

Osteomalacia with Looser zones caused by celiac disease

Nayyereh Saadati^{1*}, Mandana Khodashahi¹, Bahram Naghibzadeh² and Elaham Adibi³

¹Department of Internal Medicine, Ghaem Medical Centre, School of Medicine, Mashhad University of Medical Sciences (MUMS), Mashhad, Iran. ²Rheumatic Disease Research Center (RDRC), Ghaem Medical Center, MUMS, Mashhad, Iran. ³Intern, Ghaem Medical Centre, School of Medicine, Mashhad University of Medical (MUMS), Mashhad, Iran

Celiac disease is considered a malabsorption syndrome and is characterized by chronic small intestinal disease caused by hypersensitivity to the gliadin fraction of gluten. Celiac disease comes with diarrhea, occasional steatorrhea, weight loss, and other complications which might be caused by anemia. Reports of osteomalacia as the only symptom of celiac disease are very rare; however, osteomalacia can be a detected sign of celiac disease. Herein is described a case of osteomalacia with a Looser zone in a 39-year-old woman who had low bone mineral density caused by severe osteomalacia associated with chronic celiac disease. In patients with pain in the spine and proximal muscle, the risk of osteomalacia should be considered in any kind of diagnosis.

Keywords: bone loss, celiac disease, Looser zone, osteomalacia.

Introduction

Celiac disease is an autoimmune inflammatory disease of the small intestine caused by the ingestion of gluten, a part of wheat protein, in genetically susceptible people [1]. Typically, the disease demonstrates diarrhea, occasional steatorrhea, weight loss, and anemia [2]. There are a handful of reports of osteomalacia with Looser zones as the first presenting symptom of celiac disease. Celiac disease is known to be associated with an increased risk of osteoporosis. Osteomalacia, as a symptom of celiac disease, is believed to be the result of decreased absorption of Vitamin D that occurs, in turn, because of improper functionality of the small intestine. It has been reported that the prevalence of celiac disease in Iran, even in low-risk subjects, is higher than that of western countries, being one out of every 166 healthy blood donors [3]. The present article discusses a patient who was referred to the medical center with low bone mineral density due to longstanding osteomalacia with a Looser zone and celiac disease.

Patient and Observation

A 39-year-old woman was referred to the Rheumatology Clinic in Ghaem Medical Center, Mashhad University of Medical Sciences, Mashhad, Iran, in June 2016. She complained of experiencing pain in her spine and proximal muscle for the past three

years. Because of her body pain which lasted a long time, fibromyalgia was first considered, but a bone chemistry analysis revealed low vitamin D, calcium, and phosphate levels, elevated bone alkaline phosphatase, and high parathyroid hormone (PTH) levels which are typical in celiac disease. Plain films showed a Looser zone in the left femur. Clinical examination indicated bilateral proximal muscle atrophy, and the patient complained of weakness in the upper and lower extremities. Her hip range of motion was limited and accompanied by pain. The patient had a waddling gait. Laboratory tests (Table 1) were significant for microcytic anemia, hypocalcemia, hypophosphatemia, and high serum alkaline phosphatase. Her PTH level was high and Vitamin D (25-OH Vitamin D) level was low. Results of anti-gliadin and anti-endomysial antibody tests were positive.

Results of further laboratory investigations, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), creatinine, and thyroid function tests, were within normal ranges. Bone mineral density was measured using dual energy X-ray absorptiometry (DEXA) Lunar DPX-L (Lunar Corporation, Madison, WI), and results were low: 0.813 g/cm² (2.33 SD below the mean) for the femoral neck and 0.806 g/cm² (2.36 SD below the mean) for the lumbar spine. Plain radiology films showed a Looser

* Corresponding Author: Nayyereh Saadati, Email: saadatin@mums.ac.ir, Tel: +98 915 509 0408

Received: 03 January 2017; **Accepted:** 26 February 2017

zone in the left proximal femur bone (Fig. 1). The diagnosis of osteomalacia was then confirmed. The diagnosis of celiac disease of this patient was confirmed by positive IgA and IgG anti-gliadin, anti-tissue transglutaminase antibody tests, endoscopic detection of inflammation, and atrophy of duodenal mucosa. The patient's clinical and laboratory responses to a gluten-free diet, iron, and calcium-vitamin D were good, which is indicative of celiac disease.

