A Disease Must Be Considered in the Differential Diagnosis of Ascites: Familial Mediterranean Fever

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Dear Sir,

Familial Mediterranean fever (FMF) is an autosomal recessive disease which most commonly occurs in Sephardic Jews, Armenians, Arabs and Turks. FMF is characterized by recurrent and self-limited attacks of fever accompanied by peritonitis, pleuritis, sinovitis or erysipelas-like erythema [1, 2]. Inflammation of all serosal membranes can be seen during attacks, such as pleuritis, sinovitis and pericarditis. Small amounts of peritoneal fluid are often seen at laparoscopy of FMF patients. This finding reflects a peritoneal reaction

to repetitive inflammation, which is a process that in extreme cases may develop into ascites [3]. Ascites with large amounts of peritoneal fluid is an uncommon manifestation of FMF. In this report we present 5 FMF patients with recurrent ascites.

Case Reports

Five female patients were admitted to our clinic between 2002 and 2004 with ascites of unknown etiology. In all of the cas-

es ascites were detected on physical examination. We could not detect any clinical or laboratory signs of benign (heart, liver, kidney and gynecological diseases and tuberculosis) or malignant disorders. The laboratory test results are displayed in table 1. Serum-ascites albumin gradients were found >1.1 in 2 cases. Liver biopsy was performed in case 1 and reported as reactive changes. The cell counts in the ascites samples were $\leq 250/\text{mm}^3$. The results of ascites assessments are displayed in table 2. However, all of the patients have had

Table 1. Characteristics of patients

Characteristic	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	F	F	F	F	F
Age, years	34	25	26	17	56
Time of ascites	2 years	4 years	2 months	1 month	8 years
Time of FMF	new	6 years	15 years	7 years	new
Family history of FMF	yes	yes	yes	yes	no
Proteinuria	negative	negative	negative	negative	negative
Sedimentation (normal 0–20), mm/h	13	7	25	29	30
CRP (normal 0–3), mg/dl	8.68	3.2	16.3	4.49	3
Abdominopelvic CT	manifest ascites	pelvic ascites	hydrosalpinx, pelvic ascites	minimal pelvic ascites	pelvic ascites
Amyloidosis (rectum biopsy)	negative	negative	negative	negative	positive
Mutation analysis	M694V/V726A	M694V/V726A	M694V/M694V	M694/?	M694V/M694V
Colchium response	unknown	yes	yes	yes	yes

Table 2. Results of ascites fluid examination

Characteristic	Case 1	Case 2	Case 3	Case 4	Case 5
Color	yellow	yellow	clear	clear	clear
White blood cell count, cells/mm ³	100	120	250	200	40
Albumin (normal 3.5–6.2), g/dl	2.6	3.5	2.6	2.9	2.1
Serum-ascites albumin gradient (≤ 1.1)	0.6	0.5	1.3	1.5	1.6
Glucose (normal 74–106), mg/dl	103	79	75	80	71
LDH (normal 240–480), U/l	125	115	105	138	218
Culture	negative	negative	negative	negative	negative
Cytology	benign	benign	benign	benign	benign
Adenosine deaminase (<30), IU/ml	15.3	11.6	19.9	12.5	21.9
Acid-resistant bacile staining	negative	negative	negative	negative	negative

Table 3. Patients' clinical features based on Tel Hashomer criteria

	Case 1	Case 2	Case 3	Case 4	Case 5
<i>Major criteria</i>					
Recurrent febrile episodes accompanied by peritonitis, synovitis or pleuritis	+	+	+	+	+
Amyloidosis of the AA type without predisposing disease	–	–	–	–	+
Favorable response to continuous colchicine treatment	–	+	+	+	+
<i>Minor criteria</i>					
Recurrent febrile episodes	+	+	+	+	+
Erysipelas-like erythema	–	–	–	–	–
FMF in a first-degree relative	+	+	+	+	–

complaints of episodic abdominal pain with fever lasting 1–2 days since their childhood. Some of these patients had previously received colchicine treatment in other clinics for suspected FMF diagnosis. They had reported discontinued colchicine use on their own will, after taking the drug for different periods. The clinical features based on Tel Hashomer criteria are displayed in table 3. Genetic tests of these 5 cases revealed that 2 were homozygote for M694V/M694V, 2 were compound heterozygote for M694V/726 and 1 case was heterozygote for M694V/? gene mutations. Each patient received colchicine treatment at a dose of 0.5 mg per 8 h, and at the end of an average of 6 months of treatment, ascites were resolved in cases 2–5, as opposed to case 1, and this patient had therapeutic paracentesis twice, followed by laparoscopic examination. During laparoscopy, 5 liters of ascites was drained, and perito-

neal biopsy was taken, which helped rule out tuberculosis and malignancy, and the histological examination of the specimen was well adjusted with chronic peritonitis. During the follow-up period of case 1, colchicine was continued after laparoscopy, and no further ascites collection was observed.

Discussion

In FMF, peritoneal effusion during abdominal attacks is usually mild, is not detected by clinical evaluation and disappears during clinical remission. Chronic ascites has rarely been described in patients with FMF [1, 4, 5]. Small amounts of peritoneal fluid are often seen at laparoscopy or at radiological imaging techniques such as ultrasonography or CT of FMF patients [6]. Colchicine is the most effective

treatment to control FMF attacks. In the medical literature, 3 patients with ascites have been reported, who received colchicine, and in 2 of whom the ascites resolved on follow-up, while the third had an encapsulated peritonitis and unresolving ascites that remitted with short-term corticosteroids, but relapsed when the dose was reduced, and finally was treated surgically [5, 7]. In our study, each patient received colchicine treatment and at the end of an average of 6 months of treatment, the ascites were resolved in the cases.

In conclusion, ascites may develop in FMF patients due to chronic peritoneal irritation. Colchicine treatment may help resolve the ascites. In countries like Turkey, where FMF is more frequently encountered, this disease must be considered in the differential diagnosis of ascites.

References

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