

Familial Mediterranean fever with massive recurrent ascites: A case report

Tekrarlayan masif asitle seyreden Ailesel Akdeniz Ateşi: Olgu sunumu

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A 35-year-old woman had a history of recurrent massive ascites for 12 years. She had been examined to identify the etiology of ascites and was placed on antituberculous and subsequently steroid treatment at another center before admission to our hospital for fever, abdominal distention and abdominal pain. She had massive ascites with serum-ascites albumin gradient of 1.0 g/dl. We could not find any cause for ascites including tuberculosis. We thus performed exploratory laparotomy of the abdomen. There was no evidence of tuberculosis, peritoneal diseases or of any gynecological reason for ascites. Biopsies taken from the peritoneum revealed fibrinous peritonitis. Since she had a history of attacks of abdominal pain in her childhood, she was screened for mutations causing familial Mediterranean fever and was found to be homozygous for M694V. After definitive diagnosis of familial Mediterranean fever, she was put on colchicine treatment and relief of symptoms and reduction in ascites were seen on follow-up. To our knowledge this is the first documented case of massive ascites due to familial Mediterranean fever.

35 yaşında bayan hasta, 12 yıldır tekrarlayan masifasiti vardı. Merkezimize başvurmadan önce asit etyolojisi açısından araştırılmış, antitüberküloz tedavi ve steroid tedavisi almıştı. Hastaneye ateş, karında şişlik ve ağrı ile başvurmuştu. Serum-asit albumin gradiyenti 1.0 gr/dl olan masifasiti mevcut idi. Tüberküloz dahil olmak üzere asit etyolojisi saptanamadı. Bu nedenle, eksploratif laparotomi yapıldı. Sonuçta asit yapacak tüberküloz, peritonyal hastalık ve jinekolojik nedenler görülemedi. Peritondan alınan biyopsilerde fibrinöz peritonit saptandı. Geçmiş hikayesi sorgulandığında, çocukluk çağında tekrarlayan karın ağrısı atakları olduğu öğrenildi. Bu nedenle FMF mutasyonu açısından tarandı, M694V yönünden homozigot olduğu tespit edildi. FMF'in kesin tanısından sonra kolşisin tedavisine alındı, izleminde asitin azaldığı, şikayetlerinin düzeldiği görüldü. FMF'e bağlı masifasitle seyreden ilk olgudur.

Key words: Familial Mediterranean fever, ascites

Anahtar kelimeler: Ailesel Akdeniz ateşi, asit

INTRODUCTION

Familial Mediterranean fever (FMF) is an autosomal recessive disorder characterized by sporadic, paroxysmal attacks of fever and serosal inflammation. The typical manifestations of the disease are recurrent attacks of severe pain due to serositis and fever, lasting one to three days, and then resolving spontaneously. Between attacks, patients feel entirely well. Ninety-five percent of patients with FMF have painful attacks localized to the abdomen, which is usually the dominant manifestation of the disease (1). Recurrent attacks of peritonitis may lead to adhesions. Inflammation of all serosal membranes can be seen during attacks, such as pleuritis, synovitis, and pericarditis. Genetic testing is highly specific and sensitive for diagnosis of FMF (2, 3).

Although fluid collection due to serositis can be seen during attacks of FMF, to our knowledge this is the first documented case of massive ascites accompanying FMF. In this report, we present an FMF case with recurrent massive ascites diagnosed by genetic analysis.

CASE REPORT

A 35-year-old female patient was admitted to the hospital because of fever, abdominal pain and abdominal distention.

The patient had a long history of ascites. Twelve years before admission, she applied to a hospital with complaints of diarrhea, nausea and vomiting. She did not have any abdominal pain at that time.

