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Abstract:

A 3-year-old boy presented to the emergency department with a chief complaint of “lethargy” and was found to have ptosis with eventual respiratory failure and need for emergent intubation. There is a broad differential for a patient with respiratory failure, and careful physical examination and history are imperative to reduce morbidity and prevent mortality. After further evaluation and workup, the diagnosis is ultimately revealed.

Keywords:

myasthenia gravis; respiratory distress; ptosis; myasthenic crisis

How Much Drool Is Too Much?

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A 3-year-old boy with a history of allergic rhinitis and persistent asthma presented to a pediatric emergency department (ED) in Arizona with parental concern for congestion and drooping red eyes at 10:00 PM. His father noted that earlier in the day, his speech was more difficult to understand but returned to normal after a nap. Vital signs on arrival to the ED were temperature 36.9°C, heart rate 108 beats per minute, respiratory rate 24 breaths per minute, and pulse oximetry of 99% on room air. On physical examination, there were bilateral conjunctival erythema and swollen nasal turbinates, and the patient was noted to be rubbing his eyes. He was breathing comfortably on room air with clear breath sounds, and his heart had a regular rate and rhythm. Cranial nerves 2-12 were intact, and he ambulated appropriately for age and followed commands. There were no focal neurologic deficits on examination. The patient was continued on home cetirizine, started on tetrahydrozoline eye drops, and discharged home with the diagnosis of allergic rhinitis and viral conjunctivitis.

The patient returned to the same ED with his father the next day at around 10:00 AM for a right forehead laceration after hitting his head on the edge of the bed. The injury occurred while in the care of his grandparents. There was no report of vomiting or loss of consciousness. Both the father and the provider felt the patient's behavior was at neurologic baseline for a 3-year-old at the time of arrival to the ED. Similar to his previous visit, he was afebrile to 36.9°C with a heart rate of 107 beats per minute, respiratory rate of 26 breaths per minute, and pulse oximetry of 98% on room air. The physical examination noted a 3-cm linear forehead laceration over frontal bone with surrounding hematoma. There was no mention of any other abnormal physical examination findings including eye findings. He met low-risk criteria according to the Pediatric Emergency Care Applied Research Network (PECARN) head trauma algorithm and

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thus did not receive imaging or observation. His laceration was repaired with skin adhesive, and he was discharged home with his father.

The patient returned 9 hours later to the same ED for his third visit within 24 hours. This time, he presented with his mother and with a chief complaint of lethargy. The patient lives in a split household and had been in the care of the mother since 4:00 PM. Over the last 3 hours, she had noted new-onset drooling, garbled speech which was difficult to understand, difficulty swallowing water, and increased fatigue. She also felt his eyes appeared more erythematous and watery with droopy eyelids. She denied a history of any of the above symptoms prior to this visit. Since the patient had been in her care, he had 4 episodes of urinary incontinence despite previously being fully potty-trained. The mother denied any recent illness including cough, fever, ear pain, diarrhea, or vomiting. The father arrived and recalled the child having increased secretions under his care as well. The patient pointed to back of his throat when asked if he was in pain, which the father thought may be related to molar teeth eruption.

The initial vital signs on his third ED presentation were as follows: temperature 36.7°C, heart rate 130 beats per minute, respiratory rate 30 breaths per minute, pulse oximetry 99%, and blood pressure of 113/81 mm Hg. On examination, the patient was awake and calm in his mother's arms with no acute distress. He appeared appropriate for a 3-year-old and was interactive and did not appear altered. The provider was able to understand some of his speech, although some speech was garbled, making it difficult to understand fully. His head was atraumatic other than the previously repaired laceration. His pupils were of normal size, equal, round, and reactive to light bilaterally without significant conjunctival injection. He had ptosis bilaterally. The tympanic membranes were pearly. There was no rhinorrhea, but he did have drooling and clear oral secretions. No oropharyngeal erythema, exudates, palatal petechiae, uvular deviation, or tonsillar hypertrophy or asymmetry was appreciated. There was normal work of breathing and clear lungs sounds bilaterally. When agitated, he had intermittent stridor, but at rest, he did not exhibit stridor, tracheal tugging, accessory muscle use, wheezes, or crackles. He had tachycardia but no murmurs, rubs, or gallops. There was no lymphadenopathy. His abdomen was soft, nontender, nondistended, and without hepatosplenomegaly. Neurologically, the patient had bilateral ptosis but no other gross cranial nerve deficits. He had 5/5 strength bilaterally in his upper and lower extremities. Gross sensation was intact. His patellar reflexes were 2+ bilaterally, and providers were unable to

reliably elicit other reflexes. Anal sphincter tone was normal. He was able to ambulate without difficulty and had no ataxia.

