Bosphorus Medical Journal
Boğaziçi Tıp Dergisi

Case Report

DOI: 10.14744/bmj.2019.73645

Bosphorus Med J 2019;6(3):99–102

Silent Celiac Disease and Primary Biliary Cirrhosis Underlying Fibromyalgia: A Case Report

Fibromiyalji Altında Yatan Sessiz Çölyak Hastalığı ve Primer Biliyer Siroz: Bir Olgu Sunumu

Aliye Tosun,[1] Sinan Akay,[2] Ümit Seçil Demirdal,[1] Zehra Akpınar,[2] Korhan Barış Bayram,[3] Semra Ergan,[3] Ayhan Aşkın[1]

[1]Department of Physical Medicine and Rehabilitation, Izmir Katip Celebi University Faculty of Medicine, Izmir, Turkey
[2]Department of Gastroenterology, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey
[3]Department of Physical Medicine and Rehabilitation, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey

Cite this article as: Tosun A, Akay S, Demirdal ÜS, Akpınar Z, Bayram KB, Ergan S, et al. Silent Celiac Disease and Primary Biliary Cirrhosis Underlying Fibromyalgia: A Case Report. Bosphorus Med J 2019;6(3):99–102.

Received: 28.07.2019
Accepted: 09.09.2019

Correspondence:
Dr. Ayhan Aşkın. Atatürk Eğitim ve Araştırma Hastanesi Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, İzmir, Turkey
Phone:
+90 232 244 44 44 - 2738
e-mail:
ayhanaskin@hotmail.com

ABSTRACT

Fibromyalgia syndrome (FMS) is characterized by chronic widespread musculoskeletal pain, stiffness and tenderness at multiple points. FMS can be classified as primary or secondary according to the presence of other medical disorders. Irritable bowel syndrome, a comorbid disorder frequently associated with FMS, has also been reported to be associated with celiac disease (CD) in which gluten triggers an autoimmune reaction in the small intestinal mucosa, which results in inflammation, villous atrophy, and malabsorption. Primary biliary cirrhosis (PBC) is the most common reported liver disease in CD. A gluten-free diet is the only effective treatment for CD and prevents the troublesome consequences of the disease. Herein, we present a fibromyalgic female patient in whom the diagnosis of CD and PBS were established upon investigating the causes of elevated liver biochemistry tests and iron-deficiency anemia.

Keywords: Celiac disease; fibromyalgia; primary biliary cirrhosis.

ÖZET

Fibromiyalji sendromu (FMS), kronik yaygın kas iskelet sistemi ağrısı, sertlik ve çoklu noktalardaki hassasiyet ile karakterizedir. FMS, diğer tıbbi bozuklukların varlığına göre primer veya sekonder olarak sınıflandırılabilir. Sıklıkla FMS ile ilişkili komorbid bir hastalık olan irritabl bağırsak sendromunun, gluten'in inflamasyon, villöz atrofi ve malabsorpsiyon ile sonuçlanan ince bağırsak mukozasında bir otoimmün reaksiyonu tetiklediği çölyak hastalığı (ÇH) ile ilişkili olduğu bildirilmiştir. Primer biliyer siroz (PBS), ÇH'de en sık bildirilen karaciğer hastalığıdır. Glutensiz bir diyet, ÇH için tek etkili tedavidir ve hastalığın zahmetli sonuçlarını önler. Burada yüksek karaciğer biyokimya testleri ve demir eksikliği anemisinin nedenlerini araştırdıktan sonra ÇH ve PBS tanısı alan bir fibromiyaljik kadın hastayı sunuyoruz.

Anahtar sözcükler: Çölyak hastalığı; fibromiyalji; primer biliyer siroz.

