A 20-Year-Old Woman with Sudden Onset of Neurologic Deficits of Unknown Cause

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A 20-year-old woman presented with a 1-day history of low back pain, inability to micturate, weakness and tingling sensations in her lower extremities, and loss of sensation in both upper extremities. Her symptoms began caudally and spread distally. She had received a human papillomavirus vaccination 3 weeks prior to presentation. She had also recovered from a sore throat, runny nose, and intermittent fever 1 week prior to presentation.

A physical examination revealed stable vital signs and no fever. She was alert with normal mentation and intact cranial nerves. Power was 1 of 5 bilaterally in her lower extremities with reduced tone and absent deep tendon reflexes (DTR). Babinski reflex was mute. Power was 3 of 5 bilaterally with positive DTRs in the upper extremities. There was a loss of sensation in both upper extremities.

Figure 1. Magnetic resonance imaging of the spine showing increased signal in the anterior cervical cord extending from C5 to T3/T4.

For diagnosis, see page e113

Editor’s note: Each month, this department features a discussion of an unusual diagnosis. A description and images are presented, followed by the diagnosis and an explanation of how the diagnosis was determined. As always, your comments are welcome via email at pedann@Healio.com.
of sensation up to thoracic level 3 (T3). No insect bites or ticks were noted.

A complete blood count, comprehensive metabolic panel, urinalysis, and urine toxicology were all within normal range. Computed tomography of head was normal and lumbar puncture revealed normal cerebrospinal fluid (CSF) indices. Magnetic resonance imaging (MRI) of the brain and spine with gadolinium contrast showed increased signal in the anterior cervical cord extending from cervical level 5 to T3 (Figure 1). Comprehensive testing for infectious and autoimmune diseases is negative.

Diagnosis:
Idiopathic Transverse Myelitis

Magnetic resonance imaging (MRI) of the spine ruled out any compressive cord lesions that could have accounted for her symptoms. The classic signal enhancement on the MRI confirmed the diagnosis of transverse myelitis.

The patient was given intravenous methylprednisolone at a dose of 1 g/day for 5 days. The strength in her arms improved slightly, but weakness persisted over both lower limbs along with persistent sensory deficits up to level T3. Due to minimal response to corticosteroid, plasmapheresis was administered every other day for 7 cycles in total. Her upper limb strength improved, but she was still unable to use her hands or lower limbs. Her sensory deficits remained at level T3. She received 2 days of intravenous immunoglobulins. She also received continuous physical and occupational therapy on a daily basis. Intermittent catheterization of her bladder twice a day and enema every other day were performed. Power in her upper extremities was noted to be 4 of 5 but power in lower extremities remained at 1 of 5. Her sensation deficit was persistent at level T3. She was transferred to a rehabilitation facility to help with continued recovery.

DISCUSSION

Transverse myelitis (TM) is a neurologic disorder characterized by motor, sensory, and autonomic dysfunction resulting from inflammation of the neuroanatomic pathways of the spinal cord. The term “transverse” describes the band-like disturbance that occurs due to a sensory level deficit. Annual incidence of TM is 1 to 8 cases per million in the United States, and approximately 20% of the cases occur in the pediatric population. TM may present in the setting of an acquired demyelinating disease (eg, multiple sclerosis or neuromyelitis optica), a systemic autoimmune disease (eg, systemic lupus erythematosus), accompanying a bacterial infection (eg, herpes zoster and herpes simplex virus), or it can present as an isolated idiopathic entity. Approximately 60% of the cases appear to be autoimmune responses to an infection or vaccination.

TM can present with an array of neurologic deficits in children, including motor weakness, numbness, ataxic gait, and incontinence of bowel and bladder. Sensory deficit is also seen in many children. Disruption of the sympathetic control center leading to unopposed parasympathetic manifestations such as arterial hypotension and bradycardia are not uncommon. Incontinence and breakdown of a signal from pontine micturation center and the sacral level leading to urinary retention are also common findings in children with TM. Similarly, constipation resulting in irritability in children may be evident.

Evidence of spinal cord inflammation between 4 hours and 21 days after the onset of symptoms can guide the diagnosis of TM. The inflammation can be seen as pleocytosis, increased immunoglobulin type G index, or enhancing spinal cord lesion on MRI. The immune-mediated infiltration seen is likely a result of multiple factors, including molecular mimicry, superantigen effect, humoral-based dysregulation, and interleukin–6–mediated toxicity. The presence of intraparenchymal and perivascular cellular infiltrates causes demyelination and neuronal injury, which lead to the symptoms seen in the disease.

There are a number of diseases that may mimic the presentation of TM. These include ischemia, arteriovenous malformation, vitamin B12 deficiency, tumors, and spinal radiation. They should be excluded prior to exploring the diagnosis of TM. Initial evaluation involves identifying any compressive lesions requiring neurosurgery. MRI of the brain and the spine with gadolinium-enhanced studies are often used for this purpose. Cerebrospinal fluid analysis and serologic tests are necessary to identify the primary cause, if any, of the disease. Testing for specific infectious agents will depend on index of suspicion.

