

Acute Onset Flaccid Paralysis as Presentation of Combined Central and Peripheral Demyelination in a Child: A Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Author AD managed the patient, designed the study, wrote the protocol and wrote the first draft of the manuscript. Author AN conceptualized the study, managed literature search and collected the data. Author DG managed the patient, analyses of the study and manuscript drafting. Author RM managed the literature searches, analyses of the study and revision of manuscript. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Introduction: Inflammatory demyelinating disease like combined central and peripheral demyelination (CCPD) could have varied clinical presentation depending upon the topographical distribution of neural involvement.

Case presentation: A seven-year-old child had presented with fever followed by acute onset flaccid paralysis and urinary retention. Weakness in the lower limbs as reported was ascending and symmetric in nature, while no history of trauma, band-like sensation or altered sensorium were documented. Superficial and deep tendon reflexes of both the lower limbs were absent. Routine blood investigations had revealed neutrophilic leucocytosis only. Serum IgM antibody for scrub typhus was found positive. CSF study didn't show cyto-protein dissociation. NCV had demonstrated absence of F wave and H reflex in the peripheral nerves of lower limbs. Anti-ganglioside antibody profiles were negative. Subsequent investigations including MRI brain and spinal cord had revealed acute onset CCPD.

Conclusion: Acute onset combined central and peripheral demyelination in a child had presented as acute flaccid paralysis of the lower limbs and the condition was temporally association with scrub typhus.

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Keywords: *Acute flaccid paralysis; demyelination; immune response; Infectious complications; scrub typhus.*

Key Messages

- Scrub typhus was observed to be an important etiology for causing acute-onset combined central and peripheral demyelination.
- Physicians should be well aware of the varied manifestations of acute-onset combined central and peripheral demyelination.

1. INTRODUCTION

Demyelination is described as a pathologic process of destruction of myelin lamellae of the neural axons or the myelin supporting cells i.e., oligodendrocytes and Schwann cells of the central and peripheral nervous system respectively. Inflammatory demyelinating diseases are recognised to be a broad group of disorders characterised by immune mediated loss of myelin or axonal degeneration which could be difficult to differentiate clinically [1]. Conventionally, inflammatory demyelinating diseases are grouped according to their topographical distribution involving either central or peripheral nervous system in isolation [2,3]. Sequential or combined central and peripheral demyelination (CCPD) of the nervous system is evidently a rare clinical entity which is yet to be explored further, especially in the pediatric population.

2. PRESENTATION OF CASE

A seven-year-old male child had presented with acute onset flaccid paralysis of both the lower limbs during early in 2019. Mild to moderate grade of intermittent rise of temperature was complained for the past one week. Sensation of tingling and numbness preceded by rapid evolution of weakness in both the lower limbs was reported over the last two days which was ascending and symmetric in nature. Subsequently the child became bedridden and was unable to move his lower limbs. In conjunction to this, urinary retention was also reported. He remained conscious throughout, without any respiratory compromise and was able to perform upper limb movements. No band like sensation or history of trauma was present. Before this unprecedented event, the child was active and playful with age appropriate built and nutritional status.

On examination the attitude of the child was supine with outer border of both the feet touching the bed. Bilateral plantar reflex was documented to be absent. Tone of the lower limb muscles was reduced. Power of the muscles in lower limbs was noted to be of grade 1 as per the MRC scale. Knee and ankle jerks were absent. All sensations in the lower limbs were absent. Although no sensory level or specific dermatomal involvement could be observed and urinary bladder was over-distended. Superficial abdominal reflexes were absent. Hearing and visual assessment were normal. No sign of any cranial nerve involvement was found. Clinical assessments including upper limbs and other systems were normal.

Further laboratory investigations revealed neutrophilic leukocytosis (N:76%; TLC:15.5*10³/μL) with all the other indices of routine blood examination lying within the normal domain. Cerebrospinal fluid (CSF) study had reported - protein: 0.76 g/L, glucose: 0.82 g/L, chloride:109 mmol/L, LDH: 7.43 μkat/L, ADA: 116.7 nkat/L and cell count: 256/μL with neutrophilic predominance (70%).

