A 7-year-old girl is brought to the emergency department by her father and aunt with a chief complaint of ongoing weight loss. She recently moved from Mexico, where she had been living with her mother and two siblings, to receive further medical attention. She was in her usual state of normal health until she was 3 years, at which time she began having difficulty walking, with worsening deformities of her arms and legs. This progressed to complete inability to walk or bear weight. One year before presentation, she was seen in a clinic in Mexico and had routine blood work, as well as an electromyography (EMG) study, and was given the diagnosis of Duchenne muscular dystrophy. Her developmental history is significant for loss of fine motor skills, with normal expressive and receptive language. She eats all types of foods with no specific restrictions; however, she has always had a poor appetite. Birth and past surgical history are unremarkable. Her family history is significant for a 10-year-old brother who has decreased range of motion of all extremities, but with normal gait and weight gain. She has a 5-year-old sister with no medical issues.

In the emergency department, her temperature is 37.5°C, heart rate 104 bpm; respiratory rate 20 breaths/minute; BP 105/64; and oxygen saturation 100% on room air. Her weight is 9.57 kg, which is 50th percentile for a 12-month-old child. Her height is 88 cm, which is 50th percentile for a 27-month-old child. She is lying comfortably in bed and is quite conversive. Her lungs are clear and cardiac exam is benign with no murmurs. There is no hepatosplenomegaly, and no masses are appreciated. She has marked scoliosis and poor oral dentition with eroded enamel but no obvious caries. There is obvious muscle atrophy, but she does not appear cachetic and has no temporal muscle wasting.

There is obvious muscle atrophy, but she does not appear cachetic and has no temporal muscle wasting.

Ronen Zipkin, MD, Academic Hospitalist, Division of Hospital Medicine, Children’s Hospital Los Angeles; and Assistant Professor, Clinical Pediatrics, USC Keck School of Medicine.

Address correspondence to: Ronen Zipkin, MD; rzipkin@chla.usc.edu.

Dr. Zipkin has disclosed no relevant financial relationships.

doi: 10.3928/00904481-20100922-04

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.
ness. She has 4/5 upper extremity strength, but is unable to lift her legs against gravity. Because of her significant short stature and poor weight gain, she is admitted for evaluation of failure to thrive.

There are three broad categories when evaluating a patient with inappropriate weight gain. Poor caloric intake is the most common etiology. Patients may also have increased losses due to GI malabsorption in disease, as seen with inflammatory bowel disease or celiac disease. They may also have increased metabolic demands, as seen in children with congenital heart defects, or certain endocrinopathies, such as hyperthyroidism. The profound nature of this patient’s inability to gain weight, joint abnormalities, and lack of other clinical findings suggestive of severe malnutrition are all inconsistent with common causes of failure to thrive.

Initial laboratory evaluation includes a prealbumin of 17.9 and a basic chemistry panel that is within normal limits, including a serum Ca of 9.7 mg/dL (8.8 to 10.8 mg/dL). A full-body skeletal survey (see Figures 1 through 4) reveals diffuse osteopenia with severe osteolysis of the metaphyseal bones. There was marked bone loss with multiple fractures at various stages of healing. Further lab testing includes a serum phosphorous of 1.8 mg/dL (4.5 to 5.5 mg/dL); alkaline phosphatase of 1,204 U/L (60 to 230 U/L); urinary phosphorous of 131 mg/dL; intact PTH of 66 pg/mL (10 to 71 pg/mL); vitamin D 25 OH of 6 ng/mL (20 to 30 ng/mL); and 1.25 dihydroxy vitamin D of 16 pg/mL (31 to 87 pg/mL).

**DISCUSSION**

Rickets is characterized by poor bone mineralization, with subsequent growth retardation. Several factors can lead to rickets, including vitamin D deficiency, inadequate exposure to ultraviolet light, poor absorption of calcium, and inherited disorders characterized by poor phosphorous reabsorption by the kidneys.\(^1\)

Vitamin D deficient rickets typically presents between 3 months and 3 years, during peak growth rates. The most common reason for poor vitamin D intake is inadequate sun exposure and exclusive breastfeeding without appropriate vitamin D supplementation.\(^2\) Vitamin D3 (either synthesized in the skin or ingested) undergoes a series of hydroxylations and is ultimately converted into 1.25 dihydroxy vitamin D in the kidney, which is regulated by parathyroid hormone (PTH).\(^3\) This biologically active form of vitamin D works to increase GI absorption of calcium and phosphorous. Therefore, low serum levels of vitamin D lead to hypocalcemia, hypophosphatemia, and an elevation of PTH. Clinical findings can include frontal bossing with evidence of craniotabes, widening of the wrists, beading of the ribs, known as rachitic rosary, as well as lower extremity bowing. Due to the preventable nature of this disease, the American Academy of Pediatrics (AAP) has recommended that all exclusively breastfed infants, as well as those receiving less than 1,000 cc of formula per day, be supplemented with 400 IU per day of vitamin D.\(^4\)

The most common non-nutritional form of rickets is familial hypophosphatemia. Most cases are X-linked dominant; however, autosomal dominant and autosomal recessive cases have been re-
ported. Toddlers often present with lower extremity bowing related to weight bearing. They can also develop a waddling gait and short stature; adult heights in untreated cases average 4 feet, 9 inches. They lack tetany, pectus deformities, or evidence of rachitic rosary that is often seen with calcium or vitamin D deficient rickets. Those with autosomal dominant hypophosphatemic rickets have a mutated form of the peptide fibroblast growth factor 23 (FGF 23), which is synthesized in osteocytes. This peptide causes a defect in proximal tubular reabsorption of phosphorous, as well as inhibiting activation of 25 hydroxy vitamin D to 1,25 dihydroxy vitamin D. This leads to severe phosphaturia, hypophosphatemia, low levels of biologically active vitamin D, and, ultimately, rickets.

CONCLUSION
Regardless of the genetic basis of hypophosphatemic rickets, the treatment is aimed at replacing serum phosphorous and vitamin D levels while trying to prevent secondary hyperparathyroidism. Because of the increased risk of developing nephrocalcinosis, a renal ultrasound is recommended upon diagnosis. With early diagnosis and treatment, ongoing bowing deformities can be minimized and a normal adult height may be achieved. However, it is unclear if significant bone damage and short stature can be reversed when left untreated for a prolonged period of time, as was seen in our patient.

REFERENCES