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Case Report

Acute transverse myelitis in a 7-month-old boy after diphtheria–tetanus–pertussis immunization

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Study design: Case report of a 7-month-old boy, who developed acute transverse myelitis after diphtheria–tetanus–pertussis immunization.
Objectives: To describe the clinical course of acute transverse myelitis in an infant and to review the literature regarding the association of acute transverse myelitis and vaccinations.
Setting: Department of Pediatrics, University of Kentucky, Lexington, Kentucky, USA.
Methods: Case report.
Results: Magnetic resonance imaging (MRI) on admission demonstrated diffuse spinal cord edema with increased signal on T-2 weighted images and faint enhancement with gadolinium infusion. Urologic symptoms improved with steroids but motor function was never fully regained. Repeat MRI of the spinal cord several months later showed diminution of cord diameter with resolution of edema and signal abnormality.
Conclusion: Based on the clinical course and MRI findings, the daignosis of acute transverse myelitis was made. The association of previously received DPT immunization and the genesis of transverse myelitis is explored.
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Keywords: myelitis; immunization; diphtheria; tetanus; pertussis

Case history

Our patient is a 7-month-old Caucasian male without any significant past medical history who was admitted to the University of Kentucky Children's Hospital for leg weakness. He received diphtheria, tetanus, acellular pertussis (DTaP) vaccine (Aventis-Pasteur, Lot U0952AA) 17 days prior to admission. Previous DTaP doses given at the age of 2 and 4 months were well tolerated. He had an upper respiratory tract infection 2 weeks prior to admission. He initially developed constipation for which he was admitted to the local hospital and fleet enemas were given. Subsequently, he developed urinary dribbling, priapism, and lower extremity weakness. He had no breathing or feeding difficulties. He was then transferred to our hospital. So far, his developmental milestones had been normal. Birth, maternal, and perinatal history had all been unremarkable. Family history is negative for neuromuscular disease or for any recent illnesses. His parents and 7-year-old sister had been well. He had no known drug allergies and was not on any medications.

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On admission, he was alert, smiling, and was focusing and tracking well. Physical examination was remarkable only for a large 1.5×1.5 dark colored nevus on the right frontal scalp area. He was not dysmorphic and he did not have any neurocutaneous stigmata. Pulmonary, cardiovascular, and abdominal examinations were normal. A detailed examination of his back did not reveal any abnormalities. No tenderness was elicited on palpation. No sweat level was identified. He had priapism and urine was intermittently dribbling from the urethral meatus. He had flaccid paraplegia and he exhibited a triple flexion response to noxious stimulation of the lower extremities. Deep tendon reflexes were $+1$ on lower extremities and $+2$ on the upper extremities. Plantar responses were equivocal and no clonus was elicited. He had no abdominal reflexes. Cremasteric reflexes were present bilaterally. Anal tone was patulous and no anal wink was elicited.

Laboratory evaluation included a complete blood count showing an increased white blood count of 16 000 with 67% neutrophils. Comprehensive metabolic panel, erythrocyte sedimentation rate, urinalysis, and C-reactive protein were all normal. Cerebrospinal fluid analysis showed two red blood cells/μl, seven white blood cells/μl with four lymphocytes and three monocytes, glucose of 63 mg/dl and a total protein of 30 mg/dl. Cerebrospinal fluid oligoclonal bands were negative and IgG Index

was normal. Myelin basic protein was increased at 4.90 mg/dl with a normal of 0–2.30. Cerebrospinal bacterial and viral cultures for adenovirus, Influenzae A and B, Parainfluenzae 1, 2, and 3, cytomegalovirus, enterovirus, and varicella zoster were negative. Cerebrospinal fluid HSV-DNA PCR and Enteroviral-RNA PCR was negative. Arboviral serology for California encephalitis, Eastern Equine and Western Equine encephalitis and St Louis encephalitis were negative. Antibodies for Lyme disease, Lymphocytic choriomeningits, Mycoplasma, Ebstein–Barr virus, Bartonella henselae, and Human Immunodeficiency virus were negative. Urine heavy metal screen was negative.

