A 16-year-old girl presents to the inpatient pediatrics service following a 1-week history of double vision and nausea of sudden onset. She denied any recent illnesses, vaccinations, or sick contacts. She was not experiencing any chest pain, shortness of breath, palpitations, or diaphoresis. She had also been experiencing a sharp, shooting pain in her right thigh, most often occurring with ambulation for the past week and a half that she attributed to a basketball injury. Her medical history is significant for type 1 diabetes mellitus (DM) controlled with an insulin pump. She has no history of migraines, seizures, or diabetic retinopathy.

PHYSICAL EXAMINATION

On admission she was afebrile with a pulse rate of 70 beats per minute and a blood pressure of 125/62 mm Hg. The physical examination was significant for a small vertical strabismus on right gaze, mild bilateral horizontal nystagmus (leftward on left gaze, rightward on right gaze), and decreased adduction of the left eye. The patient had intact visual acuity, and there was no papilledema noted on fundoscopic exam. Otherwise, cranial nerves II to XII were intact and the patient had 5/5 motor strength and normal sensation in upper and lower extremities bilaterally. She did not exhibit any dysdiadochokinesia, and finger-to-nose test was normal bilaterally. Gait examination was significant for imbalance. Her basic metabolic panel and complete blood count were within normal limits.

HOSPITAL COURSE

The patient was seen by the neurology department, and imaging and several laboratory studies were ordered. A magnetic resonance imaging (MRI) scan of the cervical spine revealed a nonspecific enhancing lesion at the spinal cord at C5-6. An MRI of the brain and orbits performed prior to admission demonstrated multiple enhancing lesions with increased intensity in periventricular, deep, and juxta cortical white matter regions of both cerebral hemispheres, as well as increased signal intensity in the left cerebellar hemisphere and in both cerebellar peduncles in a pattern consistent with central nervous system (CNS) demyelination (see Figure 1, page 316). No masses were noted. The patient subsequently underwent a lumbar puncture. The resulting cytology and Gram stain did not reveal any evidence of bacterial or viral infection, but cerebral spinal fluid (CSF) analysis was significant for the presence of oligoclonal bands. Serum thyroid-stimulating hormone (TSH) and vitamin B12 levels were found to be normal. An anti-nuclear antibody (ANA) panel was found to be negative, whereas anti-thyroid peroxidase (anti-TPO) immunoglobulin G (IgG) was elevated at 120.1 mg/dL. A serum angiotensin-converting enzyme (ACE) level was also found to be elevated at 64 U/L (normal range for adults is 8 UL to 53 U/L, but the pediatric range can be as much as 50% higher than...
Case Challenge

the adult range). The patient was started on intravenous (IV) methylprednisolone (1 g per day).

Over the course of her hospital stay, the patient’s visual symptoms continued to improve and her diplopia was almost completely resolved by the fifth day of hospitalization. She remained on IV methylprednisolone during her stay. She was discharged home on a tapering dose of oral prednisone and scheduled to have outpatient follow-up with a neurologist.

**Diagnosis:**

Multiple Sclerosis

**DISCUSSION**

Multiple sclerosis (MS) is a central nervous system demyelinating disorder that affects approximately 2.5 million people worldwide, including 400,000 Americans. The pathogenesis of this often debilitating disease involves immune-mediated attack causing degeneration of the myelin sheath in both the brain and spinal cord. Diagnosis involves integration of clinical, laboratory, and imaging evidence. The McDonald criteria are commonly used in the diagnosis of MS and allow for early diagnosis based on clinical presentation as well as the presence of demyelinating lesions in the classic locations for MS (periventricular, juxtacortical, infratentorial, and cervical spine). Symptoms vary depending on the location of demyelinated lesions and can include visual changes, slurred speech, urinary incontinence, diplopia or total loss of vision, numbness or weakness of extremities, and tingling or painful sensations. As was the case with our patient, visual abnormalities are often a prominent symptom in MS. Therefore, it is important to perform a thorough eye exam in any patient who might have an underlying neurologic condition. A detailed description of exam findings can play a crucial role in localizing CNS lesions. For example, a vertical strabismus, as was seen in our patient, may represent skew deviation (an acquired vertical eye misalignment that typically occurs in patients with brainstem or cerebellar lesions) or a fourth cranial nerve palsy, among other possibilities. Further, the decreased medial excursion of the left eye on rightward gaze might suggest a lesion in the ipsilateral medial longitudinal fasciculus leading to internuclear ophthalmoplegia and horizontal diplopia, one of the classic ophthalmic findings in MS. Recognition of any abnormalities on the eye exam should prompt referral to an ophthalmologist for a more extensive evaluation.