Because of the history of head injury earlier in the day with new-onset neurologic complaints, a computerized tomography (CT) study of the head without contrast was ordered in addition to soft tissue neck radiographs due to the increased drooling and stridor. A respiratory pathogen polymerase chain reaction panel (RPP) nasopharyngeal swab; complete blood count; complete metabolic panel; urine drug screen; and ingestion laboratory tests including aspirin, acetaminophen, and alcohol levels were sent. An electrocardiogram (ECG), as part of the toxicological workup, was also performed.

The result of the CT head was normal. The neck radiographs showed “mild narrowing of the subglottic airway with loss of normal shouldering, suggesting croup” (Figure 1). Complete blood count and complete metabolic panel were unremarkable, and aspirin, acetaminophen, and alcohol levels were negative. RPP was positive for coronavirus. ECG result was likewise normal.

Approximately 2 hours after initial evaluation, the providers were called back into the room by his nurse who had noticed labored breathing, tachycardia to 146 beats per minute, and a decreased respiratory rate to 20, and he was now on 1.5 L oxygen flow via nasal cannula to maintain oxygen saturations above 90%. The patient was less active and alert than his previous examination and had more copious clear oral secretions, labored pattern of breathing, diffuse crackles throughout bilateral lung fields, and inspiratory stridor. He was



Figure 1. Neck soft tissue radiograph showing steeple sign concerning for croup.

tachycardic but without any murmurs, rubs, or gallops and no appreciable hepatomegaly. Other than being less active, there were no other acute changes in his neurologic examination. The decision was made to intubate the patient for airway protection, and he underwent rapid sequence intubation with fentanyl, midazolam, and rocuronium. He was easily intubated on the first attempt with a 4.0Fr microcuffed endotracheal tube (ETT), which was downsized intentionally because of concern for increasing stridor and potentially narrowed airway. No caustic burns or other airway abnormalities were appreciated during direct laryngoscopic visualization. The patient oxygenated and ventilated without difficulty following intubation, although when the ETT cuff was deflated for repositioning of the ETT following radiograph, copious amounts of clear secretions from the patient's mouth were noted. The rapid urine drug screen was negative, and the patient was admitted to the pediatric intensive care unit for further care.

DIFFERENTIAL DIAGNOSIS

The differential for a patient presenting to the ED with acute respiratory distress is broad and includes infection, ingestion, trauma, envenomation, muscular disorders, and autoimmune etiologies. Scorpion envenomations along with other insect bites are common in Arizona and can be a cause of drooling and increased secretions. This was at the top of the differential upon evaluation and the need for emergent intubation. Scorpion envenomation often presents with respiratory distress along with increased drooling, abnormal eye movements, muscle twitching, and agitation. The patient did have

respiratory distress, drooling, and ptosis of his eyes, but no abnormal eye movements were appreciated. Additionally, the patient initially presented without respiratory distress and progressed, which is not characteristic of envenomation. Grading and treatment of scorpion envenomation (Table 1) are based on location of pain, location of paresthesia, cranial nerve involvement (oral secretions, blurry vision, tongue fasciculations, nystagmus), and skeletal neuromuscular dysfunction (abnormal movements or flailing of the extremities).¹

Additionally, with stridor and drooling, infectious etiologies were on the top of the differential. Most common bacterial etiologies include *Streptococcus* species and *Staphylococcus aureus*.² There are many viral etiologies as well, including rhinovirus, adenovirus, enterovirus, coronavirus, and influenza. The patient was coronavirus positive on RPP. Additionally, the patient had stridor along with an radiograph concerning for subglottic narrowing, most consistent with croup. Croup, also referred to as *laryngotracheitis*, is an upper respiratory illness caused by parainfluenza 1 or 2.² The other etiologies for croup include influenza A and B, measles, adenovirus, and respiratory syncytial virus. Croup is diagnosed based on signs and symptoms including stridor, barking cough, or hoarseness. A neck radiograph will show the traditional narrowing of the trachea known as a *steeple sign*.³ However, a radiograph is not routinely performed for diagnosis because croup is usually a clinical diagnosis. Although the patient had coronavirus and concern for croup, this did not explain his ptosis and other neurologic findings.

Ingestion along with trauma is often also at the top of the differential as it typically presents acutely, and prompt diagnosis and treatment are critical. In

TABLE 1. Scorpion envenomation grading.

