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Case 1 Presentation
A female infant is born by normal vaginal delivery after induction for prolonged pregnancy. The prenatal course was unremarkable. Apgar scores are 6 at 1 minute and 9 at 5 minutes. When attempting to breastfeed at 2 hours of life, she develops opisthotonos-like posturing, hyperextending her neck and arching her back. Physical examination reveals an infant lying on a warmer, sucking vigorously on a nurse’s finger. Her weight is 3,520 g, heart rate is 130 to 150 beats/min, respiratory rate is 30 to 40 breaths/min, pulse oximetry level is 98% to 100% on room air, and rectal temperature is 37°C (98.6°F). The remainder of physical findings are normal, except for the abnormal posturing, which occurs when she is touched.

White blood cell count is $27.9 \times 10^9$/L (27,900/cu mm), with 45% segmented neutrophils, 5% bands, 36% lymphocytes, 4% monocytes, and 10% atypical lymphocytes. Measurement of hematocrit, platelets, chemistry screen 7, and liver-associated enzymes yields normal findings, as does ultrasonography of the head. Lumbar puncture reveals red-tinged cerebrospinal fluid that does not clear. The fluid contains 35,453/cu mm erythrocytes and 77/cu mm leukocytes (86% mononuclear and 14% polymorphonuclear cells), a glucose level of 2.11 mmol/L (38 mg/dL), and a total protein level of 1.59 g/L (159 mg/dL). Gram stain of the fluid reveals no organisms.

A further diagnostic procedure is performed.

Case 2 Presentation
An 11-year-old boy is found unresponsive by his mother. He has suffered from autism, asthma, and morbid obesity. For the past 2 weeks, his mother has noted a dramatic increase in his thirst, frequent urination, and bed-wetting. He has had nausea and vomiting for the past 3 days and has felt warm. There has been a 9 to 13.5 kg (20 to 30 lb) weight loss over the past 2 months. The mother reports no known ingestions.

On arrival in the emergency department, the patient has a diminished level of consciousness, moans in response to painful stimuli, and does not speak. His temperature is 37.2°C (99.0°F), heart rate is 130 beats/min, respiratory rate is 24 breaths/min, blood pressure is 119/42 mm Hg, and pulse oximetry reading is 100% on oxygen therapy. His head shows no signs of trauma, pupils are equal and reactive to light, and mucous membranes are dry. Cardiac examination reveals tachycardia with no murmur. The lungs are clear to auscultation. The extremities are cool, and the skin shows hyperpigmentation in the axillary region.

Administration of 2 mg naloxone intravenously elicits no effect. A rapid toxicology screen yields negative results, and acetaminophen and salicylate levels are undetectable. A urine dip test shows trace ketones. Blood and urine cultures are drawn, and results of one laboratory test suggest the diagnosis.

Case 3 Presentation
A 17-month-old Hispanic boy is found to have a metaphyseal fracture of his distal right femur after experiencing minor trauma. On a subsequent outpatient visit motivated by pain and tenderness of his left thigh, a radiograph reveals a metaphyseal fracture of his distal left femur. Suspicion of child abuse prompts a report to child protective services. Skeletal survey and whole body scan reveal only those two fracture sites. His developmental milestones are...
normal when not influenced by the fractures.

One month later, the patient is hospitalized again because he is unable to move his legs, has swollen and bleeding gums, and is passing dark, tarry stools. On examination, the boy appears pale, very irritable, and apprehensive, making no voluntary movements of his lower extremities. There are scattered areas of petechial hemorrhage over his extremities and trunk. His thighs are tender and edematous. Arthrocentesis of both knee yields a bloody fluid that is sterile. Computed tomography of the abdomen and pelvis demonstrates extensive soft tissue edema of the abdominal musculature and bowel wall. Further radiographs and additional nutritional history lead to the diagnosis.

**Case 1 Discussion**

Computed tomographic (CT) scan of the head revealed increased attenuation over the superior aspect of the left cerebellar hemisphere and to a lesser extent over the right cerebellar hemisphere, extending along the tentorium. This finding was consistent with subdural and subarachnoid hemorrhage layering along the tentorium. No evidence of cerebral or cerebellar edema was noted.

Intracranial hemorrhage in term neonates most commonly is subarachnoid in location and is associated with trauma or asphyxia. Obstetric factors, such as prolonged second stage of labor, precipitous delivery, and forceps delivery, also have been suggested as risk factors. None of these risk factors was present in this delivery.