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Table 1. Blood chemical values and hematologic laboratory findings

Variable	Value On admission	2 nd day of admission
Glucose (mg/dl)	67	
Urea nitrogen (mg/dl)	16	
Creatinine (mg/dl)	0.8	
Aspartate aminotransferase (U/liter)	24	
Alanine aminotransferase (U/liter)	26	
Alkaline phosphatase (U/liter)	189	
Protein (g/dl)	7.8	
Albumin	4	
Globulin	3.8	
Lactate dehydrogenase (U/liter)	272	
Total Bilirubin (mg/dl)	0.6	
C- reactive protein (mg/dl)	72.4	101
Fibrinogen	normal	decreased
CA-125	normal	
CA-15.3	normal	
CA-19.9	normal	
Carcino Embryogenic Antigen	normal	
Alpha-feto protein	normal	
Antinuclear antibody	negative	
Proteinuria (mg/day)	75	
HbsAg	negative	
Anti HbsAb	negative	
Anti HCV	negative	
Anti HIV	negative	
Hematocrit (%)	36	
Mean corpuscular volume (μm^3)	77	
Erythrocyte sedimentation rate (mm/hr)	50	76
White-cell count (per/ mm^3)	10,000	12,500
Differential count (%)		
Neutrophils	65	78
Band forms	7	8
Lymphocytes	23	10
Monocytes	5	4
Platelet count (per/ mm^3)	363,000	370,000

Abdominal ascites had been determined. She was evaluated but nothing could be determined about the etiology of peritoneal fluid collection. She claimed that she was put on an empirical antituberculous treatment with isoniazid, rifampicin, ethambutol and streptomycin.

On the fifth month of antituberculous therapy, she was admitted to the hospital because of massive ascites causing difficulty in respiration. In order to determine the etiology of the massive ascites, laparoscopy was performed and liver and peritoneal biopsies were obtained. It was reported that nothing specific for peritoneal tuberculosis was seen at laparoscopy. Liver biopsy result revealed normal findings; however, on peritoneal biopsy, fibrinous peritonitis was reported. Histopathological findings of the collected biopsies were not consistent with peritoneal tuberculosis. According to reports of the medical center, large volume paracentesis was done and around 15 liters of fluid were removed at that time. The antituberculo-

us therapy was then discontinued and she was put on prednisolone (60 mg daily for 2 months and then with tapering doses for 3 years). At the end of the three years, since she had no ascites, prednisolone therapy was discontinued. She was then ascites-free and without any complaint for seven years.

She applied to our hospital because of abdominal pain with fever and abdominal distention. Her temperature was 38°C, pulse 85/min., and respiration 18/min. Blood pressure was 100/70 mm Hg. On examination, the patient appeared well. Her head and neck were normal. Her lungs were clear and heart was normal. No palpable lymphadenopathy was detected. On abdominal examination, a fluid wave was noted, without any tenderness or guarding. There was no organomegaly. She had an erythematous, nontender, palpable skin lesion on the medial part of right ankle without swelling of any joints. There was no peripheral edema or digital clubbing. Neurologic examination was normal. Laboratory tests were performed. The blood

chemical values including tumor markers were normal except for sedimentation rate and C-reactive protein (CRP).