Nerve conduction velocity (NCV) studies of both the lower limbs demonstrated distal latencies, absence of F response and H reflex in common peroneal and posterior tibial nerves, whereas compound motor action potential amplitude was found to be within normal limits for them. Bilateral sensory nerve action potential (SNAP) latencies were recorded normal in sural nerves. Tracing of F wave and H reflex in right tibial nerve shown in Fig. 1 and the findings of NCV study in Table 1. Electromyographic studies recorded normal insertional muscle activity but absence of spontaneous activities and reduced motor unit recruitment.

Magnetic resonance imaging (MRI) study of the brain and spinal cord depicted acute demyelinating lesions. T2 weighted and fluid attenuated inversion recovery (FLAIR) sequences had revealed bilateral hyperintensity involving the parieto-occipital region of the brain; although grey-white differentiation was maintained. Similar increased signal intensity and swelling were observed on MRI for the entire length of the spinal cord, shown in Fig. 2.

Ganglioside antibody profile had failed to demonstrate significant titre of anti-GQ1b, GD1a, GD1b and G11b antibodies with immunoblot method. In concordance to the clue provided with fever, the investigation panel for infective etiologies as per the epidemiological profile of the region, had revealed presence of IgM

antibody for the scrub typhus which was detected by ELISA method. The findings of CSF protein electrophoresis by isoelectric focusing was observed normal alongside absence of anti-MOG and aquaporin-4 antibodies in indirect immunofluorescence assay.

Table 1. Findings of motor and sensory nerve conduction velocity study of both the lower limbs

Motor nerve study	Recording site	Latency, ms	Amplitude, μV	Velocity, m/s
R. PTN	Knee	7.7	6.8	43.4
R. PTN	Ankle	2.6	10.4	43.1
R. CPN	Knee	6.9	0.8	44.2
R. CPN	Ankle	2.6	1.1	44.0
L. PTN	Knee	8.0	9.0	
L. PTN	Ankle	3.1	11.9	46.7
L. CPN	Knee	6.9	2.4	
L. CPN	Ankle	2.8	2.9	46.7
Sensory nerve study	Recording site	Latency, ms	Amplitude, μV	Velocity, m/s
R. Sural	Mid-Calf	1.42	31.5	
L. Sural	Mid-Calf	1.38	24.0	46.4

Abbreviations: R, right; L, left; PTN, Posterior tibial nerve; CPN, Common peroneal nerve



Fig. 1. Tracing of F wave (Recruitment Station: Abductor Hallucis, Stimulation Station: Ankle) and H reflex (Recruitment Station: Soleus muscle, Stimulation Station: Popleteal fossa) in right tibial nerve shown in [A] and [B] respectively

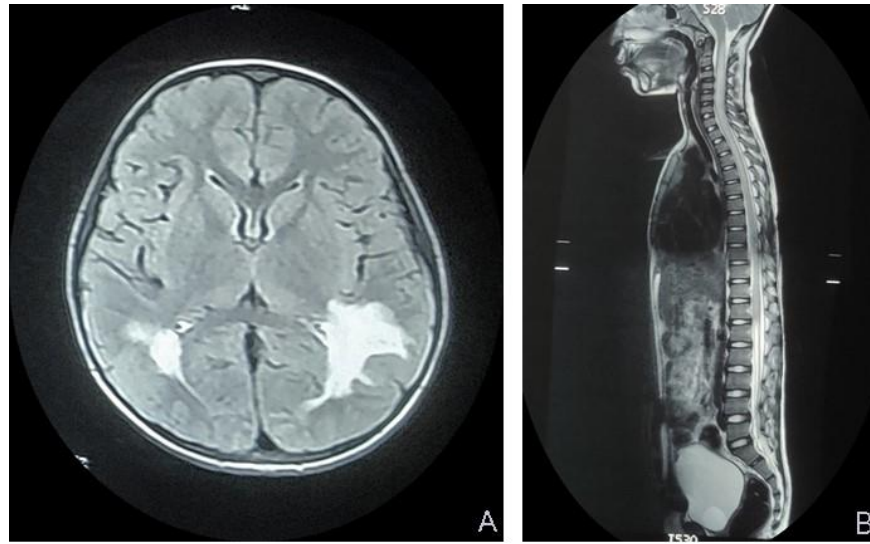


Fig. 2. T2 FLAIR MRI images showing acute demyelinating lesions in the bilateral parieto-occipital region on axial section of brain (A) and on sagittal section of spinal cord (B)

3. DISCUSSION

In the current scenario, acute flaccid paralysis (AFP) in a child preceded by nonspecific febrile illness could fairly be presumed as the presentation of Guillain-Barre syndrome (GBS). Apart from GBS, transverse myelitis was also known for being frequently encountered in the post-polio era [4]. The pattern of progression, predominant site of involvement and type of loss of neuronal functions had helped over the years to constrict the differentials. Additionally, the clinical findings from meticulous systemic examination ought to be of great value in these setting. In presence of the features suggestive of spinal cord and/or cerebral involvement, certain exploration might be required beyond the conventional affair.

