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Myelofibrosis due to Secondary Hyperparathyroidism in a Case of Celiac Disease

Nasim Valizadeh[1], Neda Valizadeh[1], Shahin Nateghi[1], Negar Aghamohammadi[1]

1. Urmia University of Medical Sciences,Urmia, Iran;

Corresponding author: Nasim Valizadeh, Assistant Professor of Hematology/oncology ; Urmia University of Medical Sciences,Urmia, Iran; (Tel/Fax: 09125474755, Email:valizadehn@sums.ac.ir)

Abstract

Myelofibrosis is reported in patients with primary hyperparathyroidism. It is also was reported in patients with secondary hyperparathyroidism due to end-stage renal disease or Vitamin D dependent rickets .We present a case of celiac disease and osteomalacia which leads to secondary hyperparathyroidism and myelofibrosis.

Keywords: Celiac disease, Hyperparathyroidism, Myelofibrosis

Introduction

Celiac sprue is an autoimmune disease caused by gluten-containing diet in genetically predisposed persons. Pathogenesis is presence of antibodies to tissue transglutaminase, endomyosium, reticulin, and gliadin.[1] It leads to malabsorption of nutrients in small intestine such as iron, folate, and calcium.[2] Presentations of patients with celiac disease are different including chronic diarrhea, short statue, iron deficiency anemia, osteomalacia, neurologic problems, and other unusual manifestations. Associated conditions include dermatitis herpetiformis, selective IgA deficiency, and other diseases which have autoimmune bases such as type 1 diabetes mellitus, thyroid disease, and liver disease.[1] In females with celiac disease, chronic malabsorption and nutritional deficiency can alter the function of hypothalamic-pituitary axis and lead to primary amenorrhea and failure of development of secondary sexual characteristics.[3] Secondary hyperparathyroidism is a physiologic response to hypocalcemia and is seen in patients with end stage renal disease,[4,5] vitamin D-dependent rickets,[6] and rarely in celiac disease.[7] PTH activates osteoclasts,[8] increases renal clearance of phosphorus, bone resorption, serum levels of 1,25-dihydroxy vitamin D and intestinal absorption of calcium, and decreases renal clearance of calcium.[7] In patients with celiac disease, hypocalcemia may persist despite secondary hyperparathyroidism and lead to stimulation and enlargement of the parathyroid glands. Parathyroid carcinoma has been reported in patients with celiac disease.[9,10] In patients with celiac disease with hypocalcemia and Vitamin D deficiency, presence of hypophosphatemia associated with low to normal Calcium and elevated PTH level is suggestive of secondary hyperparathyroidism.[7]

Literature review demonstrates that hyperparathyroidism is an important cause of myelofibrosis.[11] Kumbasar et al reported a young female with primary hyperparathyroidism and pancytopenia whose bone marrow biopsy revealed myelofibrosis. She underwent total excision of parathyroid adenoma .After surgery, complete blood count (CBC) and other clinical abnormal findings slowly recovered without another intervention.[12] Nomura et al reported a woman undergoing hemodialysis with secondary hyperparathyroidism who recovered from myelofibrosis after a total parathyroidectomy.[4]

Here, we present a case of celiac disease with osteomalacia, secondary hyperparathyroidism, and myelofibrosis.

Case Report

An 18-year-old girl was admitted to hematology department with pancytopenia and splenomegaly. She had positive history of chronic diarrhea since childhood, and primary amenorrhea. Physical examination revealed short statue, clubbing, splenpmegaly, and failure of development of secondary sexual characteristics. Laboratory

findings included leukocyte count of 1400/mm^3 (polymorphonuclear= 54%, lymphocyte= 35%), hemoglobin of 7.1 g/dl, platelet count 52,000/mm^3, alkaline phosphatase of 654 U/L (high), total billirubin of 1.35 mg/dl (normal<1.2), direct billirubin of 0.45 mg/dl (normal<0.2), prothrombin time of 15 seconds, partial thromboplastin time of 58 seconds, serum albumin of 4.3g/dl, erythrocyte sedimentation rate of 16 mm/h, ferritin of 20 ng/ml, normal iron and total iron binding capacity, lactate dehydrogenase of 808 U/L (Nl<480), and negative direct and indirect Coombs. ANA was 0.4 IU/ml, calcium 7 mg/dl (normal: 8.5-10.3), phosphorus 1.5 mg/dl (normal: 1.7-4.5), potassium 2.9 mEq/L, parathyroid hormone 226 pg/ml (high), creatinine 0.7 mg/dl, and blood urea nitrogen normal. Urine analysis, stool exam, and thyroid function tests were all normal. Serum folate level was 2.03 ng/ml (normal: 3.1-17.5), vitamin B12 level 176 pg/ml (normal: 191-663), prolactin 17 ng/ml (normal), anti-endomyosial antibody (Ig A) 170 U/ml (high). Abdominal ultrasonography revealed hepatomegaly and huge splenomegaly (span=210 mm). Peripheral blood smear showed anisocytosis, poikylocytosis, macrocyte, microcyte, tear drop, and hypochromia. Bone marrow aspiration showed dry tap. After many attempts, bone marrow was aspirated which showed severe hypocellolarity with increased number of osteoclasts, giant cells, and osteoblasts. Bone marrow biopsy and reticulin staining revealed myelofibrosis. Upper gastrointestinal endoscopy revealed fissures in the second part of duodenum. Biopsy revealed marked villous atrophy and mucosal flattening. Diagnosis of celiac disease and secondary hyperparathyroidism with myelofibrosis and central hypogonadism due to systemic illness was made. We started gluten-free diet and calcium, vitamins including vitamin D, B12, C, E and folic acid.

Discussion

Patients with celiac disease and other malabsorption syndromes with vitamin D deficiency and hypocalcemia are susceptible to secondary hyperparathyroidism which may lead to myelofibrosis. Bone marrow aspiration and biopsy are recommended in patients with celiac disease who have pancytopenia, organomegaly, and elevated PTH level. Searching for hyperparathyroidism should be recommended in patients with celiac disease and myelofibrosis. Many cases of myelofibrosis due to primary and secondary hyperparathyroidism have been reported.[12,13] In patients with primary hyperparathyroidism, total excision of parathyroid adenoma improves myelofibrosis.[9,11,12]

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