



The reader is encouraged to write possible diagnoses for each case before turning to the discussion. We invite readers to contribute case presentations and discussions. Please inquire first by contacting Dr. Nazarian at LFredN@aol.com.

Case 1 Presentation

A 15-year-old African-American boy is seen in late February complaining of 2 weeks of “tingling and cramping in my hands and feet after basketball.” He has been well and is taking no medications. His diet consists mainly of “fast foods and cola.”

Physical examination reveals a youth who looks well. All vital signs are normal. His growth has consistently followed the 75th percentile for height and 50th percentile for weight. Physical findings are completely normal. He has sexual maturity rating stage 4 genitalia, normal cranial nerve examination results, and normal strength and deep tendon reflexes.

Initial laboratory study results include: calcium, 4.9 mg/dL (1.23 mmol/L) (normal, 8.5 to 10.2 mg/dL [2.13 to 2.55 mmol/L]); phosphorus, 4.9 mg/dL (1.58 mmol/L) (normal, 2.5 to 4.5 mg/dL [0.81 to 1.45 mmol/L]); magnesium, 1.9 mg/dL (0.78 mmol/L) (normal, 1.7 to 2.2 mg/dL [0.70 to 0.91 mmol/L]); alkaline phosphatase, 576 U/L (normal, 100 to 390 U/L); albumin, 3.6 g/dL (36 g/L) (normal, 3.6 to 5.0 g/dL [36 to 50 g/L]); and creatinine, 0.7 mg/dL (61.9 μmol/L) (normal, 0.7 to 1.5 mg/dL [61.9 to 132.6 μmol/L]). Thyroid-stimulating hormone, complete blood count, liver and pancreatic enzymes, and the remainder of the serum electrolytes are within normal limits.

On re-examination, the patient is noted to have an absence of Trousseau or Chvostek signs. Electrocardiography demonstrates normal sinus rhythm with a corrected QT interval of 451 ms (normal, 425 ms maximum). Radiographs of the long bones reveal no deformity, pathologic fractures, or demineralization.

Case 2 Presentation

An 18-month-old boy has a 3-day history of worsening cough, tachypnea, and increased work of breathing. He has had no fever, anorexia, vomiting, diarrhea, cyanosis, abdominal pain, or rashes. His immunizations are up to date, including influenza. He has experienced three episodes of “atypical pneumonia” involving the right middle and lower lobes, all requiring hospitalization. He was a second-born twin delivered at 34 weeks’ gestational age and had significant respiratory distress starting in the delivery room that required positive pressure ventilation for 3 days and a 16-day stay in the neonatal intensive care unit. In addition, he sustained Erb-Duchenne palsy following a traumatic delivery. His growth and activity always have been less than that of his twin brother.

On physical examination, the boy is afebrile and has a regular pulse rate of 170 beats/min, a respiratory rate of 75 breaths/min, and a pulse oximetry reading of 88% on room air. Other positive findings include nasal flaring, subcostal and intercostal retractions, very little bulging of the abdomen on inspiration, and decreased breath sounds at the right base.

A chest radiograph shows right lower lobe atelectasis, with elevation of the right hemidiaphragm. Despite therapy with 3 days of oxygen and cefuroxime as well as aggressive chest physical therapy, he shows little improvement. You order a procedure that clarifies the diagnosis.

Case 3 Presentation

A previously healthy 17-year-old boy is brought to the emergency department because of acute alteration of his mental status, having been found at home by his sibling in an agitated,

delusional state. The initial history obtained from the patient's mother and sibling reveals no history of trauma, fever, drug ingestions, or seizurelike activity.

The boy is unable to follow simple commands, is combative, and has slurred speech. His pulse is 124 beats/min in a regular rhythm, blood pressure is 154/90 mm Hg, temperature is 99.5°F (37.5°C), and respiratory rate is 18 breaths/min with 100% oxygen saturation on room air. He also has dry oral mucosa, rare bowel sounds, and mydriasis. The rest of the physical findings are normal.