Fibromyalgia syndrome (FMS) is characterized by chronic widespread musculoskeletal pain, stiffness and tenderness at multiple points.[1] It has recently been discussed that FMS shares similar abnormalities of causation with, and clinical features of, several other disorders that make up central sensitivity syndrome, such as irritable bowel syndrome (IBS), chronic fatigue syndrome, myofascial pain, migraine, low back pain, restless leg syndrome, chronic pelvic pain, primary dysmenorrhea, temporomandibular joint disorders, posttraumatic stress disorders and interstitial cystitis.[2]

IBS, a comorbid disorder frequently associated with FMS, is a common gastrointestinal disease characterized by the presence of chronic abdominal pain or discomfort associated with changes in bowel habits, consisting predominantly of di-

arrhoea, constipation or alternating patterns, defecation urgency and abdominal distension. It has been reported that a non-negligible percentage of IBS patients are celiac disease (CD) patients in whom gluten triggers an autoimmune reaction in the small intestinal mucosa, which results in inflammation. A gluten-free diet (GFD) is the only effective treatment for CD, and it usually results in recovery of the small intestinal mucosa; therefore, an earlier diagnosis is of great importance.[3, 4] However, since CD has a diverse clinical heterogeneity ranging from asymptomatic to severely symptomatic patients, most of the cases remain undiagnosed although the estimated prevalence of CD has been reported to be 1% in the general population. An increased overall and cancer mortality (e.g., esophageal cancer, small intestine adenocarcinoma) has been reported in adult patients with CD, which lends support to the clinical importance of this disorder.[5–8]

Liver abnormalities are often seen in CD, most of which normalize when the patients convert to a gluten-free diet. However, primary biliary cirrhosis (PBC), an autoimmune disease of the liver, is reported to be the most common liver disease in CD. The diagnosis of PBC should not be overlooked, especially in patients with persisting liver abnormalities since timely diagnosis is of particular importance.[9]

In this study, we present a fibromyalgic female patient in whom the diagnosis of CD and PBC were established upon investigating the causes of elevated liver biochemistry tests and iron-deficiency anemia.

Case Report

A 51-year-old female patient was presented with a history of widespread musculoskeletal pain for one year. She also complained about morning fatigue, restless sleep, abdominal pain, bloating and constipation. Her medical history was unremarkable. On physical examination, neck and lower back movements were painful and slightly limited in all directions. On palpation, 15 tender points were detected. The neurological examination was normal. Erythrocyte sedimentation rate was 67 mm/h, Hg was 10.7 g/dl (11-16), Hct 33.1%, MCV 74.6 fL (80-100), platelet 419000 K/uL, AST 52 U/L (5-34), ALT 70 U/L (0-55), GGT 191 U/L (9-36), serum Fe 29 ug/dL (50-170), IBC 501 ug/dL (228-425), ferritin 4 ng/mL (10-291), PTH 88 pg/mL (19.8-74.6) and 25 (OH) vitamin D 17.8 µg/L (20-120). Remaining tests, including C-reactive protein, RF, TSH, renal function tests, serum glucose, electrolytes, vitamin B-12, folic acid and ANA, were in normal ranges. The patient was fulfilling the American College of Rheumatology (ACR) 1990, as well as the ACR 2010 criteria for FMS.[10, 11] The patient consulted Gastroenterology clinics, and antimitochondrial antibody was found to be positive, as well as positive antigliadin endomysium IgG and IgA antibodies. Anti-smooth muscle antibody, Hepatitis B and C serologies were negative. Histopathology of the liver biopsy (bx) revealed minimal inflammatory changes. Chronic atrophic gastritis and duodenitis were seen in endoscopy, and increased intraepithelial lymphocyte infiltration in duodenum compatible with CD was revealed on bx. Screening for osteoporosis revealed osteopenia. Musculoskeletal pain and other symptoms resolved and liver function tests decreased (AST was 35 U/L, ALT 45 U/L, GGT 65 U/L) in the first month of the treatment, including GFD for CD and ursodeoxycholic acid for PBC. Descriptive features of the case are shown in Table 1.

