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□ ORIGINAL ARTICLE □

Frequency of Abdominal Surgery in Patients with Familial Mediterranean Fever

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Abstract

Objective Familial Mediterranean fever (FMF) is characterized by recurrent episodes of peritonitis. Abdominal FMF attacks can be indistinguishable from those of an acute abdominal emergency, and patients may undergo one or more laparotomies before the true nature of their disease is documented. The objectives of this study were to investigate the frequency and reasons for abdominal surgeries performed on patients with FMF.

Methods We retrospectively reviewed the files of 254 patients with FMF (127 males, 127 females, mean age 27.2±6.3 years). We also included 182 healthy individuals for this study (89 males, 93 females, mean age 27.6±5 years; range 11-43) to make a comparison between FMF and healthy controls (HC) with respect to frequency of abdominal operations.

Results The number of patients with abdominal surgery in FMF group was 74 (29.1%). The number of surgeries performed in 74 patients with FMF was 92. The first abdominal surgery before the diagnosis of FMF was appendectomy in 68 patients (26.6%). In HC group, the number of abdominal operations was found to be 16 (8.7%). Of these abdominal operations, 9 (4.9%) were due to appendectomy. The rate of total abdominal operations and appendectomy were significantly higher in FMF group than in HC group (p= 0.0001).

Conclusion Abdominal attacks of FMF patients may cause an unnecessary laparotomy prior to the diagnosis of FMF. FMF patients can present with abdominal emergency while they are receiving colchicine. Therefore, each abdominal pain should be carefully determined according to clinical findings. The purpose of this study was to emphasize the misdiagnosis of appendicitis.

Key words: familial Mediterranean fever, abdominal surgery

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Introduction

Familial Mediterranean fever (FMF) is a disease seen mostly in people of Middle East and Mediterranean descent, with autosomal recessive inheritance and is characterized by recurrent and self-limiting fever and abdominal pain, pleuritis, and arthritis attacks. Recurrent peritonitis is one of the chief manifestations of FMF and it can range from mild to severe and may present as diffuse or localized (1). The presence of recurrent peritonitis may lead to peritoneal adhesions and intestinal obstructions. In clinical practice, appendicitis, ileus/subileus, cholecystitis, and renal colic may be perceived as causes of abdominal pain before a reliable diagnosis of FMF has been achieved, which may lead to misdiagnosis and inappropriate treatments. In this report, we evaluated the frequency and reasons for abdominal surgeries performed on patients with FMF.

Methods and Patients

We retrospectively reviewed the files of 254 patients with FMF (127 males, 127 females, mean age 27.2±6.3 years) who fulfilled the Livneh diagnostic criteria for FMF (2). Disease duration was 16.8±7.4 (range 5-23 years). As we compiled information about abdominal operations to deter-

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Table 1.

	FMF Patients n=254	Healthy control n=182
F/M	127/127	93/89
Mean age	27.2±6,3	27.6±5
Disease duration (years)	16.8±7.4	-
The number of patients with abdominal operations	74	16
The number of abdominal operations	92	16
Abdominal operations (prior to diagnosis of FMF in FMF patients)		
-Appendectomy	68	9
-Ileus and/or subileus	9	-
-Ovarian surgery	3	3
-Cholecystectomy	2	-
- Umblical hernia	1	-
-Hiatus hernia	-	1
-Stomach perforation	-	1
-Ectopic pregnancy	-	1
-Myomectomy	-	1
Total	**83**	**16**
Abdominal operations after the diagnosis of FMF		
-Ileus and/or subileus	4	-
-Explorative laparotomy	2	-
-Umblical hernia	1	-
-Cholecystectomy	1	-
-Ovarian surgery	1	-
Total	**9**	-

mine the details, we took advantage of use of their hospital records, apart from interviewing the patients or simply interviewing via telephone. Because most of the abdominal operations had been performed in other hospitals, we could not access the hospital records, which could have helped us determine the definite reasons for laparotomy. Therefore, we had to rely on the statements of patients and on the information in their files. To make a comparison between FMF and healthy controls with respect to frequency of abdominal operations, we also included 182 healthy individuals for this study (89 males, 93 females, mean age 27.6±5 years; range 11-43). The comparison between FMF patients and healthy control in terms of frequency of abdominal operations was performed by chi-square test.

Results

No significant differences were found between FMF group and healthy control group in terms of age and sex distribution. The number of patients with abdominal surgery in FMF group was 74 (29.1%). The number of surgeries performed in 74 patients with FMF was 92. The first abdominal surgery before the diagnosis of FMF was appendectomy in 68 patients (26.6%), ileus/subileus in 9 patients (3.5%), ovarian surgery in 3 patients (1.1%), cholecystectomy in 2 patients (0.7%), and umbilical hernia in 1 (0.4%) patient. In HC group, the number of abdominal operations was found to be 16 (8.7%). Of these abdominal operations, 9 (4.9%) were due to appendectomy. Other operations consisted of ovarian operation in three patients, ectopic pregnancy in one, hiatus hernia in one, stomach perforation in one, and myomectomy in one patient. The rate of appendectomy was significantly higher in FMF group than in HC group (p=0.0001).