Levels of electrolytes and liver transaminases, findings on urinalysis, and complete blood count all are normal. Computed tomography of the head yields normal findings. A comprehensive urine toxicity screen is sent for analysis. The patient is admitted for further evaluation and management.

Case 1 Discussion

Low serum calcium ion concentrations can destabilize the resting cell membrane potential and increase peripheral neuromuscular irritability. Signs and symptoms of prolonged hypocalcemia in the older child or adolescent can include tetany with perioral and extremity numbness, tingling, stiffness, clumsiness, cramps, laryngospasm, carpopedal spasm, diarrhea, unusual behavior, and seizures. Patients who have a gradual onset of hypocalcemia tend to have fewer and less severe symptoms. Other metabolic factors that may increase the severity and frequency of symptoms include respiratory alkalosis (hyperventilation), hypokalemia, and sympathetic overactivity.

Etiology

The origin of hypocalcemia in children can be categorized into causes that result in a loss or sequestration of calcium from the circulation and those that result in decreased entry of calcium into the circulation. Hypoalbuminemia, hyperphosphatemia, rhabdomyolysis, alkalosis, chelation, pancreatitis, malignancy, renal tubular disorders, sepsis, and the effects of medications can lead to a loss of calcium from the circulation. Hypoparathyroidism; hypomagnesemia; the effects of medications; and abnormalities in vitamin D intake, absorption, metabolism, or action can result in decreased entry of calcium into the circulation.

Diagnosis

The diagnosis of hypocalcemia should be confirmed by repeated measurement of serum calcium and, if in doubt, should be corroborated by measurement of serum ionized calcium, if available. Based on history and physical examination, a cause for the hypocalcemia should be sought next. Laboratory tests that may be helpful include measurement of serum creatinine, alkaline phosphatase, albumin, amylase, phosphorus, magnesium, parathyroid hormone (PTH), 25-hydroxycholecalciferol, and 1,25-dihydroxycholecalciferol.

Further laboratory evaluation of this patient revealed a PTH level of 225 pg/mL (23.7 pmol/L) (normal, 10 to 65 pg/mL [1.05 to 6.8 pmol/L]), 1,25-dihydroxycholecalciferol level of 35 pg/mL (91 pmol/L) (normal, 17 to 53 pg/mL [44.2 to 137.8 pmol/L]), and 25-hydroxycholecalciferol level of less than 7.0 ng/mL (17.5 nmol/L) (normal, 10 to 68 ng/mL [25.0 to 169.7 nmol/L]). This patient's hypocalcemia was due to vitamin D deficiency, which resulted from his unbalanced diet.

He lived with an elderly grandparent who was lactose-intolerant and did not purchase any dairy products. The boy's diet was primarily foods such as soda, French fries, and fast food chicken and hamburgers.

Pathogenesis

The integrated regulation of the serum calcium concentration depends on bone resorption and renal excretion of calcium under the control of PTH and intestinal absorption of calcium under the control of vitamin D. Calcium is absorbed poorly from the gastrointestinal tract, and even under homeostatic conditions with an adequate supply of vitamin D, there is a net absorption of only 10% of the intestinal calcium. In the absence of vitamin D, the active gastrointestinal absorption of calcium can fall below that required to maintain normal serum calcium levels. Vitamin D also is needed for PTH to have its desired effect on end-organ tissue. In the absence of vitamin D, PTH is much less effective at maintaining calcium concentrations through bone resorption.

The term "vitamin D" refers to a group of steroid molecules. 25-hydroxycholecalciferol is the major circulating form of vitamin D and the form that should be measured to diagnose vitamin D deficiency. Irradiation of skin by sunlight is one source of the vitamin. Most foods contain little or no vitamin D, but fortified milk, fortified cereals, cod liver oil, and some saltwater fish such as salmon, herring, and sardines are good sources of the vitamin.

The level of PTH becomes elevated in vitamin D deficiency to compensate for hypocalcemia, thereby increasing serum calcium concentrations through both kidney reabsorption and bone resorption of calcium. The classic metabolic presentation of vitamin D deficiency is hypocalcemia

with hypophosphatemia, but hyperphosphatemia is believed to occur in approximately one third of patients who have vitamin D deficiency, as in this boy.