Table 1. Descriptive features of the case

Age/Gender	51/female
Complaint	Widespread musculoskeletal pain, morning fatigue, restless sleep, abdominal pain, bloating and constipation
Medical history	Unremarkable
Physical examination	Painful and limited neck and lower back movements, 15 tender points
Laboratory findings	Hgb: 10.7 g/dL (11-16) Platelet: 419000 K/uL MCV: 74.6 fL (80-100) AST: 52 U/L (5-34) ALT: 70 U/L (0-55) GGT: 191 U/L (9-36) Fe: 29 ug/dL (50-170) IBC: 501 ug/dL (228-425) Ferritin: 4 ng/mL (10-291) PTH: 88 pg/mL (19.8-74.6) 25 (OH) vitamin D: 17.8 µg/L (20-120) Antimitochondrial antibody: positive Antigliadin endomysium IgG and IgA antibodies: positive
Liver biopsy	Minimal inflammatory changes
Endoscopy and biopsy	Chronic atrophic gastritis and duodenitis, increased intraepithelial lymphocyte infiltration in the duodenum
DXA	Osteopenia
Prognosis	Musculoskeletal pain and other symptoms resolved and liver function tests decreased at the first month of the treatment, including a gluten-free diet for CD and ursodeoxycholic acid for PBC.

PBC: Primary biliary cirrhosis; CD: Celiac disease; IgG: Immunoglobulin G; IgA: Immunoglobulin A; HgB: Hemoglobin.

Discussion

FMS is a complex chronic pain syndrome affecting 1% to 3% of the people worldwide. The pathogenesis of FMS remains elusive; both immunologic and environmental factors contribute to its pathological process. FMS is frequently associated with other diseases, including rheumatic disorders, infections and other systemic illnesses.[3] Patients with FMS commonly report gastrointestinal symptoms, and signs and IBS is the disorder that has been most commonly studied and correlated with FMS.[3, 12]

IBS affects 2.4-15.5% of the western populations. The challenge for the clinician is to exclude organic abnormality based on history, clinical examination, and absence of features, such as weight loss, rectal bleeding, nocturnal diarrhea, or anemia. It has been reported that a non-negligible percentage of IBS patients are CD patients whose symptoms can improve and in whom long-term CD-related complications may possibly be prevented with a strict lifelong GFD. [3, 13] CD is a chronic inflammatory disease characterized by flattened villi on the small bowel mucosa and is induced in genetically susceptible people by the ingestion of gluten-containing foods, such as wheat, rye, and barley.[5] CD has a prevalence of 1% in the general population; however, only about 10% of all cases may be diagnosed. Thus, 90% of the cases remain undiagnosed. Common signs and symptoms of CD include anemia, arthralgia, fatigue, infertility, neuropathy, and weight loss, in addition to typical gastrointestinal symptoms, including abdominal pain, anorexia, bloating, constipation, and diarrhea. However, these symptoms can be minimal or even be paradoxical in many patients.[5, 6, 8] Likewise, abdominal pain, bloating and constipation were present in our patient, but she felt no need to seek medical advice. Widespread musculoskeletal pain was the major complaint of our patient.

Many patients with CD have few or no outward symptoms, but certain biochemical signs of malabsorption are indicative of the disease (e.g., deficiencies in folate and iron). Iron deficiency anemia was also present in our patient, which led us for further investigation as well as elevated liver function tests. Autoimmune disorders are commonly associated with CD, incidences of which increase 3-10 times in respect to the general population. The link between CD and PBC is also well established, with a 3-20 fold increase in PBC risk. Elevated aminotransferases are commonly found in untreated CD patients, and the possibility of liver disease must be evaluated if they do not normalize after initiation of GFD. In patients with persisting liver abnormalities after the introduction of a gluten-free diet, the diagnosis of PBC should be looked for by the analysis of AMA[5, 8, 9, 14] PBC was also timely diagnosed in our patient. Fortunately, the liver biopsy revealed only minimal inflammatory changes. Liver function tests, especially GGT, significantly decreased in response to treatment with ursodeoxycholic acid and GFD.

