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Familial Mediterranean fever: abdominal imaging findings in 139 patients and review of the literature

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Abstract
Background: The purpose of this study was to investigate the imaging findings in patients with familial Mediterranean fever (FMF) during and between acute attacks.
Methods: Computerized search of medical records from 1989 to 1998 identified 139 patients with a discharge diagnosis of FMF. Medical records, imaging studies, and pathologic findings were reviewed.
Results: Sixty-eight patients had a documented acute attack of FMF, and 71 patients known to have FMF were asymptomatic. Imaging was performed in 68 patients. Radiologic findings included ascites, splenomegaly, hepatomegaly, lymphadenopathy, focal peritonitis, peritoneal cysts, renal changes, and other incidental findings.
Conclusions: Radiologic findings in symptomatic and asymptomatic FMF patients are not uncommon. Imaging in selected cases may facilitate diagnosis and show complications.

Key words: Familial Mediterranean fever—Polyserositis—Periodic peritonitis—Imaging—Computed tomography—Ultrasound.

Familial Mediterranean fever (FMF), first described by Siegal in 1945 [1] as "benign paroxysmal polyserositis," is a disease characterized by recurrent, self-limited attacks of fever and inflammation of serosal, synovial, and pleural membranes. The disease is also known as "recurrent hereditary polyserositis," "periodic peritonitis," and "familial paroxysmal polyserositis." Despite the name implying a familial or hereditary mode of transmission, family history has been reported to be between 28% and 43% [2]. The mode of inheritance is thought to be autosomal recessive secondary to an aberration of the short arm of chromosome 16 [3]. Nevertheless, it is likely that the disease has a polygenic mode of inheritance in which multiple extraneous factors, other than a single gene, influence the penetrance of the disease [4].

FMF is common among patients of Mediterranean heritage and affects predominantly Sepharadic Jews, Arabs, Turks, and Armenians [5]. The most common clinical manifestations are peritonitis, articular disease, and pleurisy accompanied by fever. Signs and symptoms proceed gradually within several hours and, in the majority of cases, subside completely within 24–48 h [6]. Laboratory findings include leukocytosis and an increase in acute-phase proteins and C-reactive protein.

The clinical and laboratory findings often mimic acute abdominal catastrophe, referred to as "the false acute abdomen" by Althausen et al. [7]. Judicious use of imaging may prevent unnecessary surgical intervention.

The English-language literature contains only a few reports on the radiologic findings in FMF patients, and most of them are case reports. We present our experience with 139 patients with FMF who underwent one or more radiologic examinations during or between attacks. Our results represent the total spectrum of radiologic findings of the disease.

Patients and methods

The medical records of 139 patients with FMF seen between 1989 and 1998 at the Shaare Zedek Medical Center were reviewed. The diagnosis of FMF was based on familial history, previous attacks, typical clinical symptoms and signs, and compatible laboratory tests. Demographic parameters including patients' gender, age, and origin were obtained from the charts and from data regarding the clinical symptoms and sites of involvement. According to the identification numbers, the radiologic files were reviewed to investigate which imaging examinations (plain film, KUB; abdominal ultrasound; computed tomography, CT) had been

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Table 1. Summary of examinations performed

	Acute attack			Asymptomatic		
	M	F	Total	M	F	Total
KUB	14	20	34	7	7	14
US	13	21	34	10	11	21
CT	2	4	6	6	8	14
US+CT	2	3	5	4	5	9

performed on these patients. The images were interpreted by two senior radiologists.

Ultrasound was performed with an ATL using 3.5-, 5-, and 7.5-MHz transducers, and CT images were obtained with either conventional (Elscint 1800, Elscint, Haifa, Israel) or helical (Helict II, Elscint) machines.

Two patients with known pathologies (Crohn's disease and abdominal trauma, exhibiting imaging findings of ascites and splenomagaly, respectively) were included in the study.

Results

All of the patients were either Arabs or Sepharadic Jews from countries around the Mediterranean or Middle East, mainly Iraq and Kurdistan. There were 64 males and 75 females (age range = 1–89 years, mean age = 33.2 years). Sixty-eight patients had a documented attack of FMF in their medical records. Peritonitis was the feature seen most frequently (62 patients, 91.1%). Arthritis was second in frequency, seen in five patients (7.3%), and pleuritis was relatively rare, appearing in two patients (2.9%). One patient had arthritis and peritonitis concomitantly in the same attack.

Only 68 of the 139 patients had one or a combination of imaging examinations including plain films, abdominal ultrasound, abdominal CT, and upper gastrointestinal (GI) series. Forty-seven of these patients had been examined during an acute attack. Twenty-seven asymptomatic patients were examined for other indications. Six patients had been examined both in an asymptomatic period and during an acute attack. One hundred twenty-three imaging examinations were performed in 68 patients. The results are summarized in Table 1.

