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Case Report

CASE REPORT

Rickets and gross motor delay in a child with atopic dermatitis

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Abstract

We report a case of a 14-month-old boy with atopic dermatitis (AD) who presented to our hospital with hypocalcemic tetany and gross motor delay. Further laboratory and imaging confirmed the diagnosis of vitamin D deficiency and rickets. He was breastfeeding and on a restricted diet due to presumed multiple food allergies. He received calcium and vitamin D supplementation which corrected his hypocalcemia. The patient developed *Staphylococcus aureus* bacteremia and superficial septic thrombophlebitis for which he was treated with antibiotics and anticoagulation. An elimination diet should be avoided in AD patients as true food-induced AD is rare and management should focus on optimal skincare. AD patients have a higher rate of *S. aureus* skin colonization, which increases their risk for infectious complications. This case also highlights the importance of maintaining a high index of suspicion for rickets in children with isolated gross motor delay, especially in those with risk factors.

INTRODUCTION

Rickets results from impaired bone mineralization and typically affects children during periods of accelerated growth. It is usually classified as calcipenic rickets and phosphopenic rickets. Although rickets is rarely seen in resource-rich, developed countries, this case was unique in demonstrating how elimination diets can lead to severe micronutrient deficiency. We further discuss the pathophysiology of rickets in the context of vitamin D metabolism and investigate its complex relationship with AD management.

CASE REPORT

A 14-month-old African American boy presented to our hospital during the winter with hand stiffening that started on the day of presentation. His mother noticed that his hands were stiff and bent inward while he was playing. He had no fever, seizure-like activity, upper respiratory symptoms, vomiting, nor diarrhea. His medical history was significant for atopic dermatitis (AD) since the age of 3 months and a recent diagnosis of iron deficiency anemia. His diet, in addition to breast milk, was limited to rice, chicken, potatoes and broccoli; all of which have low vitamin D content. He had an even more restricted diet due to presumed food allergies to dairy products, eggs, wheat, soy, almonds and peanuts, which were based on elevated allergen-specific IgE levels. He was taking iron supplements, but no other medications. He had no developmental regression, but he was still unable to walk or to even pull himself up to stand. He could crawl but fatigued quickly. The patient was born full-term and the pregnancy was complicated by maternal gestational diabetes, hypothyroidism and vitamin D deficiency. A physical examination revealed an alert child with normal vital signs and no dysmorphic features. He weighed 10.5 kg (60th percentile) and

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Table 1: Laboratory findings are consistent with vitamin D deficiency with resultant hypocalcemia and secondary hyperparathyroidism

	Value	Reference range
Total Ca	5 mg/dL	8–10.5
Ionized Ca	0.75 mmol/L	1.1–1.35
Phosphorus	2.2 mg/dL	4–6.5
Alkaline phosphatase	990 U/L	150–350
25 (OH) vitamin D	< 5 ng/mL	>20
PTH	290 pg/mL	15–65

his length was 77 cm (25th percentile). He had diffuse xerosis on his cheeks, trunk and flexural areas. His hands were stiff and contracted, but there were no visible skeletal deformities such as joint widening or genu varum. He had mild hypotonia; he was able to sit unassisted and to stand briefly with support but could not walk. His reflexes were normal with no fasciculations, and the remainder of the examination was unremarkable. The laboratory findings shown in Table 1 in addition to radiography findings (Fig. 1) were consistent with calcipenic rickets, most likely a consequence of his vitamin D and calcium deficient diet. A further consequence of his limited diet was microcytic anemia due to iron deficiency as was evident by his complete blood counts and iron studies. Aspartate transaminase (AST) and alanine transaminase (ALT) were 137 and 90 U/L, respectively (normal < 45), and his albumin, total bilirubin, γ-glutamyl transferase levels, electrolytes, and renal function were normal. A liver ultrasound was obtained due to ALT and AST elevation, and it was normal. His alkaline phosphatase isoenzyme was found to have originated in the bone as was expected. His ALT and AST mild elevation were likely due to muscle spasms and not due to liver etiology, and they normalized later. Celiac serology antibodies were normal, ruling out the concern for malabsorption. Electrocardiography (ECG) showed a sinus rhythm with prolonged QTc interval of 480 milliseconds (normal < 445), which was consistent with his hypocalcemia.

