

## Diphtheria, pertussis, and tetanus vaccine-induced extensive longitudinally extensive transverse myelitis: A case report

Bal Mukund<sup>1</sup>, Ashok K Yadav<sup>2</sup>, Ved Pratap Tiwari<sup>3</sup>, Narendra R Taralkar<sup>4</sup>

From <sup>1</sup>Assistant Professor, <sup>2</sup>Associate Professor, Department of Pediatrics, INHS Asvini, Mumbai, <sup>3</sup>Senior Resident, Department of Pediatrics, Raigarh Medical College, Pune, Maharashtra, <sup>4</sup>Specialist, Department of Pediatrics, INHS Jeevanti, Vasco-da-Gama, Goa, India

**Correspondence to:** Dr. Bal Mukund, Department of Pediatrics, INHS Asvini, Near RC Church, Colaba, Mumbai – 400005, Maharashtra, India. E-mail: bmdoc2002@rediffmail.com

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### ABSTRACT

Transverse myelitis (TM) has been reported in association with vaccination, including post-diphtheria, pertussis, and tetanus (DPTw) vaccination. Here, we report the case of a 21-month-old female child presented with loss of neck control with a history of DPTw booster vaccination approximately 4 weeks before this illness. The child was referred to the tertiary care service hospital. Magnetic resonance imaging of the spine revealed longitudinally extensive TM in the cervical segment. Extensive investigation effectively excluded causes other than vaccination-associated TM. Following treatment with corticosteroids and intravenous immune-globulin, the child had a complete recovery. Early diagnosis and prompt treatment with immunotherapy are associated with a good outcome.

**Key words:** Immunotherapy, Intravenous immunoglobulin, Prognosis, Vaccine-associated transverse myelitis

**T**ransverse myelitis (TM) is a focal inflammatory demyelinating disorder of the spinal cord. It commonly occurs due to an autoimmune process and the prevalence of the condition ranges from 1 to 8 cases/million per year [1]. TM is usually characterized by focal magnetic resonance imaging (MRI) signal abnormality in the spinal cord and/or cerebrospinal fluid (CSF) pleocytosis. Although the involvement is never transverse, the term has been retained due to the importance of a sensory level in the spinal segment, an essential element in the diagnosis [2].

TM is commonly divided on the basis of the extent of spinal involvement, i.e., acute complete TM (ACTM) and acute partial TM (APTM). ACTM classically presents with moderate-to-severe loss of function distal to spinal level in comparison to APTM, which is characterized by incomplete to patchy involvement of at least one spinal segment with mild-to-moderate weakness, asymmetric, or dissociated sensory symptoms [1]. Lesion extending >3 spinal segments in length is diagnosed as longitudinally extensive TM (LETM). LETM has been associated with various vaccines such as hepatitis B, measles mumps rubella (MMR), rabies, oral polio vaccine, and influenza but rarely associated with post-DPT vaccination [3,4]. Here, we present the case of extensive involvement of the cervical segment in a 21-month-old child and confirmed the diagnosis of a severe form of DPT vaccine-induced LETM.

### CASE REPORT

A 21-month-old female toddler referred from dependent hospital to our center with a history of loss of the control of neck of

1-day duration. There was no history of difficulty in swallowing, breathing, or difficulty in passing urine or stool or history of altered sensorium. There was no history of fall, trauma, or antecedent history suggestive of gastroenteritis or upper respiratory tract infection. There was a history of booster DPTw vaccination 27 days before presentation to the dependent hospital.

On general examination, the child was found to have non-significant cervical lymphadenopathy, pallor, and full neck flop. On central nervous system (CNS) examination, the child was conscious with Glasgow Coma Scale of 15/15 and hypotonia in the neck muscles. The power as per muscle research council (MRC) was 3/5 for neck flexors and 2/5 for neck extensors. Limb powers in both the upper and lower limbs were normal at all the joints. Reflexes were normal in the lower limbs, however, were poorly elicitable in both the upper limbs. Plantar was flexor bilaterally and other superficial reflexes were normal. There were no signs of cerebellar involvement or any signs of meningeal irritation. There was no evidence of sensory or autonomic involvement. Her fundus examination and other systemic examinations were also normal.

On laboratory investigation, the child had aspartate aminotransferase 364 IU/dl and alanine aminotransferase 569 IU/dl which normalized after 6 days of admission. Her CSF examination showed no cells, normal sugar (53 mg with a blood sugar of 92 mg/dl), and protein of 22 mg/dl with an absence of the oligoclonal band. CSF culture for bacteria and fungus was negative. Her initial MRI done after 2 days of illness in the referring hospital was normal; however, repeat MRI done on the 6<sup>th</sup> day of presentation for spine and brain showed T2 hyperintense

