A 15-Year-Old Girl with a History of Depression and Weight Loss

Robert Listernick, MD

A 15-year-old girl with a history of depression presented after 6 months with a 70-pound weight loss with subsequent cessation of her menstrual cycle. She stated that she does not have any trouble eating but she becomes full quickly. She sleeps most of the day and only has time for 1 to 2 meals. She denies any vomiting, diarrhea, or abdominal pain. Her mother commented on how slowly she eats and how she picks at food on her plate. Her mother has noted that her daughter’s speech has changed in the past 5 months; she feels that her daughter is slurring her words and sometimes has trouble finding a word that she’s trying to use. Her gait has changed as well; she walks more slowly and shuffles. She has gone to several doctors as well as to several different hospitals for evaluation of the weight loss but has not been provided with any answers besides a recommendation for her to see a psychiatrist. She had one inpatient psychiatric admission 2 weeks prior to this presentation. She reported there that she was eating three full meals each day. She says she’s tried her best to finish them, but felt full early in her meal. She feels that this hospitalization might have helped her depression and the feelings of sadness and emptiness that persist. She reports that she has been struggling with depression since last August when she was having issues at school.

On review of systems, she indicated having trouble eating with early satiety starting 1 month ago. She complains of pervasive body aches. Her walk to school became even more difficult because of her pain, particularly in her back. She’s had no incontinence or difficulties urinating or stooling. Her menses, which had been regular, stopped completely 4 months previously.

She lives at home with her father and siblings. Her father is not home during the day. She sleeps most of the day and has only been to school two times since these symptoms started. Her past history was unremarkable. Her family history is remarkable in that her sister died of a “pineal tumor;” no other information is available.

On physical examination, her pulse was 112 beats per minute and her blood pressure was 106/72 mm Hg. Her body mass index was 14 kg/m². She was a cachectic young woman. Save for difficulty taking full inspiration and decreased muscle mass, her general examination was normal. On neurologic examination, she was oriented to person, place, and time and had a good fund of knowledge. She avoided direct eye contact. Her speech waxed and waned in clarity but improved when she was asked to repeat herself. Her peripheral vision and hearing were intact. Her facial sensation was intact. Her palate was symmetric. There was no hoarseness to her voice. Her cranial nerve function was normal. Her reflexes were 2+ throughout. Sensation, vibration sense, and proprioception were normal. Cerebellar testing was normal and she had a negative Romberg test.

On the first round of blood tests, her complete blood count was normal. Basic metabolic profile revealed sodium of 139 mEq/L, potassium of 3.9 mEq/L, chloride of 93 mEq/L, and bicarbonate of 39 mEq/L.

Robert Listernick, MD, moderator: So, she has an eating disorder, right?

Robert Tanz, MD, general academic pediatrician: If you had to throw a dart at a dartboard at one diagnosis in a teenager who has lost this much weight, you’d say anorexia nervosa. But you’re making it sound like her general affect is one of depression, which wouldn’t fit well with anorexia, and her electrolytes need explaining. Certainly if she had bulimia with chronic vomiting you might see low serum chloride and elevated se-
rum bicarbonate but she shouldn’t have had this degree of weight loss.

Edna Romero, PhD: I was part of the team that consulted when she was first admitted; she consistently denied purposefully restricting her diet as well as any distortions in body image. That’s unusual for a teenager with an eating disorder.

Dr. Listernick: What about depression? She sounds depressed to me.

Dr. Romero: That was hard to tease apart because the onset of her depressive symptoms also seemed to correlate with the onset of her physical symptoms. She reported that she felt more fatigued and less engaged in activities that she normally enjoyed and was just more tired overall. We determined that her symptoms were more of an adjustment disorder that correlated with the onset of her physical symptoms and not necessarily a pervasive, persistent pattern of saddening.

Dr. Listernick: We pediatricians always get frustrated when we ask the psychiatrist whether a patient’s symptoms are organic or psychiatric and you don’t oblige us.

