

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 involvement.

Case presentation: A seven and half year-old child had presented with fever followed by acute onset flaccid paraparesis 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 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.

Comment [JA2]: Better to say seven or eight years

Conclusion: Acute onset flaccid paraparesis could be observed as presentation of CCPD which had a temporal association with scrub typhus infection.

Keywords: Acute flaccid paralysis; Demyelination; Immune response; Infectious complications; Scrub typhus.

Key Messages:

- Acute onset flaccid paraparesis could be found as presentation of acute onset combined central and peripheral demyelination.
- Scrub typhus was observed to be an aetiology 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 myelin damage and often accompanied by axonal loss which has resulted in abnormalities in transmission of the neuronal electrical impulses [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 very uncommon clinical entity yet to be explored in the paediatric population.

Comment [JA3]: rare

Presentation of case:

A seven and half year-old male child had presented with acute onset flaccid paralysis of both the lower limbs. 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

Comment [JA4]: The case is that of an eight year old male or female child who.....

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 the outer border of both 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 and the 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 full. Superficial abdominal reflexes were absent. Clinical assessments including upper limbs and other systems were normal.

Further laboratory investigations revealed neutrophilic leukocytosis (N:76%; TLC: $15.5 \times 10^3/\text{ml}$) with all the other indices of routine blood examination within the normal domain. Cerebrospinal fluid (CSF) study had shown- protein:76mg/dl, glucose:82mg/dl, chloride:109mEq/l, LDH:445U/l, ADA:7U/l and cell count: $256/\text{mm}^3$ with neutrophilic predominance (70%).

Nerve conduction velocity (NCV) studies of both the lower limbs demonstrated latencies in propagation of the electrical impulses and absence of F wave and H reflex in common peroneal and posterior tibial nerve, where compound motor action potential amplitude was found to be within normal limits. Bilateral normal sensory nerve action potential (SNAP) latencies were recorded in sural nerves [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 [Figure 1].

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 onset flaccid paraparesis (AFP) preceded by nonspecific febrile illness could be fairly presumed as a presentation of Guillain-Barre syndrome (GBS). Apart from GBS, transverse myelitis had also known to be frequently encountered in the post-polio era which had similar presentation in the child age group [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, clinical findings obtained from the meticulous systemic examination ought to be of great value in these settings. In the sight of 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 demyelination. Concomitant acute-onset demyelination affecting the peripheral nerves, brain and spinal cord had suggested the clinical entity like CCPD. The CSF study including cyto-protein ratio and absence of characteristic serological markers had ruled against the established forms of immune mediated demyelinating diseases involving the peripheral nerves or central nervous system in isolation. Additionally, absence of disseminated demyelination in space and time couldn't meet the definitions of the demyelinating diseases which were known for central nervous system involvement exclusively. 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 know the pathological form of peripheral neuropathy, could be considered as a limitation of the present study.

Further, this condition was observed to have occurred in association with scrub typhus infection. Scrub typhus, a zoonotic disease which had remained prevalent in the tropical region, was known for its' neurological manifestation either due to primary involvement causing meningitis, meningoencephalitis or secondary immune mediated affliction causing acute demyelinating encephalomyelitis (ADEM) [5]. 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. Immunologic cross reactivity elicited by the pathogen with the biomolecules of central and peripheral nerves sharing structural similarity could be observed to have pivotal role in producing auto-antibodies resulting into acute demyelination [6,7].

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 with primary neuronal involvement by the 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 had included systemic steroids for five days followed by tapering dose of oral prednisolone. General supportive care and physiotherapy also had an important role in the long-term recovery [1,8].

Conclusion:

Conventionally, combined central and peripheral demyelination (CCPD) had described as inflammatory demyelinating disease associated with either infectious or autoimmune origin. Here, a child suffering from acute onset combined central and peripheral demyelination was found to be presenting with acute-onset flaccid paraparesis and it was temporally associated with scrub typhus infection. Thus, it was desirable for the practitioners in the rural area especially with the resource poor setting, to be intuitive in considering acute onset CCPD as an important differential amongst the other causes for AFP in the children.

Comment [JA5]: Please you might want to rephrase your conclusion based on the case reported
.....Scrub typhus can be a cause of AFP due to CCPD.....

Comment [JA6]: Recommendation is better in the discussion

References:

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Legends:

Legend 1- Figure 1. 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 2- Table 1. Findings of motor and sensory nerve conduction velocity study of both the lower limbs

Figure 1.

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)

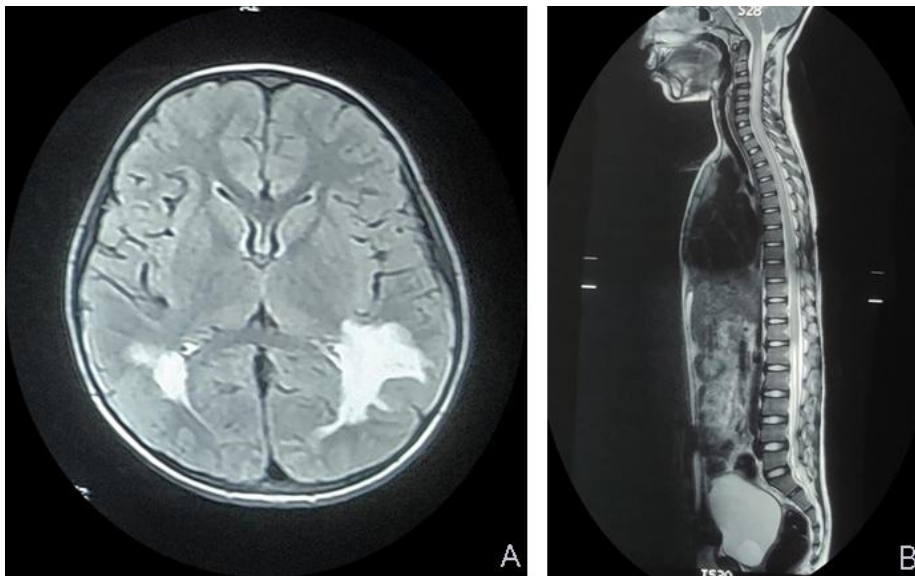


Table 1.

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]