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Celiac disease presenting as rickets in Saudi children

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BACKGROUND AND OBJECTIVES: Rickets is commonly seen as a sign of malabsorption like celiac disease if it is not treated appropriately with vitamin D and calcium supplements. The aim of this study was to examine the frequency of diagnosis of celiac disease among children with unexplained rickets in Saudi children at a tertiary hospital setting.

DESIGN AND SETTING: Retrospective review of records of patients referred over 10 years to a pediatric gastroenterology and hepatology unit.

PATIENTS AND METHODS: The study included all patients referred for evaluation of unexplained rickets and osteomalacia and screened for celiac disease. The diagnosis of rickets was made on the basis of history, physical examination, biochemical and radiological investigations. The diagnosis of celiac disease was made based on the ESPGHAN (European Society for Pediatric Gastroenterology, Hepatology, and Nutrition) criteria.

RESULTS: Twenty-six children with a mean (SD) age of 9.5 (4.6) years (5 males, range 1-15 years) were referred for evaluation of unexplained rickets and were screened for celiac disease. The diagnosis of celiac disease based on small bowel biopsy findings was confirmed in 10 (38.4%) patients with rickets. Serological markers for celiac disease including antiendomyseal antibodies and antitissue transglutaminase antibodies were positive in all ten children.

CONCLUSION: Rickets is not an uncommon presentation of celiac disease in Saudi children and pediatricians should consider celiac disease as an underlying cause for rickets.

Vitamin D deficiency rickets remains prevalent in developing countries and ranks among the five most common diseases in children.[1,2] The prevalence of nutritional rickets in developed countries appears to be increasing. Vitamin D deficiency rickets is also prevalent in Saudi Arabia.[3] Sedrani et al studied the prevalence of clinical (1.4%) and subclinical (3.1%) rickets in Saudi children admitted to Sulimania Children's Hospital in Riyadh. The majority of children with rickets (88%) were breast fed.[4]

Rickets is usually secondary to dietary deficiency of vitamin D/calcium or insufficient intestinal absorption. Another rare cause is decreased vitamin D activity due to an inability to convert to the active metabolite or end-organ resistance to the active metabolite.[5] Patients with rickets usually develop secondary hyperparathyroidism and characteristic changes of the growth plates and metaphyseal bone, which include widening of wrists and ankles, bowing of the legs, craniotabes, ricketic rosary and Harrison sulcus.[6,7]

Celiac disease (CD) is an immune-mediated disorder that affects primarily the gastrointestinal tract. It is characterized by small bowel inflammatory changes resulting in mucosal injury and subsequent malabsorption in genetically susceptible individuals following exposure to gluten.[8,9] Classical symptoms of CD include abdominal pain, diarrhea and growth failure. However, CD can be asymptomatic.[10,11] The objective of this study was to examine the prevalence of celiac disease presenting as rickets in Saudi children at a tertiary hospital setting.

PATIENTS AND METHODS

Charts over a period of ten years (January 2000 to December 2010) of all children who were referred for evaluation of rickets to the Pediatric Gastroenterology Unit at King Khalid University Hospital, Riyadh Saudi

Arabia were reviewed. The diagnosis of rickets was made on the basis of history, physical examination, biochemical, and radiological investigations. Diagnosis of celiac disease was made based on the ESPGHAN (European Society for Pediatric Gastroenterology, Hepatology, and Nutrition) criteria.[12] The data analyzed included age, sex, presenting symptoms and the clinical signs. Investigations included complete blood count, liver and renal function tests, bone profile, serum 25-hydroxyvitamin D [25-(OH)D] and total IgA levels. Parathyroid hormone level and 1,25-hydroxyvitamin D [1,25 (OH02 D) were performed if clinically indicated. We also included antiendomyseal antibodies and IgA antitissue transglutaminase antibodies as screening tests for celiac disease. If the screening tests were positive, gastroduodenoscopy with small bowel biopsies was performed to confirm the diagnosis of celiac disease.