Hepatic stores of vitamin D tend to become depleted in individuals who have poor dietary intake of vitamin D coupled with inadequate exposure to sunlight. Although fortified milk and cereals have reduced the incidence of vitamin D deficiency in the United States greatly, many diets still remain poor in vitamin D. This dietary insufficiency predisposes individuals to vitamin D deficiency, especially during the late winter months or at geographic latitudes where exposure to sunlight is limited. Darkly pigmented skin, which is believed to be less efficient at synthesizing vitamin D from sunlight, also may contribute to low stores of vitamin D. Human milk contains variable amounts of vitamin D. Babies who are breastfed, have minimal exposure to sunlight, and are not given supplemental vitamin D are susceptible to vitamin D deficiency, especially if they have dark skin.

Long-term Effects

Rickets, a childhood disease, and osteomalacia, an adult condition, are bone demineralization disorders characterized by soft, malleable, low-density osteoid. These processes can be sequelae of calcium deficiency or of vitamin D deficiency, as decreased total body calcium stores stimulate bone resorption and reallocation of calcium from mineralizing of bone to maintain serum calcium levels.

Abnormal mineralization of bone can lead to craniotabes, rachitic rosary, bowing of the long bones, enamel and eruption defects of teeth, scoliosis, bone pain, fractures, and growth failure.

This patient had no symptoms, findings on physical examination, or

radiologic changes consistent with rickets, demonstrating that hypocalcemia can occur before significant skeletal changes are present. Although hypocalcemia can be corrected before skeletal changes develop if it is detected in time, hypocalcemia itself can be fatal.

Therapy

Treatments for vitamin D deficiency include oral supplementation with vitamin D and increased exposure to ultraviolet (UV) light (sunlight or UV lamp) while ensuring adequate dietary or supplemental calcium intake. Vitamin D supplementation can be achieved with one of several vitamin D analogs, including vitamin D₂ (ergocalciferol) and calcitriol (1,25-dihydroxycholecalciferol). Calcitriol often is reserved for use in patients who have renal disease and otherwise cannot manufacture necessary quantities of the steroid in their kidneys.

Serum and urine calcium levels should be monitored at 1- to 3-month intervals to prevent hypercalcemia and nephrocalcinosis. The prognosis for vitamin D deficiency is excellent with adequate supplementation and monitoring.

This patient was started on oral ergocalciferol and calcium supplements. After 6 weeks of therapy, his calcium concentration had risen to 9.5 mg/dL (2.37 mmol/L), PTH had normalized to 50 pg/mL (5.27 pmol/L), and 25-hydroxycholecalciferol level had risen to 8.8 ng/mL (22.0 nmol/L). He and his grandparent received dietary counseling through the endocrinology service of the medical center.

Lessons for the Clinician

Hypocalcemia can result from many causes, including vitamin D deficiency because of a poor diet. Acute effects of hypocalcemia include mus-

cular, cardiac, and neurologic derangements, which can be fatal. Over time, striking changes can occur in the bones, especially in growing children. Clinicians should be aware of the manifestations of hypocalcemia so that they will test for this condition and treat it before any further damage is done. (*Brian T. Fogarty, MD, James G. Lamphear, MD, PhD, Wiesbaden Army Airfield, Germany*)

Case 2 Discussion

Real-time fluoroscopy was performed to evaluate the motion of the diaphragm. Motion of the left hemidiaphragm was normal, but paradoxical motion of the right hemidiaphragm indicated paralysis.

The Condition

Diaphragmatic paralysis, which results from phrenic nerve injury, may occur in isolation or in association with brachial plexus injuries (80% to 90% of cases of diaphragmatic paralysis). Brachial plexus injuries occur in 0.1% to 0.5% of deliveries. The most common type is Erb-Duchenne palsy, resulting from injury to cervical nerves 5, 6, and 7. On physical examination, the infant is unable to abduct the affected arm at the shoulder, rotate externally, or supinate the forearm.