Admission magnetic resosonance imaging (MRI) of the brain was normal. MRI of the spinal cord showed diffuse edema of and increased T2 signal within the spinal cord from the level of C3–T6. Dorsal and ventral spinal veins were of normal caliber and there was no evidence of a dural AV fistula. There was a faint and patchy enchancement of the spinal cord on gadolinium infusion (Figure 1). Intravenous prednisolone at 1.5 mg/kg/day for 7 days followed by oral Prednisone taper (Orapred) at 1 mg/kg/day for 2 weeks. We also treated him with Acyclovir pending the results of his CSF HSV-DNA PCR. Supportive therapy in terms of bladder and bowel care and rehabilitative services were also initiated. Within a week, priapism resolved. At discharge, he had mild hypertonicity of the lower extremities and he had demonstrable clonus. At 3 weeks after discharge, he had good urinary stream and constipation had resolved. Paraplegia persisted and pyramidal signs were more pronounced. A repeat MRI of the spine done 3 months later showed resolution of cord edema and signal abnormality but reduction in cord caliber (Figure 2). At 10 months from initial presentation, he continued to have paraplegia and spasticity of the lower extremities.

Discussion

Our patient's clinical course, neurologic findings and neuroimaging studies support the diagnosis of acute transverse myelitis 17 days after DTaP vaccination. In our review of the literature, acute transverse myelitis during infancy is rare. Several authors have described acute transverse myelitis in childhood. Knesbusch[1] described nine patients, ages 2–15 years with transverse myelitis. Yamamoto[2] described acute transverse myelits in a 15-month-old female and Garcia Zozaya[3] did likewise in a 7-month-old boy. An early report by Atkinson[4] described a 7-month-old girl within are flexic paralysis of both legs associated with a T10 sensory level and a lax anal sphincter 24 h after an intramuscular Penicillin injection. The symptoms were ascribed to particulate injection into the gluteal artery.

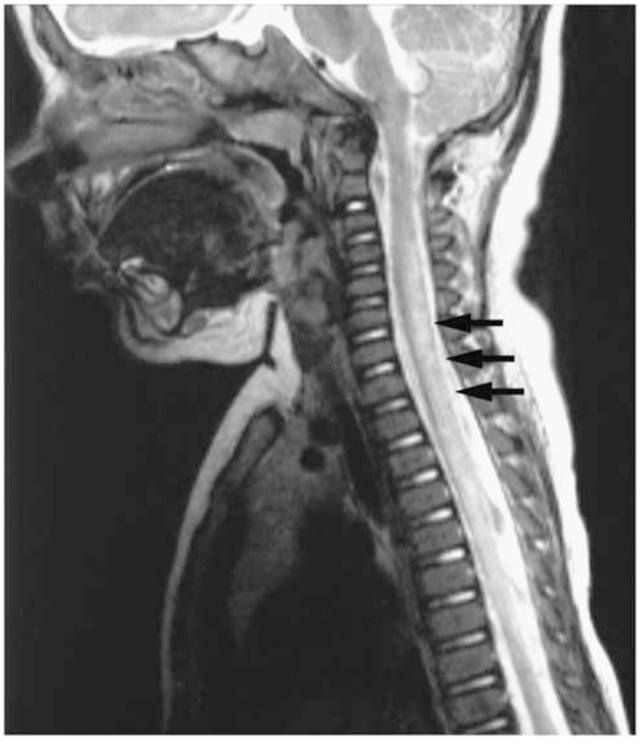

Figure 1 Initial sagittal T_2-weighted images of the spinal cord showed diffuse cord edema and increased signal intensity from C3 to T6

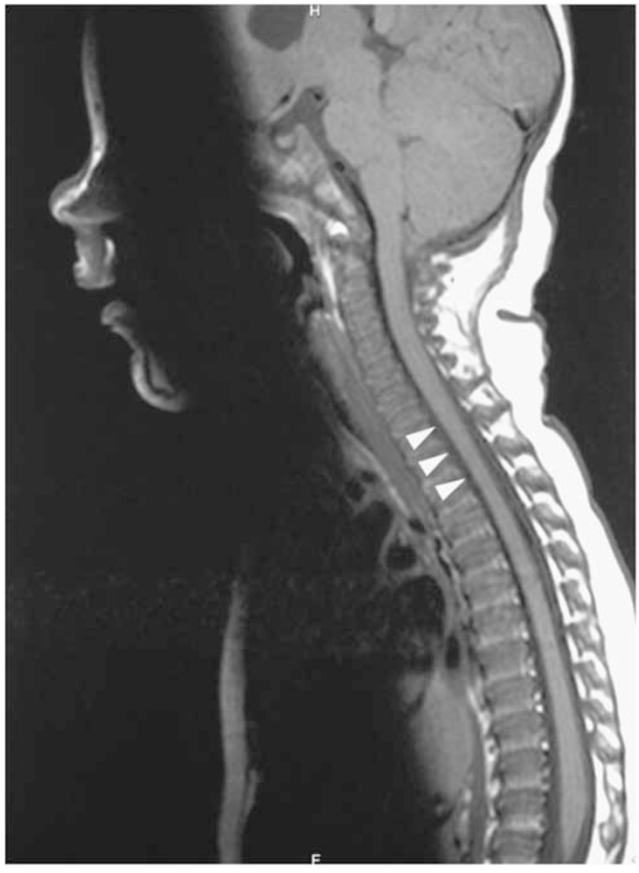

Figure 2 After 3 months, sagittal images showed resolution of the cord edema and signal abnormality but the cord had marked reduction in caliber