Considerable effort must be made to differentiate idiopathic TM from disease-associated TM, as it may influence the decision for closer follow up or prophylaxis treatment to reduce the recurrences. Central nervous system diseases that may have TM as an initial presentation include multiple sclerosis (MS) and neuromyelitis optica (NMO). MS often presents with asymmetric clinical findings with predominant sensory symptoms. Radiologic findings in MS include MRI lesions extending over fewer than two spinal segments, and multifocal areas of demyelination on brain MRI. Presence of oligoclonal bands in the CSF may indicate MS. NMO typically
Causess both TM and optic neuritis, and evaluation often reveals aquaporin 4 immunoglobulin G antibodies. Other rheumatologic diseases, such as systemic lupus erythematosus and antiphospholipid antibody syndrome, may have a component of TM but they often present with systemic symptoms along with autoimmune markers such as antinuclear antibody, anti–double-stranded DNA antibody, and antiphospholipid antibodies.²

Clinical presentation of weakness, depressed reflexes, and incontinence may be similar to Guillian-Barre Syndrome (GBS). However, sensory deficits are often not prominent in GBS, and subtle changes in MRI results can differentiate the two entities. In a patient with GBS, an MRI would demonstrate enhancement of spinal nerve roots and the absence of intramedullary disease. CSF analysis usually shows pleocytosis and elevated protein content in TM; however, absence of albumino-cytologic dissociation differentiates TM from GBS.⁸

Initial management of TM includes securing the airway, breathing, and circulation. A patient with TM with concurrent cervical lesion can have loss of upper airway patency and weakness of the diaphragm. Autonomic dysfunction can result in hypotension, bradycardia, and urinary retention, all of which require close monitoring. Although class 1 evidence for patients with TM is not available, clinical experts agree that first-line treatment should be with intravenous methylprednisolone at 30 mg/kg per day for 5 to 7 days with a maximum dose of 1 g/day, followed by a tapering dose of an oral corticosteroid over a period of 3 to 4 weeks.² Small studies looking at children with TM revealed that when compared to no treatment, those receiving steroid treatment had a faster and complete recovery from symptoms.⁹¹¹ For those with no improvement or worsening of symptoms after initiation of corticosteroid treatment, plasma exchange therapy can be offered. Plasma exchange has been used for other demyelinating conditions. In TM, six exchange transfusions are performed over a period of 2 weeks, on average. Limited data are available for additional therapies; use of intravenous immunoglobulin and immunomodulator agents such as cyclophosphamide have been suggested.²

Rehabilitation remains the cornerstone of treatment in patients affected with TM. After completion of treatment with steroids and plasmapheresis, patients are likely to benefit from inpatient rehabilitation programs. Importance is given to maintaining range of motion, strengthening of muscles, and use of adaptive equipment for bladder and bowel evacuation. Children with neuromuscular disability secondary to spinal cord lesions are at an increased risk of depression and anxiety, so providing psychologic support for patient and family is vital.¹²¹⁴

A vast majority of cases of idiopathic TM are monophasic, but approximately 10% to 25% recur.² Prognostic factors include extent of spinal cord involvement, rate of progression of symptoms, autonomic involvement, and duration of presentation. Limited data are available on prognosis in children, but case series suggest that 30% to 50% of patients have complete recovery and 10% to 20% have poor outcome.¹⁵¹⁶ A 2012 study on prognosis looked at 38 children with acute TM. Of these children, 16% were wheelchair bound and 22% had sphincter dysfunction at a 3-year follow-up.⁷ Similar results were suggested in a review of center-based analysis of children with TM, in which recovery often took months and even years.⁵

This case illustrates some of the salient features of TM, including clinical presentation and management. Although immunomodulating therapy offered some improvement, the patient did not completely return to her normal self at the time of discharge. One year later, repeat MRI of the spine showed increased intramedullary T2 signal beginning at the level of C4/C5 and severe cord atrophy extending to T3, which further confirmed her diagnosis of transverse myelitis. Almost 2.5 years after her initial diagnosis, the patient remains unable to ambulate without support and requires assistance with activities of daily living. She continues to receive physical therapy and recently started using knee-ankle-foot orthosis.

Even though the cause of her condition is unknown, the history of recent vaccination or the recent viral illness may have been a factor in the development of TM.

CONCLUSION

The etiology of TM is multifactorial and remains poorly understood. Medical professionals should have a high index of suspicion for a child presenting with motor and band-like sensory deficits. Efforts must be made to differentiate idiopathic TM and systemic and/or disease-associated TM, because it has an effect on management and surveillance. The mainstay of management remains intravenous corticosteroids and plasmapheresis, but additional therapies such as immunoglobulin and cyclophosphamide may be used.

REFERENCES