Table 1. Results of laboratory evaluation

Laboratory evaluation	Patient	Reference values
Calcium (mg/dl)	7.5	8–10.6
Phosphate (mg/dl)	2.1	2.5–4.5
Albumin (g/L)	36	35–52
Alkaline phosphatase (U/L)	605	50–305
25-hydroxy vitamin D (nmol/L)	<9	25–150
Parathyroid hormone (pmol/L)	83	14–72
Antigliadin Ab. IgG (u/ml)	46	Up to 5
Anti-tissue transglutaminase Ab. (u/ml)	>153	up to 20

Discussion

Samuel Gee first described celiac disease in 1888. He reported patients with malabsorption associated with a reversible atrophy of intestinal mucosa of the small bowel [4]. It is suggested that celiac disease is common in Caucasian family members, and it is strongly associated with HLA phenotypes B8, BR3, and DQw2 [5]. CD is an autoimmune inflammation disease of the small intestine caused by the ingestion of gluten, a factor of wheat protein, in persons who are genetically

at risk [6]. Osteomalacia was first noted in coexistence with celiac disease more than 64 years ago. In 1953, the relationship between celiac disease and osteomalacia was first reported. The osteomalacia that is associated with celiac disease is believed to result from the decreased absorption of Vitamin D caused by improper functionality of the small intestine in absorbing this vitamin. Therefore, the recommendation is that patients with celiac disease be assessed for osteoporosis. In a similar case, Frikha et al. expressed that osteomalacia with Looser zones is a late complication of celiac disease which, in turn, occurs because of poor compliance to a gluten-free diet [7]. On the other hand, osteomalacia may be the presenting feature of celiac disease, and vitamin D supplementation could be an effective mode of therapy.

Dual Energy X-ray Absorptiometry (DEXA) bone densitometry is the best method available today for diagnosing low bone mineral density [8]. This is advocated as a showing for an antibodies test for celiac disease in young patients who have osteoporosis [9]. Clinical examination shows the indication of bilateral, proximal muscle atrophy and simultaneous weakness in the upper and lower extremities [10]. In the current case, the patient's hip range of motion was limited and painful. A recent article stressed the fact that celiac disease often presents with fatigue and anemia rather than the consequences of malabsorption. Clinical or biochemical evidence of osteomalacia in patients with celiac disease is rare now, and recently, in two large series of celiac patients, there were no reports of osteomalacia evidence [11].



Fig.1. A looser zone in the left thigh bone

Improvement in bone density in the current patient was notable after six months of treatment. Hence, a regimen of a gluten-free diet together with vitamin D supplementation was proven to be very effective. Osteomalacia is a major feature of celiac disease in young women. The current patient had both clinical and radiological signs of osteomalacia (Looser zone) that preceded the diagnosis by a significant period of time. Moreover, she had features of malabsorption as well. Celiac disease that is not treated is linked to malabsorption. Most fat-soluble vitamins are absorbed in the distal small bowel; nonetheless, extensive villous atrophy from long-standing gluten enteropathy can lead to weak absorption of vitamin D and other vitamins [12].

In osteomalacia patients, the diagnosis of celiac disease should be considered, although the biochemical features of osteomalacia appear late in the process of vitamin D depletion, and preliminary features may include some increase in parathyroid hormone and reduction in 25-hydroxy cholecalciferol levels [13]. It is also recommended that parathyroid hormone blood

levels be measured. This test helps the doctor determine whether the celiac disease is being controlled, whether excessive bone loss is going on, and whether sufficient calcium is being received by the patient. Unquestionably, a gluten-free diet is a must-have component of therapy for celiac disease [14]. After the diagnosis of osteomalacia was made in the current case, treatment with a gluten-free diet and supplementary calcium and vitamin D with bisphosphonates caused progressive improvement in symptoms as expected [15].

Conclusion

It is recommended that a celiac disease diagnosis be performed in any patient with osteomalacia. Moreover, it is essential that a gluten-free diet be imposed for the purpose of celiac disease therapy [16]. Due to the risk of osteomalacia, the treatment of celiac disease should be started to prevent bone loss complications.