**Clinical Features**

The clinical manifestations of intracranial hemorrhages vary with location. Subarachnoid hemorrhage can present with apnea, episodes of cyanosis, persistent resting sinus bradycardia, and seizures. Massive hemorrhage associated with tears of the tentorium or falk cerebri may present with rapid deterioration and death. Subdural hemorrhage can present in a fashion similar to that of subarachnoid hemorrhage. Subdural hemorrhage with a slowly expanding subdural fluid volume can have a delayed presentation that is characterized by megalencephaly, frontal bossing, bulging fontanelle, seizures, and anemia. Intraventricular hemorrhage presents with the sudden onset of shock and associated metabolic acidosis, mottling, anemia, coma, bulging fontanelle, and apnea, often on the second or third day of life. Opisthotonos is a rare sign, but has been reported in cases of subarachnoid, intracerebral, and intraventricular hemorrhages.

**Diagnosis**

The diagnosis of intracranial hemorrhage in neonates is based on history (including knowledge of the birth weight and specific risk factors for the various types of hemorrhage), clinical manifestations, transfontanelle cranial ultrasonographic findings, or pattern on CT. Ultrasonography is an excellent technique for detecting germinal matrix and ventricular hemorrhage in the preterm baby. CT scan is indicated for term infants in whom intracranial hemorrhage is suspected because ultrasonography does not visualize the periphery well, where such hemorrhages often occur in term infants, and may not detect intraparenchymal hemorrhage or infarction. Ultrasonography also is relatively insensitive in detecting abnormalities in the posterior fossa. In this case, the hemorrhage was not seen with ultrasonography because the blood layered thinly along the tentorium.

Subarachnoid hemorrhage can be diagnosed or suspected by findings from a nontraumatic lumbar puncture. Usually the cerebrospinal fluid contains elevated protein levels as well as many red blood cells, as was seen in this case. However, the cerebrospinal fluid can be clear in the presence of severe subdural or intracerebral hemorrhage if there is no communication with the subarachnoid space.

The primary clinical manifestation of the subarachnoid hemorrhage in this case was the patient’s opisthotonic posturing. Opisthotonos is defined as a position of the body in which the head, neck, and spine are arched backward. Causes of opisthotonos in the newborn period include intracerebral or intraventricular hemorrhage (from birth trauma, bleeding diathesis, arteriovenous malformations, tumors), kernicterus, tuberous sclerosis, hydrocephalus, neonatal tetanus, and Dandy-Walker syndrome. Other reported causes that would be less likely to present in the newborn period include thiamine deficiency, effects of various anesthetics (propofol, enflurane, nitrous oxide, thiopental), water intoxication, carbamazepine overdose, and dextromethorphan overdose.

In this case, the patient suffered a subarachnoid hemorrhage without having experienced birth trauma or perinatal asphyxia. Therefore, the possibility of an underlying bleeding disorder was addressed. There was no family history of a bleeding disorder, hemostasis after blood draws occurred normally, and the patient had normal prothrombin and partial thromboplastin times.

**Lessons for the Clinician**

Intracranial hemorrhages can occur in term neonates, even when there is no history of a traumatic delivery. The presentation can vary and can
HNKH and DKA, in which hypernatremia does not occur, is the earlier use of hypotonic saline in HNKH to correct the hypernatremia. Serum sodium values should be corrected for hyperglycemia because an apparent “normal” laboratory value actually represents hypernatremia in the face of significant hyperglycemia. Once recognized, the hypernatremia should be corrected slowly to avoid cerebral edema. Potassium replacement should begin as soon as urine output is established because patients are depleted of total body potassium, as are patients who have DKA. Replacement of magnesium, phosphate, and calcium is not supported in the literature. Precipitating infections are common, with pneumonia occurring most frequently, followed by urinary tract infections. In this case, the patient’s urine grew *Proteus vulgaris*, and he was treated with trimethoprim/sulfamethoxazole.

Serious complications of HNKH include cerebral edema, thromboembolic events, seizures, electrolyte abnormalities, rhabdomyolysis, adult respiratory distress syndrome, and progressive underlying infection. Cerebral edema is more common in younger patients and can be prevented by avoiding rapid rehydration and preventing the rapid fall in glucose and sodium associated with excessive insulin dosing and hypotonic fluid administration.

Because HNKH can be a complication of type 1 or type 2 diabetes mellitus, long-term therapy can range from dietary control to daily insulin injections. This patient best fit the classic type 2 description, being obese and having insulin resistance. His young age was not a feature traditionally associated with type 2 diabetes, although that disorder is becoming increasingly common among children and adolescents. He was sent home on 1.3 U/kg per day of subcutaneous insulin, with the hope of transitioning him to oral therapy in the future.

