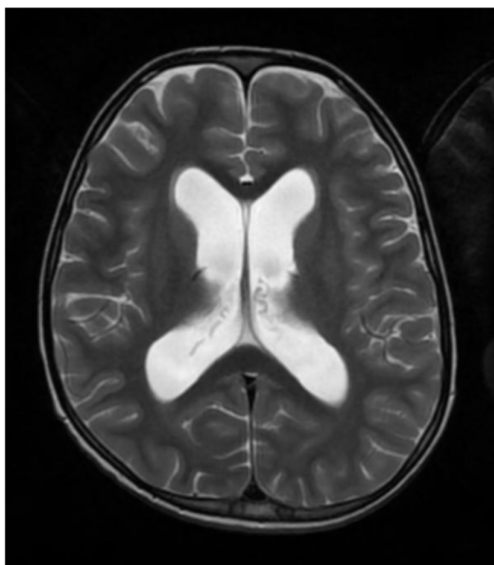


Figure 1: T2 axial MRI image showing dilatation of both lateral ventricles

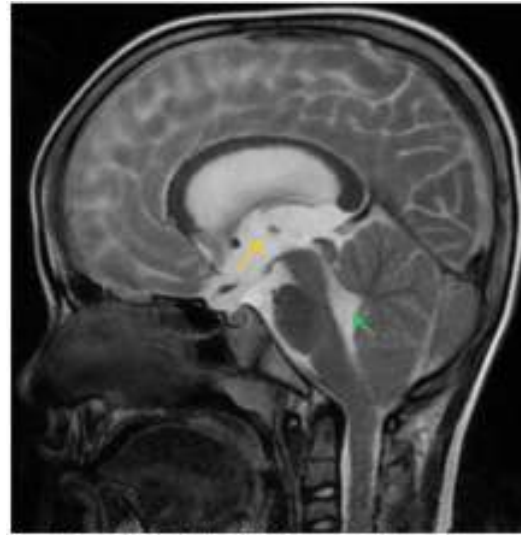


Figure 2: T2 sagittal MRI showing dilated third (yellow arrow) and fourth ventricle (green arrow)

Case 3

A 7-year-old girl was brought with fever for 5 days, vomiting for 3 days, abdominal pain and headache for 2 days and a history of 1 episode of up-rolling of eyes without any posturing present. Fever was high grade, continuous, without chills and rigors and not relieved with medication. On admission, child was conscious, oriented and febrile (104°F). Her radial pulse rate was 120bpm. Child had generalised oedema, without pallor, icterus, rash, lymphadenopathy or neck rigidity. Abdomen was soft and distended with minimal tenderness over right hypochondrium. Liver was palpable 3 cm below costal margin and bowel sounds were present. Cardiovascular and CNS examinations were normal. Due to probable diagnosis of meningoencephalitis, patient was shifted to PICU, kept nil by mouth and started on fluids and injectable antibiotics.

Computed tomography (CT) scan of brain was normal. Lumbar puncture was done and CSF had 240 cells/cu mm, mainly lymphocytes, proteins 102mg/dL, glucose 58mg/dL, gram stain and AFB negative. Paracheck, dengue NS1 and Widal tests were negative. Serum transaminases were raised (aspartate transaminase 180U/L, alanine transaminase 210U/L) with serum albumin low (2.2g/dL). CBC and renal function tests were normal. Ultrasound scan of abdomen and pelvis showed minimal ascites with hepatomegaly. Scrub typhus IgM was positive. Hence child was started on tab doxycycline; despite that patient continued to have fever spike so inj. doxycycline was started. Patient responded well in 48 hours, symptoms improved, oedema decreased and oral intake improved so doxycycline was continued for 10 days. As child was clinically stable, she was discharged from hospital. Table 1 is a summary of the investigations carried out in the 3 cases.

Table 1: Summary of the investigations carried out in the 3 cases

Investigations	Case 1	Case 2	Case 3
Haemoglobin level	77g/dL	107g/dL	8.57g/dL
Total leucocyte count	26,000/cu mm	9800/cu mm	10,200/cu mm
Platelet count	53,000/cu mm	197,000/cu mm	150,000/cu mm
Serum bilirubin	0.5mg/dL	0.6mg/dL	5mg/dL
Aspartate transaminase	64U/L	39U/L	180U/L
Alanine transaminase	43U/L	50U/L	210U/L
Serum urea	16mg/dL	18mg/dL	20mg/dL
Serum creatinine	0.5 mg/dL	0.5mg/dL	0.5mg/dL
Cerebrospinal fluid (CSF) protein	101mg/dL	100mg/dL	102mg/dL
CSF sugar	50mg/dL	50mg/dL	58mg/dL
CSF cells	247/cu mm	50/cu mm	240/cu mm
CSF polymorphs	10%	30%	20%
CSF lymphocytes	90%	70%	80%
Magnetic resonance imaging of brain	Normal	Dilatation of both lateral ventricles, dilated third and fourth ventricles	
Computed tomography scan of brain			Normal

Discussion

Severe CNS involvement has been reported in adults with *Rickettsia conorii* infection⁵, but rarely in children⁶. Neurologic sequelae include meningitis, encephalitis, acute disseminated encephalomyelitis, unilateral facial nerve palsy⁷, cerebral infarction⁸, visual loss⁹ and ataxia. In our case series, the first patient had altered sensorium with status epilepticus, the second had episodes of drowsiness noticed only during fever with clinical features of raised intracranial pressure and the third had fever with headache and normal sensorium. CSF of all 3 patients showed increased cell count and high protein suggestive of meningoencephalitis. In one patient MRI of brain showed ventricular dilatation suggestive of hydrocephalus which has not been documented in any of the previous case reports. Other complications like pneumonia, acute respiratory distress syndrome, cardiac involvement, kidney failure, thrombocytopenia and severe anaemia have been reported¹⁰.

Weil-Felix test is based on the detection of immune-response to certain Proteus antigens which cross react with *Rickettsia*. This test should not be considered a confirmatory method for diagnosis due to its low sensitivity and specificity¹¹. Indirect immunofluorescence assay (IFA) is the preferred serologic test for detecting scrub typhus due to its high sensitivity and specificity but cross-reacting antibodies becomes positive only in the late phase of the disease¹². Enzyme linked immunosorbent assay (ELISA) allows differentiation of IgG and IgM antibodies and is considered more sensitive than IFA as it detects low antibody level even in the acute phase¹³. In our setting we diagnose patients with the Weil Felix test and Immunochromatographic Kit test.

Treatment of choice for children with probable rickettsial fever is doxycycline 2.2 mg/ kg in two divided doses for children under 40 kg weight and 100 mg twice daily for children above 40 kg weight for a total of 7 days. Severe or complicated cases may need 10 days of therapy. It can be given orally, by nasogastric tube or intravenously in severe disease. In most patients, fever decreases within 48 hours of initiation of doxycycline. If fever persists, we need to add some alternative treatment or think of coinfection¹¹.

Rickettsial diseases causes widespread systemic illness in children and is always challenging to paediatrician to diagnose the illness in the early stage due to non-specific signs and symptoms and non-availability of a low cost, rapid diagnostic test.

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