Conflict of interest

The authors declare no conflicts of interest.

References

- Muhairi SJ, Mehairi AE, Khouri AA, Naqbi MM, Maskari FA, Al Kaabi J, Al Dhaheri AS, Nagelkerke N, Shah SM. Vitamin D deficiency among healthy adolescents in Al Ain. United Arab Emirates. *BMC Public Health* 2013; 13:33. doi: 10.1186/1471-2458-13-33.
- Gannage MH, Abikaram G, Nasr F, Awada H. Osteomalacia Secondary to Celiac Disease, Primary Hyperparathyroidism and Graves' Disease. *Am J Med Sci* 1998; 315(2):136-9. doi: 10.1016/S0002-9629(15)40289-7.
- Rostami Nejad N, Rostami K, Emami MH, Zali MR, Malekzadeh R. Epidemiology of Celiac Disease in Iran: A Review. *Middle East J Digestive Diseases* 2011; 3(1): 5-12.
- Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology* 2001; 120: 636-651. doi: 10.1053/gast.2001.22123.
- Helmerhorst EJ, Zamakhchari M, Schuppan D, Oppenheim FJ. Discovery of a Novel and Rich Source of Gluten-Degrading Microbial Enzymes in the Oral Cavity. *PLoS One* 2010; 5(10): e13264. doi: 10.1371/journal.pone.0013264. 2010.
- Koning F, Schuppan D, Cerf-Bennussan N, Solid LM. Pathomechanisms in celiac disease. *Best practice and research-Clin Gastroenterol* 2005; 19: 373-387. doi:10.1016/j.bpg.2005.02.003.
- Frikha F, Snoussi M, Bahloul Z. Osteomalacia associated with cutaneous psoriasis as the presenting feature of celiac disease: a case report. *Pan African Medical J* 2012; 11: 58.
- Pantaleoni S, Luchino M, Adriani A, Pellicano R, Stradella D, Ribaldone DG, Sapone N, Isaia GC, Di Stefano M, Astegiano M. Bone Mineral Density at Diagnosis of Celiac Disease and after 1 Year of Gluten-Free Diet. *The Scientific World J* 2014. doi: 10.1155/2014/173082.
- Lindh E, Ljunghall S, Larsson K, Lavo B. Screening for antibodies against gliadin in patients with osteoporosis. *J Intern Med porosis* 1992; 231:403-6. doi: 10.1111/j.1365-2796.1992.tb00951.x.
- Hepner GW, Jowsey J, Arnaud C, Gordon S, Black J, Roginsky M, Moo HF, Young JF. Osteomalacia and celiac disease: response to 25-hydroxyvitamin D. *Am J Med* 1978; 65: 1015-1020.
- Tahiri L, Azzouzi H, Squalli G, Abourazzak F, Harzy T. Celiac disease causing severe osteomalacia: an association still present in Morocco. *The Pan African Medical J* 2014; 19(43). doi: 10.11604/pamj.2014.19.43.2757.
- García-Porrúa C, González-ay MA, Avila-Alvarenga S, Rivas MJ, Soilan J, Penedo M. Celiac disease and osteomalacia: an association still present in western countries. *Rheumatology* 2000; 39 (12): 1435. doi: 10.1093/rheumatology/39.12.1435-a.
- Moreno ML, Vazquez H, Mazure R, Bai JC, et al. Stratification of bone fracture risk in patients with celiac disease. *Clin Gastroenterol Hepatol* 2004; 2(2): 127-134. doi: 10.1016/S1542-3565(03)00320-3.
- Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, and Murray JA. Diagnosis and Management of Celiac Disease. *Am J Gastroenterol* 2013; 108: 656-

Osteomalacia and celiac disease

676. doi: 10.1038/ajg.2013.79.
15. Saadati N, Rajabian R, The effect of bisphosphonate on prevention of glucocorticoid-induced osteoporosis. *Iranian Red Crescent Medical J* 2008; 10(1): 8-11.
16. Basu RA, Elmer K, Babu A, Kelly CA. Coeliac disease can still present with osteomalacia! *Rheumatology (Oxford)* 2000; 39(3): 335-6. doi: 10.1093/rheumatology/39.3.335.