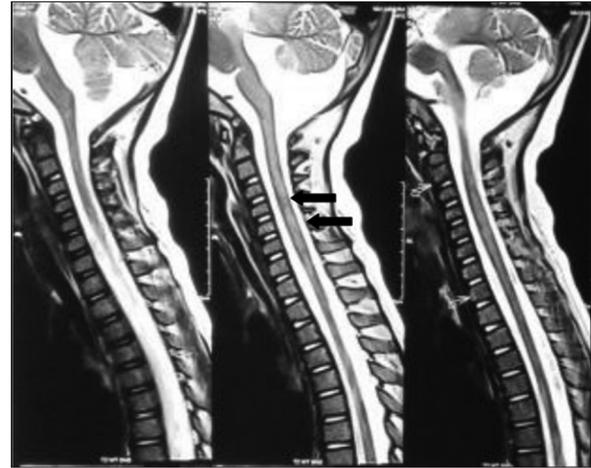
signal in cord parenchyma from C2 to C6. Rest of the spine and brain parenchyma revealed no significant demyelinating changes. MRI images demonstrated LETM (Fig. 1). The child was investigated for the presence of tuberculosis, Epstein–Barr virus, enterovirus in a polymerase chain reaction, and anti-aquaporin 4 antibodies in CSF and all the investigations were found negative. Her serum anti-aquaporin 4 antibody, antinuclear antibody, cytoplasmic antineutrophil cytoplasmic antibodies, and perinuclear antineutrophil cytoplasmic antibodies for vasculitis and workup for human immunodeficiency virus, mycoplasma, and Epstein–Barr virus were also negative. Her Vitamin B12 level was 216 pg/ml (normal 200–600 pg/ml). All the above-mentioned clinical and laboratory investigations confirmed the final diagnosis DPT vaccine-induced extensive LETM.

In view of LETM, the child was started on immune modulation with intravenous immunoglobulin (IvIG) in doses of 2 g/per kg over 2 days. The child had shown only some clinical improvement in next 72 h; hence, a 5-day pulse of methylprednisolone at 30 mg/kg/day was given intravenously followed by oral prednisolone of 1 mg/kg/day. From the 4<sup>th</sup> day of methylprednisolone pulse, the child started showing improvement, and by the 7<sup>th</sup> day of starting pulse steroid, the child recovered full range of neck movement and normal power at all groups of neck muscles. Visual evoked potential done at the time of discharge was normal. The child was discharged after 14 days of admission with advice to continue prednisolone for 2 weeks followed by tapering over 3 weeks and monthly follow-up in the OPD. A follow-up spine MRI done at 3 months showed non-enhancing altered signal intensity in the cervical spinal segment from C2 to C5 (T2 sagittal) (Fig. 2).

## DISCUSSION

TM is a focal inflammatory demyelinating disorder of the spinal cord. LETM involves >3 spinal segments in length. Occasionally, it involves entire length of the spinal cord which entails a severe form of LETM [5]. At present, a bimodal distribution is observed in children under 5 years and older than 10 years of age [4,6].

Ever since vaccination is being used to control infectious disease, the pitfalls and side effects of vaccines known as adverse effect following immunization are being reported. Several most common complications related to neurological systems are documented in literature such as TM, Guillain-Barre syndrome, neuromyelitis optica, and acute demyelinating encephalomyelitis [6]. The diagnosis in the case is based on excluding other causes and with epidemiological evidence. TMCWG (TM consortium working group) has proposed criteria for the diagnosis of TM which requires exclusion of idiopathic TM, bilateral signs and symptoms (though not necessarily symmetric), and exclusion of extra-axial compressive etiology by neuroimaging [7]. This case fits in these criteria and also had MRI evidence of LETM in the cervical segment C2–C6. Since it is difficult to pinpoint the exact causal relationship with the vaccine, a hypothesis has been proposed for the possibility of TM following vaccination. Only few cases have been published in literature due to post-DPT vaccination till date [8]. Other vaccines



**Figure 1:** Sagittal images of spine demonstrating high signal intensity from C2 to C6 in T2W



**Figure 2:** Sagittal images of cervical spine demonstrating high signal intensity - arrow from C2 to C5 in T2W at 12-week follow-up

which have been implicated in TM are MMR, H1N1, and Hepatitis B vaccination. It is a vaccine adjuvant which has been specifically considered triggering agent for vaccine-associated TM [8,9].

Autoimmunity theory has been proposed which is due cross-reactivity of antibodies and T-cells to the peripheral nervous system or CNS [10]. The other hypothesis which has been proposed is “Molecular mimicry” which portends those similar proteins of microbial pathogens with human proteins result in an immune response that damages the human organ system [11]. Diagnosis is based on clinical features and confirmed by MRI of the spine. Cervicothoracic segment or thoracic segment is usually the most common area of involvement.

The treatment is essentially immune modulation by steroid or IvIG (Class IV) or by plasmapheresis. There is no randomized trial in children published in literature to prove the superiority of one over other; however, a STRIVE trial protocol has been published in 2015 and results are pending; therefore, the choice of drug is dependent on individual preferences, cost, and availability [12]. Plasmapheresis has been recently recommended by the American Academy of Neurology for a subgroup of patients who fail to respond to high-dose corticosteroid treatment. This procedure

is technically difficult and hence is not routinely done in the children. For relapsed cases or NMO related, Cyclophosphamide, Rituximab or Eculizumab have been tried occasionally. Prognosis in TM is generally good in children; however, LETM lesions with extensive involvement of  $\geq 7$  spinal segments showed poor functional recovery in at 3-month follow-up [12]. In another study of 19 patients with TM, rapid progression of symptoms, high level of deficit, and spinal shock were associated with poorer outcome [13]. In a study from North India in Pediatric TM, spinal shock, severe weakness at onset with power  $\leq 1/5$  on MRC scale, respiratory muscle involvement, and greater mean time to diagnosis and treatment had poorer outcome during follow-up [14].

## CONCLUSION

TM is an acute/subacute inflammatory disorder of the spinal cord and may be due to a cross-reaction from vaccines. This diagnosis is only by excluding other causes and with epidemiological correlation. The early diagnosis and early treatment with immune therapy yields satisfactory results.

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