The patient was admitted to the hospital and received serial intravenous (IV) and oral replacement of calcium with vitamin D supplementation, which gradually corrected his hypocalcemia and hypophosphatemia. This was done initially in the intensive care unit with close monitoring until the ECG changes resolved. His AD was managed with emollient and topical steroids. The family met with a nutritional specialist and were educated on proper diet and provided with an AD action plan. On the third day of his hospitalization, the patient developed a fever with erythema and mild swelling of his right arm at the site of the peripheral IV catheter. The ultrasonography showed basilic vein thrombosis, and a new IV catheter was placed in the left arm. Broad spectrum antibiotics were started after obtaining a blood culture, which later grew methicillin-sensitive *Staphylococcus aureus* and his antibiotics were adjusted to IV cefazolin. He had a similar presentation at the site of his peripheral IV catheter in the left arm 4 days later and ultrasonography also showed left basilic thrombosis. A thrombophilia screen including protein S, protein C, cardiolipin antibodies, antithrombin III, factor V Leiden and prothrombin gene mutation were all normal. He was started on subcutaneous low molecular weight heparin (LMWH) to prevent further clotting. The patient was discharged home after 11 days to continue calcium and vitamin D supplements for his rickets and oral cephalexin and subcutaneous LMWH for his superficial septic thrombophlebitis.

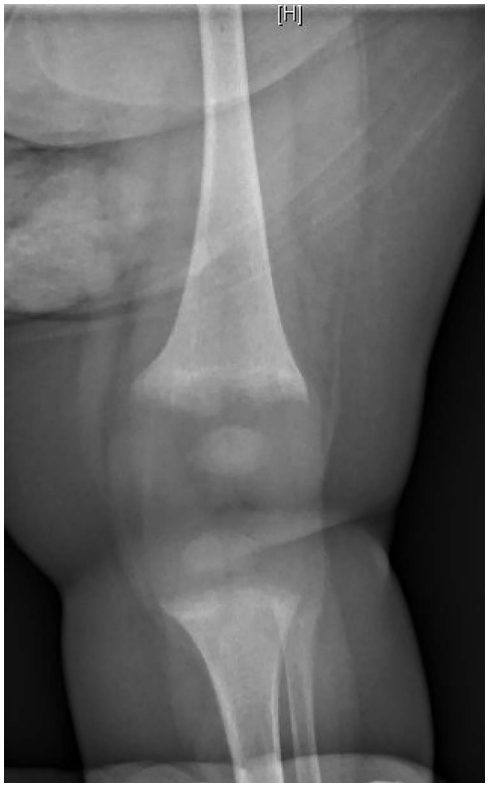

Figure 1: Radiography of the knee shows metaphyseal cupping and fraying of the tibia, fibula and distal femur.

DISCUSSION

Vitamin D is essential for calcium and phosphorus absorption in the gastrointestinal tract. Along with parathyroid hormone (PTH), vitamin D plays an important role in calcium homeostasis. Rickets is a disease that results from impaired bone mineralization and usually affects children during periods of accelerated growth [1]. It manifests mainly in infancy and early childhood but sometimes can occur during adolescent growth spurts [2]. It is usually classified as calcipenic rickets, most commonly due to dietary vitamin D and/or calcium deficiency, and phosphopenic rickets, usually due to renal phosphorus wastage. Clinical findings include genu varum, gait abnormalities, frontal bossing, craniotabes, dental abnormalities and a widening of the wrists. Rachitic rosary occurs due to the enlargement of the costochondral junction [1]. As we saw in this case, rickets can also present with muscle weakness and gross motor delay. The exact mechanism is not fully understood, but it is thought to be

