FMF and Sjogren’s Syndrome Overlap in an Elderly Patient: A Rare Coincidence or a Causal Association?

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Abstract

Sixty five-year-old female patient admitted to our clinic with complaint of intermittent fever and abdominal pain for forty years. We learned that she has mouth and eye dryness. Laboratory examination revealed elevated levels of inflammatory parameters. In chest X-ray there was reticular appearance. Then we suspect that rheumatic diseases and serological examination revealed positive ANA and anti-centromere antibodies. Minor salivary gland biopsy was reported as ‘chronic inflammation with focus score 2’. The patient was diagnosed with Sjogren’s syndrome. Because of recurrent abdominal pain with febrile episodes, we suspect of Familial Mediterranean Fever (FMF). We detected homozygous MEFV mutation in genetic mutation analysis and then FMF was diagnosed. In literature, this is the first case, coincidence of Sjogren’s syndrome and FMF, in the geriatric age group and the second case in all age groups.

Keywords

Sjogren’s syndrome, Familial mediterranean fever, Elderly

Introduction

The most common organic causes of chronic abdominal pain are; drug use with gastrointestinal side effects, peptic ulcer disease, inflammatory bowel disease, chronic pancreatitis, biliary-gastrointestinal cancers, Familial Mediterranean Fever (FMF) and endometriosis [1]. Except organic causes, functional disorders can be seen. Functional disorders must be within normal limits in laboratory values. That’s why it should not be ruled out the structural or organic diseases without evaluating anemia, serum albumin level, C-reactive protein, vitamin A-D-B12 values [1].

Common causes of fever of unknown origin (mostly prolonged 3 weeks); infection (CMV, EBV, malaria, etc.), malignancy (leukemia, lymphoma, etc.), connective tissue disease (polyarteritis nodosa, rheumatoid arthritis, systemic lupus erythematosus, etc.), drug fever, granulomatous disease (sarcoidosis, granulomatous hepatitis, Crohn’s disease, etc.), pancreatitis and pulmonary embolism. Despite all these wide spectrum of diseases; fever of unknown origin cannot be diagnosed in 10-30% of all cases [2].

Sjogren’s syndrome (SS) is a systemic autoimmune disease which especially affects the exocrine glands. SS is resulting persistent mouth and eye dryness which is often due to functional disorders of the salivary and lacrimal glands. Incidence was 0.4% [3]. It affects especially white, perimenopausal women. In large series female: male ratio has been reported as 14:1 to 24:1 [3].

FMF is a hereditary, autosomal recessive disorder characterized by 12-72 hours attacks of fever and localized serous membrane, synovial or skin inflammation.

Although the biochemical signs of inflammation remain, patients are usually full of well-being among attacks. Approximately 10% of the patients experiences first attack of FMF at the adult age. But after age 40, the first attack is very rare. Clinical criteria remain the basic for diagnosis. [Clinical criteria; attack time (12-72 hours), the repetition of symptoms (3 or more episodes) documented fever (rectal > 38 centigrade degree), pain of abdomen- breast - joints - skin lesion]. More than 1:3 patients who have typical FMF clinical signs [4].
Case Report

Sixty five-year-old female patient admitted to our clinic with complaint of intermittent fever (she didn’t know the frequency, ranging from 37-38 °C), permanent, lower quadrant abdominal pain lasting two days for forty years. In addition, chest pain and joint pain—especially at the knee, accompany these complaints occasionally. It was learned that she has intermittent fever, abdominal pain, diarrhea, nausea, vomiting for the past four months.

It was learned she had asthma and she was given antibiotic therapy one month ago because of pneumonia from the medical history. Although given antibiotic therapy, there had been increase of C-reactive protein (CRP) for one month. It was learned that she had the history of iron-deficiency anemia refractory to iron replacement for approximately five years. Endoscopic studies to find out the causes of iron deficiency anemia revealed that there were erosive gastritis and diverticula in the sigmoid colon five years ago.

Physical examination was normal except common abdominal tenderness. Vital signs were within normal limits. Laboratory examination revealed low levels of hemoglobin, elevated levels of C-reactive protein and erythrocyte sedimentation rate (Hb: 9.5 g/dL, MCV: 75 fl, sedimentation rate: 51 mm/h, CRP: 81 mg/L). Low hemoglobin was due to iron deficiency anemia. Serum iron (Fe): 19 µg/dL, Unsatuated iron binding capacity (UIBC): 303 µg/dL, Transferrin saturation; 6% serum ferritin: 66 ng/mL). Chest x ray was showed reticular appearance.

To rule out the common causes of fever of unknown origin, malignancy screening for this patient was planned. In endoscopy there was antral gastritis and hiatal hernia. No pathology was found in colonoscopy. There was no pathology in serum protein electrophoresis, serum and urine immunofixation. Because of reticular appearance in chest X-ray, thoracic CT is performed. But we could not find infection, or pathologic lymph node size, nodules, etc.

Because she had intermittent fever and reticular appearance on her chest radiography, we suspected she could have rheumatic diseases. In serological examination rheumatoid factor, C3, C4 levels were normal. Antinuclear antibodies (ANA) and anti-centromere antibodies were positive. Anti-neutrophil cytoplasmic antibodies (ANCA) were negative. We learned that patient had mouth and eye dryness. Because Sjögren’s syndrome was suspected Schirmer’s test was performed and found that 5 mm for both eyes supporting the Sjögren’s syndrome diagnosis. Minor salivary gland biopsy was reported as ‘chronic inflammation with focus score 2’. The diagnosis of Sjögren’s syndrome was made and hydroxychlorocine 2 x 200 mg treatment was started.

Due to history of intermittent fever for 40 years and family history of FMF, we suspected the patient to be having FMF diagnosis. We detected homozygous MEFV mutation in genetic mutation analysis. The diagnosis of FMF was made and colchicine 2 x 0.5 mg treatment was started. Salivary gland, duodenum and rectum biopsies revealed no amyloidosis.

Discussion

Familial Mediterranean Fever (FMF) is usually diagnosed in childhood and adolescents. First attack after 40-years-old is seen very rarely in FMF [4]. In Turks, Jews, Armenians and Italians, asymptomatic carrier rate of a single MEFV mutation is about one in five [4]. Sjögren’s syndrome affects mainly white, postmenopausal women. Disease incidence is 0.4%, and the prevalence is about 0.6-3.3% in Europe [3]. In literature, to our knowledge, our case is the first one about coincidence of Sjögren’s syndrome and FMF in the geriatric age group [5]. The case of 42-year-old woman was similar to our case that anti-centromere antibody positivity was found. Also, homozygous M694V mutation and high levels of ESR and CRP have been identified in both cases [5]. In our case, diagnosis was supported with minor salivary gland biopsy. However, in our case sialo-graphy could not be performed because of technical difficulties although it takes place in the diagnostic criteria of Sjögren’s syndrome. Tamir and Langevitz reported that the incidence of late-onset cases (> 40-year-old) of FMF as 0.05%, however most of the cases are men and M694V mutation is homozygous negative [6]. Similar to our case report, amyloidosis was not detected in the previous reports. The main cause of the negative amyloidosis may be explained by negative M694V mutation and favorable clinical course of the cases. The major difference of our case from the other reports in literature is that amyloidosis was negative although the patient had homozygous M694V mutation.

As a result; mouth and eye dryness are frequent complaints in elderly. In the presence of these symptoms, diagnosis of Sjögren’s syndrome should be considered. In case of having periodic fever and abdominal pain episodes, although it is a rare condition in elderly, diagnosis of FMF should also be kept in mind.

Conflict of Interest

The authors state that they have no conflicts of interest.

References
