

Hip Fracture as the Presenting Feature of Celiac Disease: A Case Report

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Abstract

A 38-year-old woman presented to explore the etiology of hip fracture after a slight fall. Bone mineral density showed bone demineralization and laboratory investigations were in favor of osteomalacia. Serological markers for CD were highly positive: IgA anti-endomysial antibodies (indirect immunofluorescence)+++, IgA anti-transglutaminase 2 antibodies (ELISA) = 144 RU/ml, IgA anti-deaminated gliadine peptides antibodies (ELISA) >200 RU/ml, IgG anti-deaminated gliadine peptides (ELISA) 118 RU/ml. Diagnosis of osteomalacia secondary to longstanding undiagnosed celiac disease was made. Calcium, vitamin D and iron supplementation was prescribed and gluten free diet was started.

Keywords: Celiac Disease; Osteomalacia; Hip Fracture

Introduction

Celiac disease (CD), a systemic auto-immune disease, is driven by dietary gluten in genetically predisposed subjects. CD is more common in females. This disorder could be accompanied by gastrointestinal or extra intestinal symptoms; it can even remain asymptomatic. Several complications can occur due to undiagnosed or untreated CD. It is often associated with more or less severe malabsorption syndrome responsible for nutritional deficiencies including vitamin D, calcium and phosphorus [1].

Low levels of vitamin D, calcium and phosphorus could cause bone demineralization and osteomalacia [2]. In this paper, we will present a patient with severe osteomalacia due to long-standing undiagnosed CD.

Case Report

A 38-years-old female was admitted to rheumatology department to explore the etiology of hip fracture after a slight fall for which she was operated.

On examination, the patient was small and underweight; her weight was 39 Kg and her height was 149 cm (Body Mass Index = 17,56 Kg/m²). She had pale conjunctive.

The direct inquiry revealed that she had three spontaneous miscarriages and anemia not corrected by oral iron supplementation.

Bone mineral density showed bone demineralization (low density at both lumbar vertebra L1-L4 = -5DS and femoral neck = -4,8 DS; Tscore = -5, Z score = -4).

On laboratory evaluation, increased alkaline phosphatase, low 25 hydroxyvitamin D (25(OH) D), low calcium and low phosphate values were all in favor of osteomalacia. Table 1 shows the result of phosphocalcic metabolism.

All serological markers for CD were highly positive: IgA anti-endomysial antibodies (indirect immunofluorescence)+++, IgA anti-transglutaminase 2 antibodies (ELISA) = 144 RU/ml (NV<25 RU/ml), IgA anti-deaminated gliadine peptides anti-

bodies (ELISA) >200 RU/ml (NV<25 RU/ml), IgG anti-deaminated gliadine peptides (ELISA) 118 RU/ml (NV<25 RU/ml).

Antinuclear antibodies, anti-cardiolipin antibodies, anti β 2-glycoprotein I antibodies, anti-thyroid antibodies, anti-cyclic citrullinated peptide antibodies and rheumatoid factors were all negative.

Biochemistry and hematology parameters are indicated in Table 2.

Protein electrophoresis was normal.

The diagnosis of osteomalacia due to untreated CD was made.

Calcium, vitamin D and iron supplementation was prescribed and a gluten free diet was started.

Discussion

The association CD-osteomalacia was mostly described as case reports [3,9]. In all these cases osteomalacia was revealed by bone pain or weakness. None of the patients had, like our patient's case, a severe fracture. Only Tahiri el al reported a double symptomatic fracture of the wrist and femur in a 36-year old woman [8]. Osteomalacia results from defective mineralization when the body is prived from calcium and vitamin D [2]. This disease occurs when existing bone is replaced by unmineralized bone matrix or when newly formed bone is not mineralized [2]. CD, which is the first cause of malabsorption syndrome, could be the cause of osteomalacia.

In our patient, the diagnosis of CD was made regarding the positivity of serological markers. In fact, it has been recently demonstrated that bowel biopsy is not always required to diagnose CD in patient with concordant antibody results [10,11].