related to hypocalcemia and hypophosphatemia-induced muscle dysfunction. Muscle weakness can also result from reduced weight bearing caused by bone pain and discomfort [3]. Over 90% of vitamin D in humans comes from the photoconversion of 7-dehydrocholesterol in the skin to cholecalciferol (vitamin D3) by ultraviolet B radiation. Dietary sources of vitamin D include fortified dairy products, cereals, eggs, fish and liver. Risk factors for vitamin D deficiency in children include prolonged and exclusive breastfeeding without vitamin D supplementation, prematurity, limited sun exposure, living at high altitudes, gut malabsorption and a restricted diet. Individuals with darker skin color are at risk for vitamin D deficiency due to melanin functioning as a natural sunscreen. Diets restricting dairy products such as milk also result in inadequate calcium intake, further driving calcipenic rickets [1, 4]. Our patient had many of these risk factors. The American Academy of Pediatrics recommends daily vitamin D supplementation of 400 international units for exclusively breastfed infants and infants who consume less than ~1 liter of formula per day. Although it was prescribed, the vitamin D supplementation was not taken by the patient nor his mother. It is worth noting also that his anthropometric parameters of weight and height imply that he is 'healthy' and meeting the growth velocity of his peers. These measurements do not identify children who have significant micronutrient deficiencies despite adequate caloric intake. AD is a chronic pruritic inflammatory skin disorder. It affects about 10% of children in the USA and up to 65% of cases occur in those <1 year of age. The diagnosis is usually made clinically based on symptoms of pruritis, chronic and relapsing course, and typical age-related skin distribution. In infants and young children, AD affects the cheeks, scalp, trunk and flexural areas, whereas in adolescents, the hands and feet are typically affected. Differential diagnosis includes scabies, contact dermatitis, seborrheic dermatitis, psoriasis, ichthyosis and cutaneous malignancies. The pathogenesis of AD is complex and multifactorial with skin barrier dysfunction playing a key role. This results in xerosis and the entry of allergens, which triggers an inflammatory response in genetically predisposed individuals [5, 6]. More than 90% of parents believe that food allergy is the culprit behind their child's AD. Although the prevalence of food allergy in children with AD is higher (up to 40%) than in children without AD (5%), true food-induced AD is rare. The relationship between AD and food allergy is not causative. Allergy to a certain food requires both sensitization (i.e. elevated allergen-specific IgE) and the development of symptoms upon exposure to that food. Sensitization alone is not sufficient to diagnose a food allergy. Routine food allergy testing is not recommended in AD patients, but if suspected, the patient might need to be evaluated with an oral food challenge. An elimination diet is neither recommended nor effective in treating AD symptoms and can lead to protein and micronutrient deficiency [7–9]. Instead, the management of AD should focus on optimal skincare with routine emollient application. Topical steroids and sometimes calcineurin inhibitors play an important role as well in controlling skin inflammation. Adjunctive therapy includes oral antihistamines for control of pruritis, and antibiotics for cases complicated by secondary bacterial infections [5, 6]. There has been some evidence to suggest an inverse relationship between vitamin D levels and the severity of AD in children [10, 11]. In fact, vitamin D supplementation has been shown to be beneficial in decreasing the severity of AD in children at risk for vitamin D deficiency during winter months [12]. However, there is no strong evidence to support vitamin D supplementation in children with AD if they do not have vitamin D deficiency, but it might be wise to investigate vitamin D status in these children and to treat accordingly. One study even showed an increased risk of incident AD in infants who had low cord blood vitamin D levels, which raises the question of the role of vitamin D in disease prevention [13]. Our patient developed superficial septic thrombophlebitis and *S. aureus* bacteremia. AD patients have a higher rate of *S. aureus* colonization when compared to the general population [14]. This, along with an impaired skin barrier, puts these patients at a higher risk for skin and systemic infections. Interestingly, vitamin D deficiency has been associated with hypercoagulable state and occurrence of venous thrombosis [15].

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CONFLICT OF INTEREST STATEMENT

None declared.

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PATIENT CONSENT

Parental consent obtained for publication.

GUARANTOR

Shafee Salloum, MD.

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