	Location of pain	Location of paresthesias	Cranial nerve involvement and/or skeletal neuromuscular dysfunction	Treatment
Grade 1	Local only	Local only	None	Analgesia
Grade 2	Local and proximal to envenomation	Local and proximal to envenomation	None	Analgesia +/- anxiolytic
Grade 3	Local and proximal	Local and proximal	Cranial nerve OR skeletal neuromuscular dysfunction	Analgesia, anxiolytic, Anascorp antivenom (centuroides immune Fab)
Grade 4	Local and proximal	Local and proximal	Cranial nerve AND skeletal neuromuscular dysfunction	Analgesia, anxiolytic, and Anascorp antivenom, airway protection as needed

the United States, there are an estimated 8000 organophosphate poisonings per year.⁴ Additionally, poisoning with selenium and mercury can present similarly. Treatment includes administration of atropine along with pralidoxime.⁴ Drugs that can cause hypersalivation include morphine, pilocarpine, methacholine, haloperidol, and clozapine. Cocaine and phencyclidine can also cause increased secretions. There was no history to suggest ingestion in the patient.

Muscular disorders can also cause respiratory distress and failure. Muscular dystrophy, polymyositis, and myasthenia gravis should be on the differential. The most common muscular dystrophies in children are Duchene and Becker. Both are X-linked recessive and caused by a mutation in the dystrophin gene which clinically presents with progressive weakness.⁵ Weakness often affects proximal limb muscles before distal, and lower extremities before upper extremities. The classic finding is Gowers sign, where a child uses their hands and arms to walk up their body to get to an upright position from sitting because of the lack of hip and thigh muscle strength.⁵ Physical examination findings include pseudohypertrophy of the calf, lumbar lordosis, waddling gait, shortening Achilles tendon, hypotonia, and hyporeflexia.⁵ The patient did not have any secondary symptoms of the above, and the patient had a normal gait. Polymyositis, on the other hand, is a rare autoimmune myopathy with direct T-cell invasion of the muscle fibers.⁶ The hallmark of this disease is weakness, primarily proximal muscle weakness. Lastly, myasthenia gravis is an antibody-mediated autoimmune disease that affects postsynaptic neuromuscular junction.⁷ Usually, symptoms are gradual, but patients can present in myasthenic crisis leading to respiratory failure. Most common symptoms include ptosis and diplopia which are worse with activity and improved with rest. Myasthenic crisis is a life-threatening condition defined by worsening weakness and requires noninvasive ventilation or intubation.⁸

CASE PROGRESSION AND DIAGNOSIS

The patient arrived to the pediatric intensive care unit intubated on a ventilator with a rate of 28 breaths per minute, tidal volume of 100 mL (7 mL/kg), PEEP of 7, pressure support of 10, and FIO₂ of 60%. He was sedated but had clear and equal breath sounds bilaterally. His heart had a regular rate and rhythm, and he had good perfusion throughout. No abnormal physical examination findings were found. His orogastric tube was set to low intermittent suction, and he remained on a dexmedetomidine drip at 0.4 µg/kg/h

and ampicillin/sulbactam 50 mg/kg intravenously every 6 hours pending culture results. A CT of the neck was obtained to rule out other etiologies for respiratory distress, which was negative for peritonsillar or retropharyngeal abscess. An extubation trial was done on day 2 of admission. Because of inspiratory stridor and increased work of breathing, he was given inhaled dexamethasone and racemic epinephrine with minimal improvement. He continued with poor pharyngeal tone, drooling, dysarthria, and hypoxia with oxygen saturations 80%, and he was reintubated for airway protection. During extubation, the patient was moving all his extremities, but there was concern for hypotonia. The patient was on sedating medications, which were a confounding factor. Neurology was consulted at that time because of concern for a neuromuscular process. Their recommendations included to obtain negative inspiratory force studies, magnetic resonance imaging of the thoracic and lumbar spine with gadolinium contrast, acetylcholine receptor antibody, ganglioside (GM1, GD1b, GQ1b) antibodies, lumbar puncture with standard indices plus cerebrospinal fluid (CSF) IgG, oligoclonal bands, IgG/albumin ratio, IgG index, and electromyography. CSF studies were normal with WBC 0, RBC 0, protein 19, and glucose 97. CSF West Nile Ab IgG and IgM were negative. CSF oligoclonal bands were negative, and the patient had a normal IgG to albumin ratio. A comprehensive drug screen was negative. Negative inspiratory force was reported at -40. Electromyography with 2-Hz repetitive stimulation was abnormal, which showed a greater than 10% decrement for the left deltoid/axillary, left tibialis anterior/peroneal, and left adduction digiti minimi/ulnar. Ganglioside (GM1, GD1b, GQ1b) IgG and IgM antibodies were negative. Initial acetylcholine binding and block antibodies were negative, but positive for acetylcholine receptor muscle binding (0.15 nmol/L, normal <0.02), negative striated muscle Ab titer, and AchR muscle modeling Ab 17%, therefore 17% loss of Ach receptor. Given these results, the diagnosis of myasthenia gravis was made.