James G. Mackenzie, DO, child psychiatrist: The problem is that children who have organic illnesses also will have secondary or coincidental primary emotional reactions to their circumstances. It’s extremely difficult for us at times. She may very well have an organic illness that exacerbates whatever feelings she has about her social stressors such as a bad breakup with a boyfriend.

Dr. Listernick: I think we all agree that she needs a serum pH to be able to accurately interpret the serum electrolytes. One wasn’t performed immediately. She was admitted from the emergency department. Overnight, it was noted that she was taking shallow respirations. She was not placed on pulse oximetry initially but because of the respiratory pattern her oxygen saturation was checked and was found to be between 85% and 92% on room air. An arterial blood gas was obtained and the results were a pH of 7.27, pCO₂ (partial pressure of carbon dioxide) of 89 mm Hg, and pO₂ (partial pressure of oxygen) of 56 mm Hg. A chest X-ray was normal.

Denise Goodman, MD, pediatric intensive care physician: So as to emphasize a basic teaching point, you cannot accurately interpret her electrolytes without an arterial blood gas determination. We should also not confuse the terms “acidotic and alkaleotic” with “acidemic and alkalemic.” Acidosis or alkalemia refers to a primary physiologic process that causes a change in the serum base or acid, whereas acidemia or alkalemia refers to the blood pH. Initially we knew that she was alkaleotic but didn’t know her blood pH, which is crucial in understanding the metabolic processes taking place within her. Her hyperventilation is not surprising because she has a primary respiratory acidosis with a compensatory metabolic alkalosis. Remember that when one tries to correct one’s blood pH, it is impossible to overcompensate. We know that she has a primary respiratory acidosis because her pH is low, meaning she is also acidemic, so it’s clear that the initial alkalosis was compensatory, not primary.

Dr. Listernick: What was going through the team’s mind at this juncture?

Nina Gazanfari, MD, pediatric resident: Now that we knew that she had a chronic respiratory acidosis with metabolic compensation and a normal chest X-ray, we started thinking about processes that would lead to hyperventilation or limit her respiratory effort. We were struck by her shallow respirations. We wondered about a primary neuromuscular disease or perhaps chest wall involvement from scleroderma leading to respiratory failure.

Lauren Camarda, MD, pediatric pulmonologist: Let’s not forget about the historical point that she was “sleepy all the time.” Most likely her hyperventilation was worse at night, leading to even greater CO₂ (carbon dioxide) retention and CO₂ narcosis. It’s possible that her receipt of supplemental oxygen might even exacerbate CO₂ retention if she has lost her hypoxic drive to breathe. Pulmonary function testing would be helpful in sorting this out.

Dr. Listernick: Once that arterial blood gas was obtained, she was transferred to the intensive care unit. What was your thinking?

Kelly Michelson, MD, pediatric intensive care physician: We initially cast a broad differential diagnosis. We wondered about malignancy given her weight loss but put this low on the list. I suspect that respiratory failure would be exceedingly rare in a child with malignancy unless there were significant pulmonary involvement; her chest X-ray was normal. A myopathy was entertained but she had no other signs such as sclerodactyly. She clearly didn’t have an eating disorder; when she was asked what she thought of her body she said, “I want my old body.” Ultimately, over the first day, her examination evolved and it became clear that she had profound weakness. We asked the neurology department to see her.

Tracy Gertler, MD, PhD, pediatric neurologist: When we saw her the next day we thought she had bilateral ptosis, limitation of eye movement to the right, and lower facial weakness, as she couldn’t purse her lips or puff out her cheeks. Given the bulbar muscle weakness, ophthalmoplegia, and respiratory insufficiency, we thought that myasthenia gravis (MG) was most likely. Also, I know you downplayed it somewhat in your history on purpose, but her “low speech” and swallowing difficulties in retrospect were a manifestation of weakness.
Leon Epstein, MD, pediatric neurologist: Given that we’re discussing MG, it’s important to distinguish strength from fatigability. If she rested for a period, she should be able to do a single squat. Her respiratory muscles are working all day without rest leading to respiratory failure.

Dr. Listernick: How was she evaluated for MG?