**Lessons for the Clinician**

Clinicians should be aware that a rare patient might present with a clinical picture similar to DKA but without the striking ketoacidosis characteristic of that condition. HNKH also is due to an insulin deficiency and is treated much as DKA is treated, but it is likely to be accompanied by hypernatremia, which requires special treatment. Like DKA, HNKH can have serious consequences and requires skilled management and constant monitoring. (David C. Pettigrew, MD, Oregon Health Sciences University, Portland, OR)

**Case 3 Discussion**

**Diagnosis**

Because of the evidence of bleeding, a number of laboratory investigations were performed, revealing a normal white blood cell count, differential, platelet count, prothrombin time, partial thromboplastin time, and bleeding time. His hemoglobin level was reduced, at 92 g/L (9.2 g/dL). Detailed investigation of the patient’s dietary history revealed that he was a picky eater; his diet had consisted of white (unfortified) rice, chicken, and soda pop and lacked fruits, fruit juices, milk, and vegetables. His vitamin C intake was estimated to be less than 1 mg/d (recommended daily allowance for children younger than 3 years is 40 mg/d).

Detailed examination of a new set of radiographs showed rarefaction of the bone, atrophy of the spongiosa, pathologic fracture, and an area of calcification causing a bony spur (Fig. 1). The roentgenographic findings and history of poor vitamin C intake led to the diagnosis of scurvy.
The child was treated with parenteral ascorbic acid, then switched to oral vitamin C. Within 1 week he began to crawl, and in 3 to 4 weeks he had begun to walk. Radiographs obtained 6 months later showed significant improvement in the bones (Fig. 2).

Pathogenesis
Vitamin C (ascorbic acid) is essential for human health. Its absence in the diet can lead to scurvy, which can be life-threatening. In 1753, Lind et al made clear that the etiology of this morbid condition was due to deficiency of vitamin C. Vitamin C deficiency impairs the formation of collagen and chondroitin sulfate. Poor collagen synthesis results in extravasation of blood from fragile capillaries, causing cutaneous and gingival hemorrhage. Because osteoblasts no longer form the osteoid, endochondral bone formation ceases, and the trabeculae that have been formed become brittle and fracture easily. Abnormalities are found mainly in the metaphyseal zone of tubular bones and at the chondrosternal junctions. Vitamin C deficiency also results in impaired energy metabolism, which may induce muscular dysfunction, muscular hemorrhage, and rarely peripheral nerve dysfunction due to local hematoma that may lead to muscular pain and weakness.

Clinical Features
Scurvy has become a rare disease in industrialized countries. It may occur at any age, but the majority of cases are seen in infants 6 to 24 months of age. After a variable period of vitamin C deficiency, vague clinical features such as irritability, digestive disturbances, and anorexia appear. Follicular hyperkeratosis and corkscrew coiled hairs develop. There is evidence of generalized tenderness, especially noticeable in the legs, which results in pseudoparalysis and the inability to walk. Rheumatic manifestations can result from bleeding into the muscles or joints, as in this patient. Gingival bleeding is a common finding. Petechial hemorrhages, hematuria, and subdural hemorrhages may be seen. Submucosal hemorrhage in the gastrointestinal tract may result in melena. Anemia is present in 75% of patients who have scurvy, usually in a normochromic, normocytic pattern. Although normal in this child, both the bleeding time and prothrombin time may be increased.

Differential Diagnosis
The clinical features, radiographic findings, and complete resolution of these features after administration of ascorbic acid left no doubt that this child had a forgotten disease. Scurvy can mimic many other diseases, such as vasculitis, blood dyscrasia, deep vein thrombosis, and rheumatic disorders. Osteoporotic bones in scurvy are prone to fracture, even with minor trauma, and the condition can be confused easily with child abuse. The wide variety of conditions that have been mistaken for child abuse include osteogenesis imperfecta, rickets, scurvy, copper deficiency, and syphilis.

Treatment
Treatment of scurvy is with oral ascorbic acid. One regimen is 25 mg four times a day for 4 to 5 days, followed by 25 mg twice a day until healing occurs.

Lesson for the Clinician
This case illustrates the need for continued awareness of this uncommon but potentially lethal disease and underscores the importance of a detailed nutritional history. (Sanjiv Midha, MD, Archana Watane, MD, Ashok Jain, MD, Texas A & M University at Driscoll Children’s Hospital, Corpus Christi, TX)
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