A rarer form of injury is Klumpke paralysis, which involves cervical nerves 7 and 8 and the first thoracic nerve. This injury affects the smaller muscles of the hand and wrist, rendering the infant unable to grasp with the affected hand. Some brachial plexus injuries are associated with Horner syndrome, causing ipsilateral miosis and ptosis resulting from damage to the first thoracic nerve and its sympathetic fibers.

Up to 80% of brachial plexus injuries occur on the right side, and fewer than 10% are bilateral. Difficult ex-

tractions and breech delivery are the most common precipitants.

Unilateral diaphragmatic paralysis in older children results most frequently from phrenic nerve damage, as in neonates. Causes of diaphragmatic paralysis detected after the newborn period include trauma (birth, chest wall injury), cardiac surgery (thoracotomy), spinal cord injury, neuromuscular disease (polio, peripheral neuritis, *Herpes zoster* infection), subphrenic disease (abscess, peritonitis), and idiopathic (presumed viral). Children older than 1 year of age tolerate paralysis better than do infants.

Clinical Findings

Diaphragmatic paralysis should be suspected in newborns who have respiratory distress associated with brachial plexus injuries. Infants are affected more intensely than are older children because of poor intercostal muscle development and decreased caliber of the bronchial tree. As with this patient, breathing occurs in a thoracic pattern, with little bulging of the abdomen upon inspiration.

Often the clinical course is biphasic. During the first hours after birth, respiratory distress, atelectasis, hypercarbia, and increased oxygen demand are common. During subsequent days, the condition may stabilize because positive pressure ventilation masks diaphragmatic paralysis. Over weeks, in severe cases, deterioration may be aggravated by atelectasis or infection.

As in this child, some cases of diaphragmatic paralysis related to birth injury are not noted at birth, and the condition becomes evident only when another process compromises the patient. Ultrasonography or fluoroscopy was not performed in the nursery because the patient responded to therapy, and paralysis of the diaphragm was not evident on

the radiograph at that age. Signs may appear when the patient suffers an infection, an asthma exacerbation, or atelectasis. These children often are diagnosed as having atelectasis or recurrent pneumonia without discovery of the diaphragmatic paralysis.

Diagnosis

Radiographic findings typically demonstrate reduced lung volumes, with unilateral elevation of the hemidiaphragm and sometimes atelectasis, but the elevation of the hemidiaphragm usually is not prominent early in the course. As with this patient, elevation of the hemidiaphragm may not be evident in the nursery. The involvement of the right middle and lower lobes on subsequent films obscured the elevation of the right hemidiaphragm. Phrenic nerve palsy is diagnosed in the patient who is breathing spontaneously by ultrasonography of the chest or real-time fluoroscopy, which is the most definitive study.

Prognosis and Management

The mortality rate is 10% to 15% for patients who have unilateral paralysis and up to 50% for bilateral cases. Most affected children (50% to 60%) recover within the first 6 to 12 postnatal months, with mild cases resolving by 1 to 3 months. Treatment usually is supportive, with careful monitoring of respiratory status. The infant should be placed with the affected side down and receive chest physical therapy. Oxygen administered by nasal cannula or positive ventilation has been effective. If phrenic nerve function does not return, surgical plication of the diaphragm may be indicated. A pediatric surgeon should be consulted. A physical therapist should be consulted for any infants who have palsies to prevent contractures of the affected arm.

Once this patient's pneumonia resolved, he underwent plication of the right hemidiaphragm. He tolerated the procedure well.

