Serological Diagnosis of Subclinical Gluten Enteropathy: A Case Presented As Treatment Resistant Osteomalacia

Subklinik Gluten Enteropatinin Serolojik Tanısı: Tedaviye Dirençli Bir Osteomalazi Vakası

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Abstract

Gluten enteropathy is frequently presented with minimal symptoms and signs. Atypical clinical presentation and treatment resistant osteomalacia should be screened for gluten enteropathy. Current serologic diagnostic methods have a high sensitivity and specificity. Serologic screening is recommended even in the absence of clinical symptoms and presence of minor histopathologic findings. In this case we report a patient with treatment resistant osteomalacia due to subclinical gluten enteropathy that responded to gluten free diet. *(Rheumatism 2006; 21: 118-20)*

Key Words: Gluten enteropathy, osteomalacia, serology

Özet

Gluten Enteropati seyrek olmayarak hafif semptom ve bulgularla seyreder. Atipik klinik bulgularla seyreden ve tedaviye dirençli osteomalazi olguları gluten enteropati açısından araştırılmalıdır. Günümüzdeki serolojik tanı metodları yüksek oranda sensitivite ve spesifiteye sahiptirler. Serolojik araştırma, klinik semptomların olmadığı ve hafif histopatolojik bulguların varlığında da önerilmektedir. Bu olgu sunumunda, biz glutensiz diyete cevap veren, subklinik gluten enteropatiye bağlı bir osteomalazi vakası bildiriyoruz. *(Romatizma 2006; 21: 118-20)*

Anahtar Kelimeler: Gluten enteropati, osteomalazi, seroloji

Introduction

Osteomalacia is characterized by impaired mineralization of bony matrix. Causes of osteomalacia include insufficient vitamin D intake, absorption disorders and disorders of vitamin D metabolism. Patients with osteomalacia may present with generalized pain involving the pelvis, spine, ribs or lower extremities. Clinical signs of osteomalacia include proximal muscle weakness that may result in an antalgic or waddling gait and difficulty in ambulation. Pain may be elicited by deep palpation of the tibia, ribs or pubic ramus.

Osteomalacia associated with intestinal malabsorption syndromes is a well-known entity. Occult disease is frequently present with minimal symptoms or signs. Current serologic tests, which have high sensitivity and specificity, could lead to diagnosis in patients without clinical symptoms (1).

In this case we report a patient with treatment resistant osteomalacia due to subclinical gluten enteropathy (GE) that responded to gluten free diet.

Case

A 34-year-old woman was admitted with the complaint of progressive hip girdle pain and weakness of 2.5 years history. She was unable to walk due to severity of the pain for the last 6 months. The complaints began in the hips and spread to her shoulders and knees. She previously used vitamin D and calcium preparations. She was not on any medication on admission. She had no gastrointestinal or biliary disease, no history of steatorrhea with malabsorption, no history of drug usage, had normal renal and liver functions. But she was wearing turban for religious belief that prevents exposure to sunlight.

Previous referral was orthopedic surgeon because of her protrusio acetabuli. Physical examinations revealed generalized pain especially increased with deep palpation of tibia, vertebral column and pelvis. Hip movements were limited on both sides. Also abdominal muscle weakness and diastasis recti were detected.

The laboratory data (Table 1) revealed a serum calci-

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um level of 3.5 mEq/l (normal range: 4.5-5.5 mEq/l), serum inorganic phosphorus level of 3.0 mg/dl (normal range: 1.6-6.8 mg/dl) and alkaline phosphatase (ALP) concentration of 674 IU/l (normal range: 25-150 IU/l), which was 5 times high. The 25-hydroxy vitamin D3 (25-OHD) concentration was 19 nmol/l (normal range: 25-125 nmol/l), parathyroid hormone (PTH) concentration was 125 pg/ml (normal range: 12-72 pg/ml) which was considered as secondary hyperparathyroidism. Also she had iron deficiency anemia with Hb: 9.4 g/dl. Serum iron concentration was 27 μg/dl (normal range: 37-145 μg/dl), total iron binding capacity was 650 μg/dl (normal range: 260-590 μg/dl) and serum ferritin concentration was 7,5 ng/ml (normal range: 10-120 ng/ml). Radiological examination demonstrated only mild generalized demineralization but not the looser's zones.

The whole body scintigraphy revealed multiple areas of mild to moderate increased uptake bilaterally and increased activity at costochondral joints suggesting rachitic rosary and multiple focal increased uptake on costae were compatible with pseudofractures. There were also multiple areas of increased uptake in the pelvis and mandibula. The findings were consistent with metabolic bone disease such as osteomalacia (Figure 1).