An electrocardiogram showed a normal rhythm at a rate of 70/min. Radiographs of the chest revealed a normal heart and normal lungs. An ultrasonographic study of abdomen and pelvis showed massive ascites and bilaterally located ovarian cysts. There was a single gallstone of 10 mm in diameter within the gallbladder, without evidence of cholecystitis or dilatation of the common bile duct. The liver, spleen, kidneys and pancreas appeared normal. A Doppler ultrasound examination of the portal venous and hepatic venous systems was also normal without evidence of portal hypertension or Budd-Chiari syndrome. A computed tomographic (CT) scan of the abdomen and pelvis, obtained after the oral and intravenous administration of contrast material, showed bilaterally located ovarian cysts and massive septated ascitic fluid, but no thickening or opacification of mesentery, omentum or peritoneum. There were also no enlarged lymph nodes. A paracentesis was performed. Microscopic examination of peritoneal fluid showed mesothelial cells and neutrophils; no acid-fast bacilli, other microorganisms, or cancer cells were detected. A tuberculin skin test was positive (16 x 16 mm). A test for human immunodeficiency virus (HIV) antibodies was negative. Multiple cultures, including specimens of blood, urine and peritoneal fluid, were negative. Repeated ultrasonography of pelvis showed disappearance of most of the ovarian cysts after menstruation. Vaginal cytological examination revealed normal findings without cancer cells. There was no history of tuberculosis or exposure to the disease, hemoptysis, or use of alcohol or illicit drugs. During her follow-up, she had fever with peak values between 38.3° and 38.6° C, together with abdominal pain. There was an increase in the results of synchronously checked CRP, sedimentation rate and white blood cell counts, and a decrease in serum fibrinogen level. Her temperature returned to normal after three days together with resolution of abdominal pain.

We performed explorative laparotomy of the abdomen, and found no evidence of tuberculosis, peritoneal mesothelioma or ovarian malignancy. Biopsies were obtained from mesentery and peritoneum, and lymph nodes were collected. Histopathological findings of those biopsies revealed fibrous peritonitis. Tuberculous cultures of lymph nodes were negative. Amyloid protein deposition

was not detected on biopsy samples.

The patient's parents were cousins, and it was learned that her aunt's daughter was diagnosed as FMF. When asked cautiously, she described childhood attacks of abdominal pain, swelling of joints (especially ankles), and erythematous skin lesions which disappeared in a few days.

She was screened for mutations causing FMF and was found to be homozygous for the M694V mutation by denaturing gradient gel electrophoresis. After the diagnosis of FMF by genetic testing and for 13 months after colchicine therapy, the patient has been free of any symptoms and free of ascites.

DISCUSSION

Familial Mediterranean fever is an autosomal recessive inflammatory disease linked to the MEFV gene. Five missense mutations, V726A, M694V, M694I, M680I and E148Q, have been described (4). M694V mutation (51.5%) is the most common one among Turkish FMF patients (5). Peritoneal and pleural involvement, skin lesions, arthralgia and joint involvement are all well-known features of FMF (6). Although peritoneal fluid collection of a minimal amount can be seen during serositis attacks in FMF patients, massive recurrent ascites is an unusual presentation for this genetic disease. Our patient was diagnosed as FMF by genetic testing and had massive ascites with serum-ascites albumin gradient of 1.0 g/dl. To our knowledge this is the first documented case of massive ascites due to FMF. There are two cases of FMF patients with massive ascites in the literature; however, mesothelioma associated with FMF was the cause of ascites in those cases (7). There was no evidence of peritoneal mesothelioma or of any other cause by diagnostic workup in our case, so we performed an explorative laparotomy and obtained some peritoneal biopsies just to exclude the diagnosis of mesothelioma and any other causes.

Previous response probably related to steroid tre-

Table 2. Findings on paracentesis

Variable	Value
Glucose (mg/dl)	70
Albumin (g/dl)	3
Lactate dehydrogenase (U/liter)	87
Adenosine deaminase	normal
Acid fast Bacilli	negative
White-cell count (per / mm ³)	0.2
Differential (%)	
Neutrophils	90
Lymphocytes	10
Tuberculous culture	negative

atment may be explained by immunosuppression and subsequent resolution of inflammatory activity of peritoneum or by spontaneous recovery coincidentally encountered during treatment.

After definitive diagnosis, she was put on colchicine treatment and relief of symptoms and reduction in ascites were seen on follow-up. She has now been free of abdominal pain and without any asci-

tes for 13 months after colchicine therapy.

Familial Mediterranean fever should be kept in mind in the differential diagnosis of massive ascites and atypical abdominal pain pattern like in our patient. Molecular genetic tests should be considered, especially in such patients of Mediterranean origin and with a family history of FMF.

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