Female patients had more examinations than did male patients, probably due to the need to rule out other pelvic pathologies that are more frequent in women.

Thirty-four plain abdominal films had been performed in 26 symptomatic patients. Twenty films were normal, 11 showed dilatation of the small bowel loops, and three demonstrated splenomegaly. Only 14 plain abdominal films had been performed in 9 asymptomatic patients. Seven showed no pathology, and seven shows dilatation of the small bowel loops. Four symptomatic patients had a radiographs of a painful joint: three showed no pathology and one showed swelling of the joint.

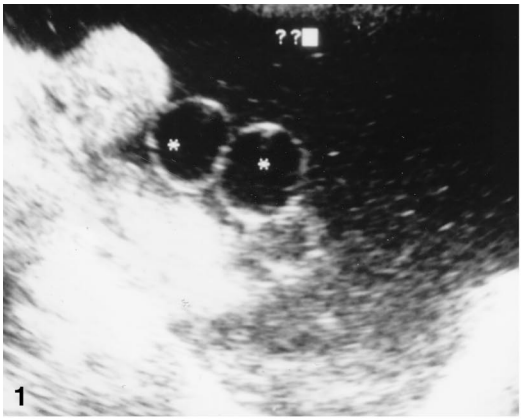
Table 2. US findings

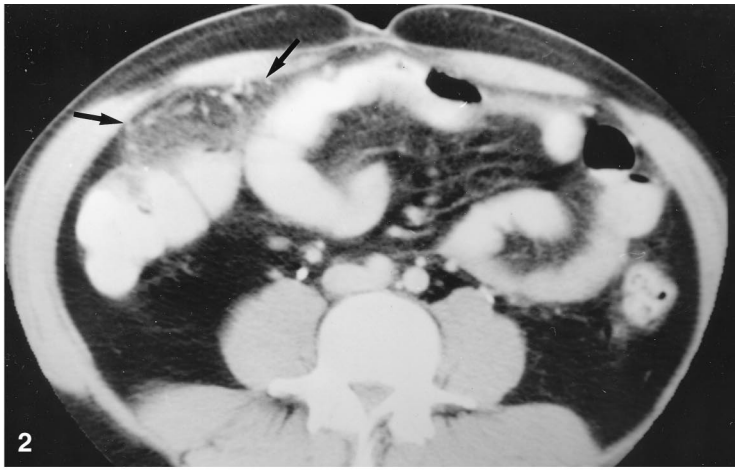
	Acute attack	Asymptomatic
n	29	15
Normal	12	10
Peritoneal fluid	6	3
Splenomegaly	8	2
Hepatomegaly	—	2
Enlarged kidneys	3	1
Hyperechoic kidneys	2	1
Lymphadenopathy	1	1
Peritoneal cysts	2	1
Dilated bowel loops	3	—
Pericardial fluid	—	1
Other	3	4

Thirty-four abdominal ultrasound examinations had been performed in 29 symptomatic patients, and 21 examinations were performed in 15 asymptomatic patients. The ultrasound results are presented in Table 2. Of the three patients with peritoneal cysts, two had single paraovarian cysts and one had multiple small cysts throughout the abdomen, a finding consistent with encapsulating peritonitis (Fig. 1). Other findings were cholelithiasis, cholecystitis, cavernous malformation of the portal vein, terminal ileitis, segmental infarct of the kidney, bleeding from a ruptured renal cyst, and an incidental ovarian dermoid cyst.

CT was performed in only five symptomatic and 10 asymptomatic patients. The CT results are presented in Table 3. Findings identified as "other" in Table 3 included cavernous malformation of the splenic vein, terminal ileitis, incidental ovarian cysts, ovarian dermoid cyst, segmental renal infarct, and bleeding from a ruptured renal cyst. CT proved to be superior to ultrasound in depicting peritonitis because of its ability to demonstrate changes in the peritoneal fat. In one patient in whom focal peritonitis was noted (Fig. 2), follow-up examination after 2 weeks showed complete disappearance of the peritonitis; the patient was without symptoms. Lymphadenopathy was demonstrated in two patients. In one case, the enlarged nodes were demonstrated at the liver hilum; in the second case, massive retroperitoneal and mesenteric lymphadenopathy was demonstrated (Fig. 3).

Other imaging examinations included an upper GI series in six symptomatic and two asymptomatic patients and was normal or showed irrelevant findings in five patients. In one patient, Crohn's disease was diagnosed. This patient also underwent a barium enema, which was compatible with Crohn's disease. One asymptomatic patient had hysterosalpingography for infertility, which showed evidence of peritoneal fluid.