RESULTS

Twenty-six children (5 males, age range 1-15 years, mean [SD] 9.5 [4.6] years) were referred for evaluation of unexplained rickets (unexplained rickets means there was no identifiable cause excluding all those with nutritional, inherited, renal or liver disease) to our unit who were screened consecutively for celiac disease over a period of ten years (January 2000 to December 2010). The main symptoms were bone pain, and easy fatigability. Signs of rickets included skeletal deformities, waddling gait, widening of wrists and ankles with rachitic rosary. All children had evidence of rickets on radiological investigations including cupping, fraying and flaying with decreased bone density. The diagnosis of celiac disease was confirmed in 10 (38.4%) patients with rickets. There were total 90 cases of celiac disease and of this 11.1% had rickets. The mean laboratory values are given in the **Table 1**. Serum concentration of 25-(OH)D ranged between 12-26 ng/mL (normal, 10-45). Parathyroid hormone level was raised in 7 patients ranging from 45 to 530 pg/nL (normal, 5-15 pg/mL). None of the patients had gastrointestinal symptoms. Serological markers for celiac disease including antiendomyseal antibodies and antitissue transglutaminase antibodies were positive in all ten children and small bowel histopathology showed evidence of celiac disease. Out of 10 patients, 7 had MARSH type IIIc, 2 had type IIIb and 1 patient had type IIIa.

Table 1. The mean laboratory values.

	Number	Mean	SD
Age (years)	10	9.5	4.6
Hemoglobin (mg/dL)	10	9.9	1.2
Calcium mmol/L	10	1.8	0.3
Phosphate mmol/L	10	1.3	0.3
Alkaline phosphatase U/L	10	868.8	298.5

DISCUSSION

Celiac disease, also known as gluten sensitive enteropathy, is a permanent intestinal intolerance to gluten and related proteins that leads to mucosal damage in genetically susceptible individuals. The prevalence of celiac disease in some parts of the Middle East is 0.53%.[13] In Saudi Arabia, a recent case series reported the characteristics of 62 children with celiac disease. Classical symptoms included growth failure as the main presentation followed by chronic diarrhea, abdominal pain and vomiting.[9]

The classical age of presentation of celiac disease is 9 months to 1 year with chronic diarrhea, anorexia, and failure to thrive, muscle wasting and abdominal distension. However, atypical disease with short stature, anemia, constipation, and ataxia has now become more frequent in older children.[14] Short stature as the only presentation has been reported in some series up to 30% of patients.[15]

Rickets and osteomalacia can be associated with celiac disease in children.[16] This study highlighted a relatively high prevalence of rickets as the only manifestation of celiac disease. Ten children who presented only with signs of rickets and gastrointestinal symptoms were proven to have celiac disease, indicating the importance of screening such patients for celiac disease. Rickets as a presentation of celiac disease had been reported in few case reports and case series.[17] Celiac disease predisposes to metabolic osteopathy and bone damage is very high with malabsorption, but it is also present in asymptomatic patients.[18] Local and systemic mechanisms may play a role in the metabolic bone disease in celiac disease. The loss of villous architecture leads to malabsorption of calcium and vitamin D leading to hypocalcemia and secondary hyperparathyroidism. In addition, the release of proinflammatory cytokines, activating osteoblast represents the main locally acting mechanisms responsible for bone derangement.[19,20]

In children, metabolic bone disease resolves with a gluten-free diet.[21] Interestingly, this finding was reported in one study of about 30 children who were followed up for a mean duration of 10.7 years. Bone mineral density and serum markers of bone metabolism completely normalized on long-term gluten-free diet.[22] However, initial addition of vitamin D and calcium seems to be

beneficial and showed significant clinical and biochemical improvements within months along with a gluten-free diet. This management is of a significant importance particularly for growing children.[23]

The study highlighted the importance of screening for celiac disease in children with unexplained rickets as early intervention does have a major impact on bone health. The limitations of the study included the small number of patients examined and the fact that it was conducted at a tertiary hospital setting. Larger community-based studies are recommended.

Rickets is not an uncommon presentation of celiac disease in Saudi children. Pediatricians should be aware of the possibility of the presence of celiac disease in any child with unexplained rickets. Large population-based studies are required to clearly document the prevalence of this association.

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