Lessons for the Clinician

It is important to look for an underlying cause for any patient who has recurrent pneumonia, such as an immunodeficiency, cystic fibrosis, foreign body aspiration, bronchial injury or malformation, or diaphragmatic paralysis. When the lung findings always occur in the same location, foreign body aspiration, bronchial injury or malformation, or diaphragmatic paralysis is more likely. Although diaphragmatic paralysis is an uncommon cause of recurrent pneumonia or atelectasis, knowledge of a brachial plexus injury at birth should suggest that condition. This case reiterates the importance of a thorough birth history, regardless of a child's age. (*Jennifer L. Watson, DO, The Children's Regional Hospital at Cooper, Camden, NJ*)

Case 3 Discussion

Shortly after admission, the urine toxicity screen was reported as being positive for atropine. Because the patient's clinical picture was consistent with anticholinergic toxicity (tachycardia, decreased bowel sounds, mydriasis, dry skin, urinary retention, hallucinations), his mother was asked to search the home for substances of potential abuse. She returned to the hospital with a glass of tea containing approximately 100 seeds and a plant later identified as *Datura stramonium*, also known as Jimson weed (Fig. 1).

Clinical Picture

Hallucinogenic plants constitute a wide variety of species, all of which affect cognition, mood, and percep-



Figure 1. Jimson weed seeds, some in tea and pods.

tion. A national survey in 1990 estimated that almost 8% of the population of the United States older than the age of 12 years had tried a hallucinogenic drug once in their lives, with the highest prevalence occurring between the ages of 18 and 25 years. In 1993, the American Association of Poison Control Centers reported that approximately 95,000 poisonings were associated with toxic plants, of which Jimson weed accounted for 318 cases.

Although ultimately they all render similar effects, hallucinogenic plants generally are categorized by their primary mechanism of action on the central nervous system, which include effects on cholinergic, monoamine, or amino acid neurotransmitters. *Datura* sp belong to the anticholinergic hallucinogen group. The numerous species of *Da-*

tura are indigenous in many parts of the world, including the United States. Historically, *Datura* has been used among Native Americans for shamanism and was introduced to popular culture in the 1960s through the writings of Carlos Castaneda. (1) Other plants having anticholinergic activity include *Hyoscyamus niger* (black henbane), *Atropa belladonna* (deadly nightshade), *Mandragora officinarum* (mandrake), *Amanita* sp (fly agaric), *Latana camara* (red sage), and *Solanum* sp (Jerusalem cherry).

The tropane alkaloids, including hyoscyamine, atropine, and scopolamine, are antagonists of the muscarinic cholinergic receptors. Of these compounds, scopolamine renders the hallucinogenic effects because it is the only one that crosses the blood-brain barrier effectively. As a

group, however, these compounds affect all muscarinic cholinergic receptors in peripheral locations, including exocrine glands, cardiac and smooth muscle, and autonomic ganglia.

Based on this set of physiologic actions, the classic observations of “hot as a hare, blind as a bat, dry as a bone, red as a beet, and mad as a hatter” are noted in patients who are under the influence of anticholinergic hallucinogens. The hallucinogenic effects can last from hours to days, depending on the ingested dose. All parts of the *Datura* plant contain tropane alkaloids, but the highest concentrations of toxins can be found in the seeds, which contain an equivalent to 0.1-mg atropine per seed.

The percentage of tropane alkaloids in plant species varies, as does the type of tropane alkaloid that predominates. *Datura* has 0.1% to 0.65% tropane alkaloids, mostly hyoscyamine and scopolamine. Belladonna has 0.33% to 0.6% tropane alkaloids, primarily hyoscyamine. The alkaloids can be transformed by drying the plant, which increases the amounts of atropine and scopolamine.

Differential Diagnosis

The differential diagnosis of acute altered mental status in an adolescent should include the possibility of toxic ingestion. Other causes to consider are meningitis, encephalitis, trauma, seizure, electrolyte imbalance, dehydration, uremia, endocrine abnormalities, space-occupying brain lesions, and psychiatric disorders.

Management

General principles of any condition resulting from the ingestion of poison dictate that the clinician focus on cardiopulmonary resuscitation and

stabilization (ABCs), diagnosis, non-specific therapy, and specific therapy once the offending agent has been identified. Patients experiencing an anticholinergic storm may present in a coma, unable to protect their airways, which mandates immediate attention to the ABCs. Once the ABCs have been addressed, nonspecific therapies, such as administration of glucose or naloxone, may be considered, along with obtaining blood and urine samples for laboratory evaluation.