Nancy Kuntz, MD, pediatric neurologist: By the time I saw her in the neuromuscular laboratory, she had bilateral ptosis and relatively immobile eyes. When I queried her extensively, I could not elicit a history of fatigability throughout the day.

Dr. Listernick: When I was in medical school in the pre-antibiotic era, I learned about the edrophonium test for diagnosing MG. Do you still use it?

Dr. Kuntz: It needs to be performed in an intensive care setting because you might invoke profound bradycardia or other serious side effects. I’m aware of several disasters with its use. In addition, children tend not to enjoy it due to some of the side effects such as bowel “gurgling.” Finally, I believe that edrophonium is no longer available. Neostigmine could be used but it is longer acting. We performed electromyography (EMG) instead.

Dr. Listernick: Can you walk us through the EMG?

Dr. Kuntz: We tried to focus on the muscle groups that are easiest and most reliable to test as well as those that are affected by the symptoms. We started with the ulnar nerve in the hand because it’s easiest to test. We saw no decrement in activity with repetitive stimulation at 2 Hz and no evidence of fatigue after 60 seconds of exercise. We next tested the cranial nerves because of the bulbar involvement. The same was true of the spinal accessory nerve at the side of the neck recording on the trapezius. However, testing of the facial musculature showed a 25% decline in function diagnostic of a neuromuscular transmission defect. Finally, testing of single nerve fibers of her forehead muscles was also confirmatory.

Dr. Listernick: So she has MG?

Dr. Kuntz: MG is not a single diagnosis; presently, there have been three separate protein targets identified in the group of acquired autoimmune myasthenias: the acetylcholine receptor, the MUSK (muscle-specific kinase) protein, and LRP4. There are probably many more targets waiting to be identified in those MG patients who don’t have identifiable autoantibodies.

Dr. Listernick: Does MG have different presentations based on the exact autoantibody?

Dr. Kuntz: Of course, because every patient is unique. However, patients with acetylcholine receptor antibody myasthenia tend to present with ptosis and ophthalmoplegia. Most of the children with this presentation develop generalized involvement of the extremities within the first 2 years of involvement. MUSK antibody-related myasthenia tends to remain confined to the respiratory, facial, and bulbar muscles more than acetylcholine receptor antibody MG does. It also occurs with a much higher frequency in people who have Mediterranean or African ancestry.

Dr. Listernick: Treatment?

Dr. Kuntz: Given the degree of involvement, I recommended that treatment be instituted immediately even before we had the antibody results. She underwent plasma exchange therapy first, followed by administration of intravenous immunoglobulin.

Dr. Camarda: She also required bilevel positive airway pressure while sleeping. It generates inspiratory and expiratory pressure gradients that complement the patient’s own respiratory cycle, optimizing the lungs’ efficiency and reducing the work of breathing. Over time,
she’s begun to tolerate the mask, and her CO₂ is slowly starting to normalize.

**Dr. Listerick:** Is her muscle damage irreversible?

**Dr. Kuntz:** I think her clinical course has been short enough that she stands a good chance of having reversible weakness. I didn’t see any muscle atrophy. She still has ptosis and ophthalmoplegia but she says that she feels 100% better. Untreated MUSK-associated MG may cause irreversible muscle atrophy due to the immune process.

**Dr. Listerick:** Hopefully she’ll do well. Thanks everyone.

---

**Key Learning Points**

1. Acidosis or alkalosis refers to a primary physiologic process that causes a change in the serum bicarbonate, whereas acidemia or alkalemia refers to the blood pH.

2. Acid-base status and serum electrolytes cannot be accurately interpreted without an arterial blood gas determination.

3. Myasthenia gravis (MG) is not a single diagnosis; presently, there have been three separate protein targets identified in the group of acquired autoimmune myasthenias: the acetylcholine receptor, the MUSK (muscle-specific kinase) protein, and LRP4.

4. Patients with acetylcholine receptor antibody MG tend to present with ptosis and ophthalmoplegia. Most of the children with this presentation develop generalized involvement of the extremities within the first 2 years of involvement. MUSK antibody-related MG tends to remain confined to the respiratory, facial, and bulbar muscles more than acetylcholine receptor antibody MG does.