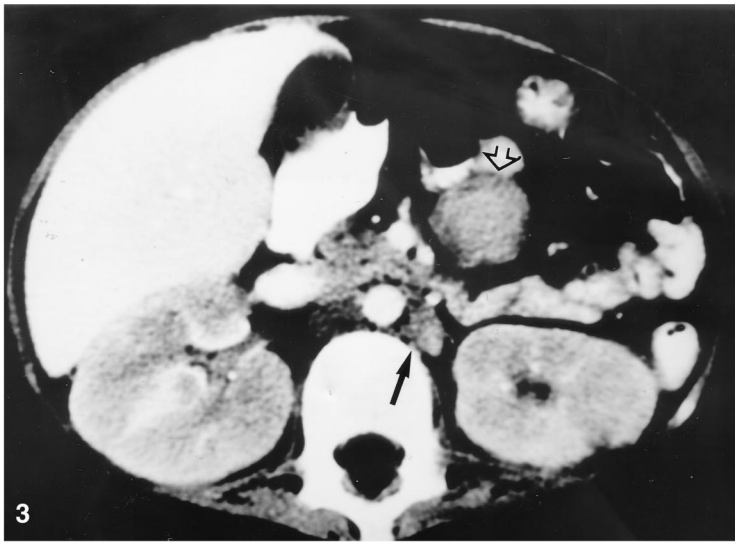


Fig. 1. Ultrasound demonstrates a large amount of unclear peritoneal fluid, with sediment consisting of particles, and two cysts, consistent with encapsulating peritonitis.

Fig. 2. CT at the level of the umbilicus shows infiltration of the greater omentum fat anterior to the ascending colon, with prominent vascular injection, consistent with focal peritonitis (*arrows*).

Fig. 3. CT at the level of the kidneys shows large, hypodense right kidney secondary to amyloidosis and enlarged lymph nodes in the retroperitoneum (*arrow*) and mesentery (*open arrow*).

Table 3. CT findings

	Acute attack	Asymptomatic
n	5	10
Splenomegaly	2	5
Hepatomegaly	—	1
Lymphadenopathy	—	1
Focal peritonitis	1	—
Peritoneal cysts	1	1
Peritoneal fluid	1	3
Normal	1	—
Other	2	6

Discussion

FMF is characterized by recurrent attacks of febrile serositis. The most common manifestation is peritonitis. According to the literature, 55% of patients suffer from peritoneal symptoms as the initial manifestation of the disease [5]. Laparoscopy or surgery during the peritoneal attack has demonstrated sterile peritoneal exudate containing fibrin and polymorphonuclear cells [5]. Recurrent acute abdominal episodes may result in formation of peritoneal adhesions that may cause small bowel obstruction [8] or encapsulating peritonitis with a pseudocystic appearance [9]. In our series, 91.1% of patients had at least one episode of peritonitis. One patient had radiologic signs for encapsulating peritonitis. Arthralgia has been reported in 75% of cases [5], especially in children [10], but was seen in only 7.3% of our patients. Pleuritis has been reported to occur in 40% of cases [11] but was evident in only 2.9% of our patients. Involvement of the reticuloendothelial system in FMF is seldom mentioned in the literature [12–15], whereas splenomegaly has been reported in as many as 57% [12]. Hepatomegaly also has been reported to occur in FMF patients [4]. Occurrence rates of both peripheral and abdominal lymphadenopathy have been reported to be 1% [14] and 6% [2]. Biopsy has shown nonspecific lymphoid hyperplasia [2, 13, 14]. Mesenteric lymphadenopathy has been encountered in

9–14% [15] of patients undergoing laparotomy during an acute abdominal FMF attack, but retroperitoneal lymphadenopathy has been anecdotally reported in the literature [13].

Pericarditis is a rare manifestation of FMF, occurring in 1.7% of the patients reported by Kees et al. [16]. Acute scrotal pain has been recognized as one form of FMF attack because the tunica vaginalis, an extension of the peritoneal sac, is likely to be affected [17]. Vasculitis in the form of Henoch-Schönlein pupura and polyateritis nodosa occurs at a greater frequency in FMF patients than in the general population, but it is not a widely recognized feature of the disease [18]. The most important complication of FMF is renal failure due to amyloidosis. Colchicine has proved to be beneficial in decreasing the incidence of renal amyloidosis and the frequency and severity of FMF attacks.

In conclusion, our large series of FMF patients demonstrates the wide spectrum of radiologic findings. Although the diagnosis of FMF is based mainly on clinical and laboratory examinations, imaging is useful for diagnosis and for demonstrating possible complications of the disease. Acquaintance with the radiologic findings is crucial and may prevent unnecessary surgical intervention.

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