Case report

Acute onset flaccid paralysis as presentation of combined central and peripheral demyelination in a child: a case report

Abstract

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

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 aware of the varied manifestations of acute-onset combined central and peripheral demyelination.

Introduction:

Demyelination is described as a pathologic process of destruction of myelin lamellae of the neuronal 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 paediatric population.

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*10^3/ µL) with all the other indices of routine blood examination 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 nerve, whereas compound motor action potential amplitude was found to be within normal limits for them. Bilateral normal sensory nerve action potential (SNAP) latencies were recorded in sural nerves. Tracing of F wave and H reflex in right tibial nerve shown in **Figure 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 of the entire length of the spinal cord, shown in **Figure 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 panel for infective aetiologies as per the epidemiological profile of the region, had revealed presence of IgM antibody for the scrub typhus which was detected by ELISA method. It is worth noting that CSF protein electrophoresis with isoelectric focussing was found normal alongside absence of anti-MOG and aquaporin-4 antibodies with indirect immunofluorescence assay.

Discussion:

In the current scenario, acute flaccid paralysis (AFP) preceded by nonspecific febrile illness could fairly be presumed as a presentation of Guillain-Barre syndrome (GBS). Apart from GBS, transverse myelitis which have similar presentation in the child age group is 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 constringe the differentials. Additionally, the clinical findings from meticulous systemic examination ought to be of great value in these settings. In sight of the features suggesting autonomic nervous system, spinal cord and cerebral involvement, certain exploration was required beyond the conventional affair.

Concurrent demyelination involving both the central and peripheral neurons had been discussed scarcely in the paediatric population. The clinical scenario may vary widely depending upon the site of neuronal 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 involvement. Absence of superficial abdominal reflexes, loss of control of bladder and bowel had indicated neuronal 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 that involve the peripheral or central nervous system exclusively. 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 alone. Thus, the clinical scenario under discussion had remained confined to a broader term of 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 could be 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 instigations, 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 neuronal affliction by auto-antibody production causing massive destruction of the myelinated neurones [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 is a zoonotic disease which has remained 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 similar 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 cerebrosides in central nervous system [6]. Yet the clarity might remain farfetched until we could identify the culprit in vivo.

Serologically positive cases of scrub typhus who received treatment with doxycycline during the acute phase of the disease had shown remarkable improvement. Treatment with antimicrobials in the patients having the primary neuronal involvement by infective organism might have a quicker response 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.

Conclusion:

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

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Legends:

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

Legend 2- Figure 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)

Legend 3- Table 1. Findings of motor and sensory nerve conduction velocity study of both the lower limbs

Figure 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

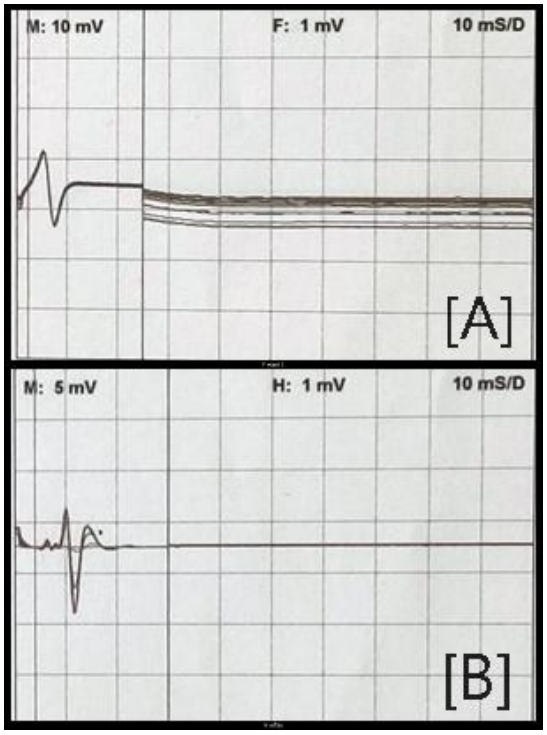

Figure 2.
T2 FLAIR MRI images showing acute demyelinating leisons in the bilateral parieto-occipital region on axial section of brain (A) and on sagittal section of spinal cord (B)

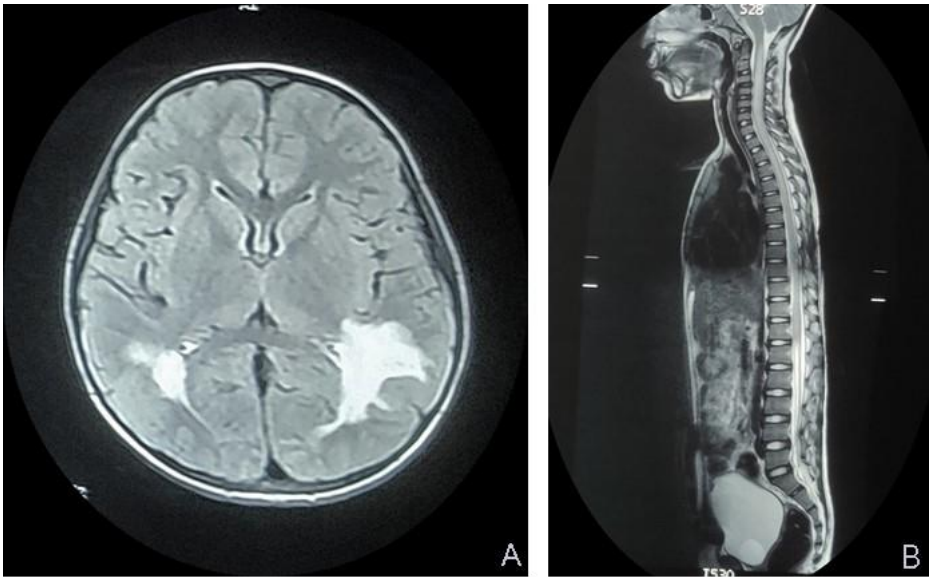

Table 1.
Findings of motor and sensory nerve conduction velocity study of both the lower limbs

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]