The arthralgia and myalgia from which suffer our patient could also due to her untreated CD. In fact, celiac disease is significantly more frequent in patients with unexplained articular manifestations than in general population [12] and the cause-effect relation was proved by a complete remission after

Table 1: Phosphocalcic Metabolism

	Calcium(2-2.5 mmol/l)	Calcium-U (2.5-5 mmol/l)	Phosphorus (0.81-1.36 mmol/l)	Phosphorus-U (22-44 mmol/l)
Day1	2.01	---	0.3	---
Day2	1.84	0.37	0.4	6
Day3	1.75	0.37	0.5	12.5

Table 2: Biochemical and Hematological Parameters

Laboratory tests	Results	Normal range
Cholesterol	3.2	3.9-6.7 mmol/l
Triglycerides	1	0.6-1.7
HDL-cholesterol	0.9	0.8-1.7 mmol/l
LDL-cholesterol	1.8	2.2-3.3 mmol/l
Magnesium	0.78	0.74-0.9 mmol/l
25 (OH) vitamin D	5.3	20-40 ng/ml
Iron	2	19-27 μ mol/l
Ferritin	9	10-280 ng/ml
Homocystein	16	5-15 μ mol/l
Folic-acid	1	5.3-14.4 ng/ml
Vitamin B12	652	208-963 pg/ml
Glycemia	5.1	3.9-6.1 mmol/l
Alkaline phosphatase	841	35-140 UI/l
ALAT	36	<40 UI/l
ASAT	66	<37 UI/l
Thyroid-stimulating hormone	1.831	0.55-4.78 mUI/l
Parathormone	214.6	15-65 pg/ml
Complement C3	1	0.9-1.8 g/l
Complement C4	0.12	0.1-0.4 g/l
Haemoglobin	8.9	12-15.5 g/dl
Mean corpuscular volume	74	83-98 fl
Mean corpuscular haemoglobin concentration	30.6	31-36 %
Leukocytes	2800	4000-11000/mm ³
Platelets	240000	150000-400000/mm ³

starting gluten free diet [13,14]. In our previous study about the frequency of CD in patients with unexplained articular manifestations, an 80-years-old woman was admitted to the hospital for arthralgia and her medical records revealed that she had one abortion and 8 children died before the age of 6 months.

Our patient had three spontaneous miscarriages. It is well known that CD increases the risk of recurrent miscarriages. During CD, there is production of anti-endomysium and anti-transglutaminase 2. The transglutaminase 2 (TG2), the main autoantigen of CD, is an ubiquitous enzyme and so expressed in endometrial cells, stromal and trophoblast placental cells. Maternal CD antibodies binding the placental TG2 may adversely affect placental function. In fact, they could cause an inhibition of syncytial TG2 impairing placental development and endometrial angiogenesis [15,16]. It was also demonstrated that spontaneous abortions in CD patients has been linked to vitamin and mineral deficiencies [15].

Our patient had moderate hypertransaminasemia probably due to untreated celiac disease. In fact, we and others [17,18] demonstrated that 9% of patients with unexplained liver cytotoxicity had CD. In CD, The increase of transaminases levels was mild [19] and the elevated levels reverted to normal in the majority of patients on strict gluten free diet [18]. Several mechanisms were involved in liver damage [19] especially the chronic intestinal inflammation causing an exposure of TG2. The autoantibodies produced during CD could reach TG2 in extra-intestinal tissues and play an important part in liver injury. Furthermore, the increased intestinal permeability induced by gliadin cause an exposure, of the hepatobiliary system, to toxins and antigens and to proinflammatory cytokines. The malabsorption and the bacterial overgrowth observed in CD have been also suggested as possible mechanisms of liver injury in CD [19].

Celiac disease is a frequent cause of hematologic disorders. Our patient's haemoglobin was 8.9 g/dl despite iron supplementation. The anemia was due to an iron malabsorption, in fact, iron and ferritin levels were decreased. Anemia is the most

frequent non gastro-intestinal manifestation of CD [20]. Our team described three cases of severe osteomalacia presenting as a major feature of CD [3]. All of them had anemia and one of these patients had a 15-years history of persistent iron-deficiency anemia despite oral iron supplementation.

The leukopenia, in our patient was probably due to reduced level of folic-acid. Indeed, severe folic-acid deficiency can result in a decrease in both leukocytes and platelets and even manifest as severe pancytopenia [20].

Within one year after starting the gluten free diet, levels of liver enzymes, calcium and phosphorus reverted to normal and arthralgia and myalgia disappeared.

Conclusion

This case report highlights, once more, the importance to be aware of the predominance of extraintestinal manifestations in CD, because a very late diagnosis can lead to serious complications which can go as far as a severe fracture of the hip.

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Mariam Ghazzi and Skander Laabidi did Immunological tests and wrote the manuscript; Sawssen Mrad did Biochemistry analyses; Khadija Baccouch and Elyes Bouajina did clinical investigations and revised the manuscript.

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