Recurrent operations were performed in eleven patients (4.3%). Appendectomy was also performed in these eleven patients earlier. One of the patients had four abdominal surgeries. Six of the patients had one abdominal surgery and four of them had two operations after appendectomy. Of these 18 abdominal operations, 13 were ileus/subileus, 2 cholecystectomy, 2 explorative laparotomy and 1 ovarian surgery. The other reasons for laparotomy in the patient with four abdominal surgeries were ileus or subileus that emerged within 12 years after appendectomy.

Of the 92 abdominal surgeries, 83 had already been performed prior to the diagnosis of FMF, while 9 were per-

formed 5.7±4.3 years (range 1.5-7.1 years) after the diagnosis of FMF. Of these 9 laparotomies, four were due to ileus/subileus, 2 explorative laparotomy for primary infertility evaluation, 1 umbilical hernia, 1 cholecystectomy, and 1 ovarian operation.

Discussion

It is well known that FMF patients may be subject to misdiagnosis before a precise FMF diagnosis and this may lead to unnecessary abdominal surgeries. Delay in the diagnosis of FMF in Turkey was approximately 6.9 years (3). In this period, some patients may be subject to unnecessary abdominal operations. The most common abdominal operation performed in FMF patients is appendectomy (3). The frequency of appendectomy in a nationwide multicenter study evaluating 2838 Turkish FMF patients was 19% (3). Since there has been no study investigating the frequency of appendectomy in the general population in Turkey, we compared the frequency of appendectomy in FMF patients with matched healthy individuals. As was expected, the frequency of abdominal operations in FMF patients was significantly higher than those of healthy individuals. In a nationwide multicenter study including 7520 patients with irritable bowel syndrome, appendectomy prevalence was found to be 4.8% (4). In a study conducted in Israel, the rate of appendectomy was found to be 9% in patients with FMF (5). The real acute appendicitis is 5% when the appendectomy material is re-examined. In another study, the frequency of appendectomy in FMF patients was reported to be 16% by Berkun et al (6).

Berkun et al also reported that even after colchicine use, FMF patients are still not far from a higher risk than are healthy individuals for developing intestinal obstruction either spontaneously or as a post-surgical complication (7). Furthermore, abdominal emergency can develop in FMF patients without prior abdominal operations. Çiftçi et al showed that intestinal obstructions can occur in 3% of patients with FMF who had not undergone a prior laparotomy (7). It has been speculated that the presence of neutrophils in the inflamed peritoneum may give rise to peritoneal adhesions (8). It is very crucial to differentiate FMF attack from adhesive intestinal obstruction because all clinical and laboratory features of FMF peritonitis such as abdominal distension, rebound tenderness, rigidity, fever, leukocytosis are also found in the course of intestinal obstruction (9). However, abdominal findings of the FMF attacks subside within 24 hours of course while the clinical picture progressively worsens in adhesive intestinal obstruction and acute appendicitis (9). Kisacik et al suggested that increased procalcitonin levels could be a useful test in the differentiation of acute appendicitis from abdominal FMF attacks (10).

Although we did not come across any patient that needed abdominal surgery but had not been operated in our group, a serious abdominal emergency that may develop in an FMF patient could be potentially considered as an FMF attack. This may delay diagnosis and lead to unwanted results. In our study, we determined 9 abdominal surgeries after the diagnosis of FMF patients who were on colchicines. These patients were not admitted to hospital in elective conditions in 4 of the 9 abdominal surgeries. Accordingly, FMF patients may be admitted to the hospital with a dangerous abdominal emergency without abdominal FMF attack.

Elective laparoscopic appendectomy has been suggested to prevent unnecessary surgery in FMF patients (11) but this has not been recommended by others, because any surgical procedure may stimulate an attack and contribute to the formation of adhesions. In addition to the financial and social loads of unnecessary operations, intra-abdominal adhesions after surgeries can lead to other laparotomies due to ileus and subileus. Therefore, increasing knowledge of pediatricians, surgeons, internists and emergency doctors on this issue may preclude unnecessary operations, as well as aide in early diagnosis of FMF. A good history taking is an absolute essential diagnostic tool in achieving a precise diagnosis of FMF and other abdominal occurrences.

The limitations of our study include a retrospective design and a relatively small sample. Another limitation is having a retrospective analysis of the patients. Because most of the abdominal operations were performed in other hospitals, we could not access hospital records, which could have helped us to determine the precise reasons for laparotomy. This factor can decrease the validity of our results. However, we had to rely on the statements of the patients.

In summary, abdominal attacks of FMF patients may cause an unnecessary laparotomy prior to diagnosis of FMF. Furthermore, once a patient is diagnosed as having FMF, there may be a tendency among physicians to relate each abdominal pain to an FMF attack, whether related to FMF or not. Therefore, we suggest that every single abdominal pain should be considered independent of each other even if a patient has been diagnosed as having FMF, in which case other possible causes of abdominal pain can be taken into consideration. The purpose of this study is to emphasize the misdiagnosis of appendicitis.

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