Table 1. The laboratory findings of the patient on admission and treatment period are shown

	On admission	3. month	6. month
Calcium (4.5-5.5 mEq/l)	3.5	4.3	5
P (1.6-6.8 mg/dl)	3.0	4.5	4.5
ALP (25-150 IU/l)	674	342	170
25-OHD (25-125 nmol/l)	19	18.7	24.5
PTH (12-72 pg/ml)	125	283.7	105
Hb (g/dl)	9.4		
Fe (37-145 μg/dl)	27		
FeBC (260-590 μg/dl)	650		
Ferritin (10-120 ng/ml)	7.5		

ALP- alkaline phosphatase, Fe- serum iron concentration, FeBC- total iron binding capacity, Hb- hemoglobin, P- inorganic phosphorus, PTH- parathyroid hormone, 25OHD- 25-hydroxy vitamin D3

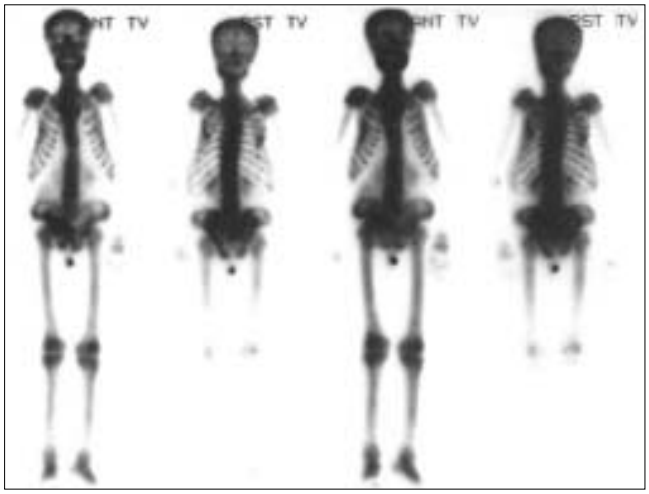

Figure 1. Whole body scintigraphy demonstrating bilateral multiple areas of mild to moderate increased uptake. Areas of multiple focal increase uptakes on costae suggest pseudofractures

With these findings she has been diagnosed as osteomalacia and was treated with a high dose vitamin D regimen consisting of im injection of ergocalciferol 300.000 IU for once. Additionally an oral supplementation of 1000 mg calcium carbonate in combination with 1.0 μg calcitriol per day was given.

After 3 months she was free of symptoms and the following laboratory results were noted: serum calcium 4.3 mg/dl; phosphorus 4.5 mg/dl; ALP 342 IU/l; serum 25-OHD level 18.7 pg/ml; PTH 283.7 pg/ml. The whole body scan did not reveal an increased uptake.

Despite the reveal of clinical symptoms, due to lack of laboratory response, the diagnosis was remained in doubt. We have thought that an initial clinical response might have been due to intramuscular vitamin D injection, following the treatment with oral therapy supplied no further response. As you know disorders of small intestine may cause malabsorption and osteomalacia. In some cases the bone disease is more evident than the gastrointestinal disease. Although our patient has not got gastrointestinal symptoms, we have made further research for malabsorption syndromes. The serum anti-gliadin IgA was 55.5 U/ml (normal range: 0-25 U/ml), anti-gliadin IgG was 26.9 U/ml (normal range: 0-25 U/ml), and endomysium antibody (EMA) was positive (+++). With these serolojic findings, intestinal biopsy was performed. Histologic examination of biopsy revealed mild changes of villi and surface epithelium. According to these results 1 μg/day calcitriol, 1000mg/day calcium carbonate, and gluten free diet were prescribed. After 6 months therapy, laboratory response has been achieved; serum calcium level 5 mg/dl; phosphorus level 4.5 mg/dl; ALP level 170 IU/l; serum 25-OHD level 24.5 pg/ml; PTH level 105 pg/ml.

Discussion

The prevalence of GE in the United States is 1:250 based on serologic testing (2). Occult disease is frequently present with minimal symptoms or signs. It has been estimated that there are 5-7 asymptomatic cases for each symptomatic case (3). Iron deficiency anemia is a common clinical presentation in adults with GE, which was also present in our patient. The prevalence of occult GE presenting with iron-deficiency anemia is approximately 2.8% (4).

To evaluate the patient for GE, serologic screening is recommended with a high sensitivity and specificity (5). Anti-gliadin antibody measurement is a highly sensitive and specific test for the diagnosis of GE. IgA EMA tests have been found to be %85-98 sensitive and nearly 100% specific in diagnosis of GE (5). Tissue transglutaminase

(tTG) test, has been identified as the antigen of Ig A EMA, has a 95% concordance rate with Ig A (6), with sensitivity of 95-98% and specificity of 94-95% (5).

The diagnosis of GE should be suspected in any patients with osteomalacia, especially resistant to the oral vitamin D supplementation. Today serologic tests are recommended for the diagnosis of GE, lessening the need for intestinal biopsy. Although our patient's intestinal biopsy revealed mild changes of villi and surface epithelium, combination of gluten free diet and vitamin D supplementation proved very effective.

As a result, like our case if we have lack of clinical and/or laboratory response to calcium and vitamin D treatment, we must remember intestinal disorders for further research. Serologic tests are highly useful, even the patients with mild changes of intestinal biopsy.

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