It is possible that our patient had a postinfectious or a postvaccination acute transverse myelitis as his symptoms occurred about 2 weeks after an upper respiratory infection and 17 days after a DTaP vaccination. There are several reports of acute transverse myelitis following vaccinations in both adults and children. An earlier report by Kulenkampff[5] described a 6-month-old baby who developed flaccid quadriparesis with respiratory compromise 17 days after a DPT vaccination. Similarly, Whittle and Robertson[6] reported a 7-month-old baby who developed flaccid paraplegia 6 days after a DT inoculation and oral polio vaccine. Zanoni *et al*[7] also reported their findings on a 15-month-old girl with acute transverse myelitis 21 days after Measles–Mumps–Rubella vaccination. More recently, Iniguez *et al*[8] reported a 15-year-old girl who had progressive right-sided weakness and numbness 1 week after receiving the first dose of Hepatitis B vaccine. A second case implicating Hepatitis B vaccination in the pathogenesis of acute transverse myelitis was reported by Fonseca *et al*.[9] Matsui *et al*[10] reported a 4-year-old girl who developed acute transverse myelitis 14 days after a Japanese B encephalitis vaccination. Lim *et al*[11] reported a 9-year-old girl who developed transverse myelitis 16 days after measles and rubella vaccination. There are similar reports in adults. One publication described a 42-year-old male who developed transverse myelitis with a Brown–Sequard syndrome following prophylactic influenzae immunization despite chronic immunosuppresion for steroid-responsive optic neuritis.[12] Another described a 36-year-old patient who developed a fatal inflammatory polyradiculopathy/myelopathy 9 days after a booster Hepatitis B vaccine.[13]

In our patient, we were not able to discover an associated agent despite an extensive diagnostic workup. The history of fever and upper respiratory symptoms 2 weeks before the onset of the symptoms suggests a viral agent. A retrospective analysis of 33 pediatric and adult patients ages 18 months–82 years showed that 15 out of 33 (46%) had a preceding infection of which 73% were respiratory, 13% had a gastroenteritis and 13% had a generalized flu-like symptoms.[14] A direct infection has not been proven. Rather, the concept of a molecular mimicry has been postulated whereby the offending agent triggers an autoimmune response to the myelin sheath of the central tracts of the spinal cord.[15] Reports of postvaccination acute transverse myelitis suggest such an immune-mediated process.

It is important to rule out intramedullary and extramedullary conditions such as tumors, spinal cord trauma, abscesses, infarction, and dural AV fistulas. In our patient, MRI features showing preservation of cord architecture with a homogenously abnormal signal on T_2 weighted images, patchy gadolinium enhancement and the lack of vascular channels makes a neoplasm and arterio-venous fistulas unlikely. Follow-up MRI performed 3 months later also showed resolution of the above abnormalities although the spinal cord appeared of smaller caliber (Figure 2).

As in adults, acute transverse myelitis in children appears to be a self- and time-limited illness and is generally monophasic. Improvement generally occurs two to 12 weeks after maximal deficit. Several authors have concluded that a rapidly progressive course generally portended a worse prognosis.[16] At 10 months after initial presentation, our patient regained very little use of motor function.

This report illustrates the clinical course and outcome in a 7-month-old child with acute transverse mellitus seventeen days following DTaP vaccination. To the best of our knowledge, our patient is one of the youngest cases ever reported. Although there is a temporal relationship between the development of transverse myelitis and DTaP vaccination in our patient, it is difficult to establish a causal relationship between the two. The occurrence could have been simply coincidental. The same is true regarding the role played by his antecedent viral upper respiratory tract infection. It is, however, possible that the concomitant exposure to these two antigens may have increased the risk of an abnormal immunologic response in a genetically susceptible individual.

In summary, this case illustrates the association between transverse myelitis and DTaP vaccination in an infant. Further studies characterizing the subset of patients who develop neurological complications in association with immunizations need to be carried out.

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