The exact cause of this autoimmune condition remains to be elucidated, but appears to involve both genetic and environmental risk factors. MS can occur at any age, but is typically diagnosed between 20 and 40 years of age. Just as with many other autoimmune diseases, women are approximately twice as likely to be affected as men. There appears to be a strong genetic component, as those with a first-degree relative with MS have a 1% to 3% risk of developing MS compared with the general population’s risk of .001%. Caucasians of Northern European descent have a much higher risk of developing MS than those of African, Asian, or Native American ethnicities. Treatment of acute episodes typically involves high-dose corticosteroids, and synthetic interferon beta analogues (glat-
Pediatric MS represents up to 10% of all cases. Symptoms are similar to those in adult patients, but children are more likely to have seizures, as well as cerebellar and brainstem symptoms. Girls are more likely to present with sensory symptoms and to recover after an initial episode than boys. MS typically has a more indolent course in children with accumulation of many lesions leading to complications in mid-adulthood. As with adult-onset MS, there appears to be a higher incidence of disease in children living in Europe, the northern United States, and southern Canada than in those inhabiting regions closer to the equator. There is some thought that this discrepancy may be at least in part related to vitamin D deficiency. There also appears to be an association of certain infections with the development of MS in both children and adults. One study found that 83% of children with MS were seropositive for EBV IgG compared with 42% of normal controls. As with adults, there appears to be a strong genetic association; children of parents with MS have a 3% to 5% chance of developing MS. The risk for identical twins has been documented to be as high as 30%. The diagnosis of MS in pediatric patients can often be difficult because an initial presenting episode could present similarly to other demyelinating disorders. Furthermore, in some pediatric cases, the demyelinated lesions on MRI scans may not initially be enhancing, making early diagnosis more difficult. Initial attacks in children with MS are often misdiagnosed as acute disseminated encephalomyelitis (ADEM). ADEM occurs more commonly in children than MS and involves widespread inflammatory damage of white matter, with 50% to 75% of cases following a bacterial or viral infection and preceded by a prodrome of fever, fatigue, headache, and nausea. These patients can present with symptoms similar to MS, such as blurred vision, imbalance, and weakness. MRI typically shows widespread white matter changes involving up to half of the total white matter volume. CSF analysis often reveals elevated white blood cell count, often with a lymphocytic predominance. The classic oligoclonal bands most commonly seen in MS have been shown to be present in 10% of patients with ADEM. A range of 15% to 20% of pediatric cases of MS present with encephalopathy and neurologic deficits and are difficult to distinguish from cases of ADEM. The presence of old demyelinated lesions along with new ones helps distinguish MS from ADEM.

One interesting component of this case presentation is that the patient suffered from type 1 DM and subsequently received this new diagnosis of MS. Although both disorders are known to be autoimmune in nature, they have been associated with distinct HLA class II haplotypes, so a link between the two was often thought to be unlikely. However, a Danish population-based study of nearly 15,000 first-degree relatives (siblings and offspring) of patients with MS showed a 63% increased risk of developing type 1 DM when compared to the general population. Furthermore, researchers found that a Danish cohort of patients with type 1 DM had a higher than expected rate of MS diagnoses during a several follow-up period. Along with this study and others like it, this case report may provide further evidence of a link between these well-known, but still incompletely understood autoimmune disorders.

CONCLUSION
This case presentation depicts the presence of an “adult” disease in the pediatric population. Due to more common illnesses in children, especially ADEM, the diagnosis of MS can be missed. The two diseases can present very similarly clinically, and as the presenting episode is most often the initial MS attack in children one cannot rely on the classic MS picture of multiple lesions separated in time and space. Delay in early diagnosis of MS may lead to inadequate therapy to prevent future relapses and their long-term sequelae. Our patient did not have the typical history of a preceding viral or bacterial infection that is seen in most cases of ADEM, but such a clinical history should not preclude the diagnosis of MS. Multiple sclerosis should remain on the differential diagnosis for any pediatric patient who presents with symptoms and imaging consistent with CNS demyelination, even in the presence of a recent history of infection because certain infections have been linked to the development of MS.

FOLLOW-UP
Following discharge home, the patient remained on a steroid taper and her diplopia gradually resolved over the next several days. She was able to return to school but continued to have some difficulty reading and focusing her eyesight for more than 15 minutes at a time. Her neurologist recommended beginning an interferon beta analogue to prevent future episodes. To date, the patient and her family are still considering this option.

REFERENCES