Acute Respiratory Failure in a 2-year-old Girl

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A 2-year-old Hispanic girl was brought to the pediatric intensive care unit (PICU) with acute respiratory distress. She was transferred from a local hospital, where she was admitted with difficulty swallowing, sore throat, and changes in her voice.

The symptoms started 2 days before hospital admission. Initially, the girl suffered from an episode of choking while she was eating a piece of sausage. Her mother immediately performed the Heimlich maneuver, which removed the sausage. One the same day, she had three episodes of large, watery, non-bloody stools. She started having generalized weakness and developed difficulty in swallowing solids and liquids, and throat pain with changes in voice. The parents took her to a clinic, where amoxicillin was given for sore throat.

A CT scan of the face and head did not demonstrate any fracture or hemorrhage.

Incidentally, the girl had suffered from a fall 2 weeks before admission while playing in her backyard. She fell and hit her face on a concrete surface and was taken to the hospital with epistaxis and facial bruises. A computerized tomography (CT) scan of the face and head did not demonstrate any fracture or hemorrhage. She remained stable until the development of current symptoms.

During the hospital admission, a comprehensive evaluation was performed. Past history and family history were unremarkable. She was born by repeat cesarean section, with a birth weight of 6 lb, 7 oz. Her immunizations were current. She met her developmental milestones. Her weight on admission was 10.2 kg, head circumference was 47 cm, and height was 93 cm. Vital signs were within the normal range. The physical examination revealed dysphagia for solids and liquids, weakness, sore throat, mild dehydration, and disturbed phonation.

Editor’s note: Each month, this department features a discussion of an unusual diagnosis in genetics, radiology, or dermatology. 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 e-mail at pedann@slackinc.com.
Muscle strength was 4 out of 5 in all extremities. Deep tendon reflexes were brisk without clonus. Initial labs showed elevated C-reactive protein and neutrophilic bands. Urinalysis showed increased leukocytes, and culture was positive for *Escherichia coli*. Basic metabolic profile, rapid streptococcal antigen test (RAST), and lumbar puncture were unremarkable. An upper gastrointestinal endoscopy was found to be negative for any pathogenic process. A nasogastric tube was inserted for feeding, and she was given intravenous fluids and cefotaxime for urinary tract infection (UTI).

On the second day of admission, the girl developed acute onset of respiratory distress and became delirious, arousable only with deep stimulation. She was pale and drooling. She was transferred to PICU with increasing shortness of breath. Urgent intubation and mechanical ventilation were performed secondary to hypercarbia (pCO2 of 106). Physical examination after intubation showed a weak gag reflex and weak respiratory effort. Magnetic resonance imaging (MRI) of the brain and cervical spine, along with the thoracic spine, were found to be normal. Lyme disease antibodies were negative. She was given one dose of intravenous immunoglobulin, with little effect.

She was tested for botulism, and while pending results, the Centers for Disease Control and Prevention (CDC) were contacted to obtain anti-toxin. An extubation attempt was made; however, she needed to be reintubated after a short period of time. Serum creatine level was found to be high. Subsequently, an electromyogram showed decremental response on repetitive stimulation (see Figure). After the results of electromyogram, another extubation was attempted after she was given physostigmine. This time, she was able to be extubated, and started swallowing and tolerating oral feeds, along with improvement in muscle strength. Modulating type anti-acetylcholine receptor (AChR) antibodies and anti-peroxidase antibodies were found to be positive.
DISCUSSION

Myasthenia gravis (MG) is an autoimmune disorder of the nicotinic AChR of skeletal muscle, characterized by muscle weakness after repeated or sustained activity. MG crisis is a severe form that can clinically present with acute respiratory failure. Most patients with MG crisis have an identifiable risk factor. The incidence rate of MG crisis is found in approximately 20% of all patients with MG and is likely to occur during the first 2 years after diagnosis. Myasthenic crisis as a first presenting symptom in the pediatric population is rare. There was no family history of MG in this patient. The precipitating factor was perhaps the development of a UTI. There are three clinical entities of MG in children: 1) a transient form in neonates born to a mother with MG; 2) congenital myasthenia; and 3) juvenile MG, which is similar to adult MG. Juvenile MG presents mostly with ocular symptoms rather than generalized symptoms. A number of case series have documented MG in the pediatric population. A retrospective review of 77 patients with juvenile MG showed a median age at onset to be 8 years. The diagnosis of MG crisis should be considered in all children with respiratory failure with uncertain etiology. There are sparse published data regarding MG crisis in children. In approximately 40% of adult MG patients, no triggering factor can be found, and crisis may be the initial manifestation of MG. Common precipitants of MG crisis are presence of infection, aspiration pneumonitis, idiopathic causes, initiation of a new medication, recent surgery, trauma, botulinum injections, and thymoma.

Disorders that may mimic MG crises in children may affect the brainstem (infarction, hemorrhage, mass lesions); spinal cord (cervical cord compression); motor neurons (spinal muscular atrophy); peripheral nerves (Guillain-Barré syndrome, acute porphyria); neuromuscular junction (Lambert-Eaton myasthenic syndrome, organophosphate poisoning, botulism); or muscle (myopathies, acid-maltase deficiency, myositis).

On physical examination, the patient with MG crisis appears restless with rapid and shallow breathing due to respiratory muscle fatigue. Stridor, a gurgling voice, disturbed phonation, and dysarthric speech are signs of loss of airway protection and reduced integrity of bulbar muscles. The shunting of pulmonary blood flow can lead to hypoventilation, hypoxia, hypercarbia, and acidosis requiring urgent intubation with mechanical ventilation. After initial stabilization of the child, routine diagnostic workup should include an edrophonium test and electromyography. A decremental response of the amplitude of compound motor action potentials of more than 10% after repetitive nerve stimulation is highly suggestive of MG.

Serum anti-AChr antibodies are typical, although are not always present, in juvenile MG. These can be divided into binding, blocking, and modulating antibodies. Binding antibodies can fixate and can lead to loss of postsynaptic membrane and AChr. Blocking antibodies may impair binding to the AChr, leading to poor muscle contraction. Modulating antibodies cause AChr endocytosis resulting in loss of receptor expression and is associated with worse prognosis. The presence of anti-peroxidase antibodies is associated with increased incidence of comorbidities, such as thyroid disorders. If these are negative, and there is still a high index of suspicion, then antimuscle-specific kinase antibody testing can be carried out. Long-term management of juvenile MG depends on clinical presentation and may include acetylcholinesterase inhibitors; systemic corticosteroids; intravenous immunoglobulin; cytotoxic immunosuppressants; and plasmapheresis. Pyridostigmine remains the first-line acetylcholinesterase inhibitor used for treatment of juvenile MG. Side effects with long-term therapy may include nausea; vomiting; diarrhea; fasciculations; muscle twitching; bradycardia; and abdominal cramps. The outcome for adult patients with MG crisis is good if therapeutic and supportive measures are used efficiently. The mortality rate is approximately 8% in adults, and about one-third will experience a recurrent episode. No such data are available for children with MG crises. In any child with MG,
careful long-term monitoring and therapeutic plans should be implemented by the pediatric neurologist and primary care pediatrician.

REFERENCES