After diagnosis, the patient was treated with IVIG and prednisone for 3 days with improvement of symptoms. He was successfully extubated on day 9 of hospitalization after treatment and remained stable throughout his 18-day hospitalization. He did not require plasma exchange. He was placed on pyridostigmine along with tapering doses of steroids prior to discharge. After discharge, the patient was followed by neurology, physical therapy, occupational therapy, general pediatrics, and immunology. He regained his baseline strength, his ptosis resolved, and he returned to his normal behavior

and activities. He was tapered off steroids in the year after discharge from the hospital and remained on pyridostigmine.

DISCUSSION

Myasthenia gravis is the most common disorder of neuromuscular transmission. The hallmark of the disorder is fluctuating degrees and variable combination of weakness in ocular, bulbar, limb, and respiratory muscles. The weakness is from the antibody-mediated T-cell response to acetylcholine receptors or receptor-associated proteins at the postsynaptic neuromuscular junction.⁷

The incidence of myasthenia gravis is about 20 per 100 000 in the United States, which includes children and adults, and a prevalence of roughly 60 000 patients affected. It is estimated that the risk of myasthenic crisis in myasthenia gravis patients may be as high as 10 to 20%, and 13 to 20% of myasthenia gravis presents with myasthenic crisis as the first manifestation.^{9,10} Precipitating factors include infection, thymectomy, pregnancy, childbirth, and tapering of immunosuppressive medications.¹¹ Medications most often associated are antibiotics (aminoglycosides, fluoroquinolones, erythromycin, azithromycin), cardiac medications (β -blockers, procainamide, quinidine), and magnesium.¹² In the case of our patient, no specific cause or precipitating factor was found except for potentially an upper respiratory illness with coronavirus and signs and symptoms of croup.

The diagnosis of myasthenia gravis is complex. Bedside tests including the ice pack test and edrophonium test are sensitive but have major limitations with false-positive results. Thus, a confirmatory test with antibodies and electrophysiological studies (repetitive nerve stimulation studies and single-fiber electromyography) are needed. An immunologic assay to detect the presence of circulating acetylcholine receptor antibodies is the first step in the laboratory confirmation of myasthenia. On the other hand, muscle specific kinase antibodies and receptor tyrosine kinases are found in less than 50% of generalized myasthenia gravis without acetylcholinesterase receptor antibodies but are rare in ocular myasthenia gravis.^{13,14}

The treatment for myasthenia gravis begins with respiratory support including intubation or noninvasive ventilation. Once disabling and often fatal, myasthenia gravis can be managed effectively with therapies that include anticholinesterase agents, rapid immunomodulatory therapies, chronic immunosuppressive agents, and thymectomy. Treatment varies based on the age of the patient, severity of disease, respiratory involvement, bulbar involvement, and progression of the disease. Goals of

treatment are to minimize adverse effects of the drug while having improvement in symptoms and return to baseline function. Symptomatic treatment with acetylcholinesterase inhibition increases the amount of acetylcholine at the neuromuscular junction, thereby improving symptoms. Pyridostigmine is often the treatment of choice and sometimes is used as monotherapy. With generalized myasthenia gravis, steroids and nonsteroidal immunosuppressive agents are used to target immune dysregulation. Likewise, plasma exchange or IVIG is an immunomodulating treatment used for bridge therapy or during acute exacerbations of myasthenia gravis. Approximately 15% of patients with myasthenia gravis are found to have a thymoma. Surgery with complete resection is indicated for these patients when possible.

SUMMARY

Myasthenic crisis is an uncommon yet important diagnosis to keep on the differential of a patient with respiratory distress, especially in a patient with ptosis and sialorrhea. It is also imperative to take a closer look at patients who present for multiple visits to the ED in a short time period even if they appear to be unrelated or benign. Our patient presented 3 times to the ED in a 24-hour period. He was diagnosed with allergic rhinitis and a facial laceration in his first 2 visits. Individually, these were not concerning, but retrospectively, they were red herrings. When assessing a child with respiratory distress requiring intubation, the differential should remain broad, but the physical examination and history are paramount for diagnosis and differentiating infectious vs other etiologies. Early recognition and consultation with specialists can help with diagnosis, treatment, and management. **+**

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