The only effective treatment for CD is strict and life-long adherence to a GFD and it usually results in recovery of the small intestinal mucosa. All food and drugs that contain gluten from wheat, rye, barley, and their derivatives must be eliminated because even small amounts can be harmful. Initiated treatment with a GFD improves the symptoms of CD. Likewise, we observed in our patient.[4, 5]

To conclude, CD, along with the PBS, were the underlying causes of FMS in our patient. Diagnosis and proper treatment of underlying CD and PBS not only provided the treatment for FMS but also, more importantly, will highly likely to prevent the troublesome outcomes of the diseases. Therefore, we assume that increased physician awareness of the clinical range of these disorders and a continued high threshold of suspicion are needed.

Disclosures

Informed consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – A.T., S.A., Ü.S.D.; Design – Z.A., K.B.B., S.E., A.A.; Supervision – A.T., S.A., Z.A., K.B.B., S.E.; Materials – A.T., A.A.; Data collection/or processing – A.T., A.A.; Analysis and/or interpretation – A.T., A.A., Ü.S.D., K.B.B., S.E., Z.A.; Literature search – A.T., A.A., Ü.S.D.; Writing – A.T., A.A.; Critical review – A.T., S.A., Ü.S.D., Z.A., K.B.B., S.E., A.A.

References

1. Yunus MB, İnanıcı F. Fibromyalgia Syndrome: clinical features, diagnosis, and biopathophysiologic mechanisms. Rachlin ES, Rachlin IS, editors. Myofascial pain and Fibromyalgia. New York: Mosby; 2002.p.3–32. [CrossRef]
2. Hawkins RA. Fibromyalgia: a clinical update. J Am Osteopath Assoc 2013;113:680–9. [CrossRef]
3. Rodrigo L, Blanco I, Bobes J, de Serres FJ. Remarkable prevalence of celiac disease in patients with irritable bowel syndrome plus fibromyalgia in comparison with those with isolated irritable bowel syndrome: a case-finding study. Arthritis Res Ther 2013;15:R201. [CrossRef]

4. Norström F, Sandström O, Lindholm L, Ivarsson A. A gluten-free diet effectively reduces symptoms and health care consumption in a Swedish celiac disease population. BMC Gastroenterol 2012;12:125. [CrossRef]
5. Di Sabatino A, Corazza GR. Celiac diseaes. Lancet 2009;373:1480–93. [CrossRef]
6. Dawidowicz K, Ea HK, Lahalle S, Qubaja M, Lioté F. Unexplained polyarthralgia and celiac disease. Joint Bone Spine 2008;75:325–8. [CrossRef]
7. Corrao G, Corazza GR, Bagnardi V, Brusco G, Ciacci C, Cottone M, et al; Club del Tenue Study Group. Mortality in patients with coeliac disease and their relatives: a cohort study. Lancet 2001;358:356–61. [CrossRef]
8. Westerberg DP, Gill JM, Dave B, DiPrinzio MJ, Quisel A, Foy A. New strategies for diagnosis and management of celiac disease. J Am Osteopath Assoc 2006;106:145–51.
9. Kummen M, Schrumpf E, Boberg KM. Liver abnormalities in bowel diseases. Best Pract Res Clin Gastroenterol 2013;27:531–42. [CrossRef]
10. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33:160–72. [CrossRef]
11. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res (Hoboken) 2010;62:600–10. [CrossRef]
12. García-Leiva JM, Carrasco JL, Slim M, Calandre EP. Celiac symptoms in patients with fibromyalgia: a cross-sectional study. Rheumatol Int 2015;35:561–7. [CrossRef]
13. Sanders DS, Carter MJ, Hurlstone DP, Pearce A, Ward AM, McAlindon ME, et al. Association of adult celiac disease with irritable bowel syndrome: a case-control study in patients fulfilling ROME IIcriteria referred to secondary car. Lancet 2001;358:1504–8. [CrossRef]
14. Caramaschi P, Stanzial A, Volpe A, Pieropan S, Bambara LM, Carletto A, et al. Celiac disease in a rheumatology unit: a case study. Rheumatol Int 2008;28:547–51. [CrossRef]