Concurrent demyelination involving both the central and peripheral neurons had been discussed scarcely in the pediatric population. The clinical scenario could vary widely depending upon the site of neural affliction and we had observed AFP as a mode of presentation of CCPD. Flaccid paralysis of the lower limbs was observed as a consequence of peripheral nerve or lower motor neuron involvement. Loss of superficial abdominal reflexes, involvement of bladder and bowel control had indicated neural affliction of higher order. Concomitant acute-onset demyelination affecting the peripheral nerves, brain and spinal cord had suggested the clinical entity like CCPD. The CSF study

including unaltered cyto-protein ratio, and the absence of characteristic serological markers had ruled against the established forms of immune mediated demyelinating diseases which could involve the peripheral and central nervous system in conjunction. Additionally, absence of disseminated demyelination in space and time couldn't meet the definitions of the demyelinating diseases which were known to involve central nervous system exclusively. Thus, the clinical scenario under discussion had remained confined to a broader term like acute-onset CCPD.

However, inability to perform peripheral nerve biopsy in order to confirm the pathological form of peripheral neuropathy like demyelinating vs. axonal neuropathy, uniform vs. segmental involvement was considered as the limitations of the present study. But the NCV study had demonstrated slowing of nerve conduction velocity, prolonged terminal latency, and conduction block which had evidently inclined the observations more in favour of demyelination. Whereas normal compound motor action potential, absence of features of denervation on EMG had ruled against the axonal neuropathy [5]. Moreover, the differential involvement of nerves had suggested acquired demyelination. The present report had raised the possibility of further investigations, to sub-classify such cases into acute inflammatory demyelinating polyneuropathy (AIDP) with central demyelination like ADEM, or childhood multiple

sclerosis with peripheral neuropathy, or the other possible combinations under the broad term of CCPD, considering the duration of illness and extent of neurological involvement [1,3,6].

A number of infectious diseases were known to be associated with secondary neural affliction by auto-antibody production causing massive destruction of the myelinated nerves [7-9]. Combined central and peripheral demyelination (CCPD) was classically known as an inflammatory demyelinating disease associated with either infectious or autoimmune origin. Here we had observed similar association with scrub typhus infection. Scrub typhus, a zoonotic disease continued to be prevalent in the tropical regions [10]. It was known for its' neurological manifestation either due to primary involvement causing meningitis, meningoencephalitis or secondary immune mediated affliction causing acute demyelinating encephalomyelitis (ADEM) [11]. The classical sign of eschar formation at the site of bite by the chigger was observed to have a variable incidence and was absent here [12,13]. From what we had understood till now immunologic cross reactivity elicited by the pathogen with the biomolecules sharing structural similarity or spatial orientation between the central and peripheral nerves, was apparently observed to have crucial role for producing auto-antibodies in such circumstances. And correspondingly, the P protein of myelinated peripheral nerves was found analogous to the cerebroside in central nervous system [6]. Yet the clarity might remain far fetched until we could identify the culprit in vivo.

Scrub typhus patients treated with doxycycline during the acute phase of illness had shown remarkable improvement. Treatment with antimicrobials of the patients with primary involvement by the infective organism, might have significant response in terms of recovery than those suffering from immune mediated secondary affliction of the nervous system. Considering the evidence of ongoing demyelination, the standard of care should include systemic steroids followed by tapering, according to the individual response [1,14]. Routine supportive care and physiotherapy also had an important role in the long-term recovery. It was desirable for the physicians in the rural area especially with the limited resources, to be vigilant enough in considering acute onset CCPD as an important differential amongst the other causes for AFP in the children.

4. CONCLUSION

It was witnessed that scrub typhus can be a cause of AFP in children due to acute onset combined central and peripheral demyelination.

CONSENT AND ETHICAL APPROVAL

We had taken approval from our institutional ethical committee for our case study and the reference no for such was - IEC/NBMC.2021-2022/48.

As per international standard or university standard guideline informed consent has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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