In managing Jimson weed toxicity, anticholinergic-induced agitation can be treated with long-acting benzodiazepines such as midazolam. For patients whose agitation is refractory to benzodiazepines, more potent tranquilizers such as haloperidol may be used. Appropriate use of soft restraints can prevent the patient from harming himself or herself and the clinicians. Numerous case reports have advocated the use of physostigmine to help reduce and sometimes reverse the hallucinogenic and agitated state observed in affected patients.

Jimson weed poisoning may result in hyperpyrexia and dehydration. The value of cooling blankets and volume resuscitation with crystalloid fluids is well documented in the literature. An indwelling bladder catheter should be placed because these patients also suffer from urinary retention. Given the anticholinergic effects on the heart and skin, monitoring heart rate and peripheral perfusion is an ineffective method of assessing the hydration status. Placement of a bladder catheter also aids in determining the patient's response to intravenous hydration.

Early gastric emptying with lavage and administration of activated charcoal are indicated to help remove the drug. Cathartics, although not used commonly in treating poisoning to-



Figure 2. Telltale inscription on the patient's palm.

day, may help in cases such as this by enhancing passage and elimination of ingested parts of the plant because these patients suffer from slowed gastrointestinal motility.

This boy required benzodiazepines and soft restraints for his agitation. In addition, activated charcoal and a cathartic were administered by nasogastric tube to eliminate the ingested seeds and reduce toxicity. He excreted hundreds of Jimson weed seeds in his stool and was discharged from the hospital in 72 hours without residual neurologic deficit.

Of interest, after identification of Jimson weed as the offending agent, noted by the patient's mother, closer examination of the patient's left palm revealed the following words, "Mr. Joe is on *Datura*," re-emphasizing the importance of a thorough physical examination in making a diagnosis (Fig. 2).

Lessons for the Clinician

When evaluating a patient who has experienced major changes in mental status, a toxic ingestion must be kept

in mind, including one involving plants. A clinical picture suggestive of atropine poisoning should alert the clinician to toxicity from an anticholinergic plant. (*Mani Mokalla, MD, Swati Agarwal, MD, Michael Bressack, MD, Lucile Packard Children's Hospital at Stanford University Hospitals, Palo Alto, CA [MM, SA], Santa Clara Valley Medical Center, San Jose, CA [MB]*)

References

1. Castaneda C. *The Teachings of Don Juan: A Yaqui Way of Knowledge*. Berkeley, Calif: University of California Press; 1968

A Special Case

The case of Jimson weed poisoning by Drs Mokalla and Agarwal, both pediatric residents, and Dr Bressack, an intensive care attending physician, came from the inaugural American Academy of Pediatrics (AAP) Resident Section Clinical Case Presentation Program held in 2003. Approximately 40 abstracts were submitted,

from which 10 were chosen for presentation and recognition at the AAP National Conference and Exhibition (NCE) in November 2003.

From the 10 abstracts, one was chosen by the editors of *Pediatrics in Review* to be written as a case for "Index of Suspicion." The criteria used to pick the finalist were interest and educational value to our readers as well as the content needs of the journal. These are the parameters by which all cases are chosen. Many cases are proposed, and most of these

have the potential to teach our readers. However, because PREP the Curriculum attempts to cover the broad spectrum of pediatric medicine in any given 5-year period and must avoid redundancy as much as possible, the content needs of the journal must be applied as a final filter.

The abstract competition continues annually, and we congratulate all participants for their efforts in sharing interesting cases with their colleagues. We look forward to selecting

another instructive case from this year's submissions to publish in "Index of Suspicion" in 2005.

Abstracts for the AAP Resident Section Clinical Case Presentation program are submitted as part of the normal NCE abstract submission process in the spring of each year. Residents and fellows who would like additional information on the competition should contact David Kaelber, MD, PhD, AAP Resident Section NCE Abstract Chair, at david.kaelber@cwru.edu.—*LFN*