



Case Report

# Familial Mediterranean fever with recurrent erysipelas-like erythema and myalgia: A case report

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## ABSTRACT

Familial Mediterranean fever (FMF) is a disease progressing with recurrent serositis episodes and usually accompanied by fever. Symptoms, such as myalgia and skin lesion, are less common in the clinical presentation of FMF. Herein, we present a 23-year-old female patient who was admitted to our outpatient clinic with myalgia. She had no findings of typical episodes for FMF. However, on physical examination, she had an unrecognized skin lesion. In conclusion, FMF should be kept in mind in patients with recurrent erysipelas-like lesions.

**Keywords:** Colchicine; erythema; muscle pain; periodic disease; skin.

Familial Mediterranean fever (FMF) is an autosomal recessive inherited disorder, which particularly affects Jewish, Armenian, Turkish, and Arabic populations.<sup>[1]</sup> The disease progresses with recurrent episodes. A typical episode reveals itself with fever and serositis. The skin and muscle involvement are not common in a typical episode. To the best of our knowledge, there is no specific laboratory test to diagnose FMF. Diagnosis is often based on clinic symptoms, ethnic origin, family history, and colchicine response.<sup>[1]</sup> Herein, we report a female case who was admitted with recurrent muscle pain and skin rash and diagnosed with FMF based on the presence of an unrecognized skin lesion on physical examination.

## CASE REPORT

A 23-year-old female patient was presented to our outpatient clinic of physical medicine and rehabilitation with a complaint of severe muscle pain. Her medical history revealed that her complaint was lasting for two days with repetition two or three times every year for the last couple of years and tended to heal spontaneously several days later. She previously applied to orthopedics and physical therapy outpatient

clinic with these complaints and received non-steroidal anti-inflammatory drugs (NSAIDs). However, she was unresponsive to this treatment. Her medical and family history was non-specific.

On physical examination, there was an erythematous lesion localized on the upper part of the right ankle (Figure 1). The lesion was an erythematous plaque with a non-well-defined border of 5x6 cm in diameter, which was hot, tense, and indurated. No pathology was detected on musculoskeletal system and neurological examination. She had similar lesions on both feet, when she had muscle pain. However, such lesions disappeared spontaneously within six to seven days. The results of the laboratory examination were as follows: hemoglobin: 11.5 g/dL (reference range [RR]: 12-18), platelet: 227.000 mm<sup>3</sup>, white blood cell: 8300/mm<sup>3</sup> (RR: 4800-10800), C-reactive protein: 105 mg/L (RR: 0-8), and sedimentation: 66 mm/h. Liver and kidney function test results were also normal. Due to the recurrent structure of the existing complaints and findings, it was suspected that this situation might be a rheumatic pathology. Amoxicillin clavulanate 2 g/day and ciprofloxacin 1 g/day were initiated with the diagnosis

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**Figure 1.** An erythematous lesion localized on the upper part of the right ankle.

of erysipelas, a bacterial skin infection, by the physical medicine and rehabilitation outpatient clinic.

At her first follow-up visit after six days, the lesion on the right foot disappeared. However, she reported that muscle pain only partially relieved. Her laboratory tests including rheumatoid factor, antinuclear antibody and human leukocyte antigen B27 were all negative. Genetic analysis for the familial Mediterranean fever gene (MEFV) revealed a homozygote mutation for M694V. The skin lesion was considered an erysipelas-like erythema (ELE) of FMF, and colchicine was prescribed as 1.5 mg/day. At 18 months, she is still free of similar signs and symptoms of FMF.

## DISCUSSION

Familial Mediterranean fever is an autosomal recessive disease characterized by recurrent episodes of fever, peritonitis, pleuritis, and arthritis.<sup>[2]</sup> Previous studies have reported that 90% of patients have abdominal, 75% have articular, and 45% have pleural episodes. Symptoms, such as myalgia and ELE, are less frequent findings of the disease.<sup>[3]</sup> In this article, we present an atypical FMF case with myalgia and skin lesion symptoms alone, but not with typical episodes of the disease.

Many skin lesions, such as purpuric rash, ELE, Henoch-Schönlein purpura, and angioneurotic edema can be seen in FMF cases. Among them, ELE is an unusual, but well-known pathognomonic skin manifestation of FMF.<sup>[4,5]</sup> It is characterized by well-demarcated, tender, erythematous, and infiltrated plaques usually located on the joints, lower extremities, and dorsal aspect of the feet. They may be induced

by physical effort and resolve spontaneously within 48 to 72 h of bed rest.<sup>[5,6]</sup>

The lesions resemble erysipelas or cellulitis and the differential diagnosis can be difficult. Considering that the fact that ELE lasts shorter (4 days on average) and is not always accompanied by fever, may occur on both feet, recovers spontaneously, and is more predominant in younger individuals, it would be easier to differentiate ELE from other infectious diseases. In such cases, it must be kept in mind that the lesion may be an inflammatory skin rash, such as ELE. In general, ELE is associated with M694V homozygous, severe FMF clinic phenotype, and amyloidosis.<sup>[7]</sup> However, several studies showed that in FMF patients whose the initial disease presentation was ELE and who did not have other systemic findings, a milder disease picture could be seen and, therefore, the diagnosis could be delayed.<sup>[7]</sup> Similarly, our patient was not aware of her rashes and existing lesion which were detected on physical examination. The patient's lesion was unilateral, tender, hot, and located in the right ankle. Contrary to the frequent ELE lesions, the patient was afebrile and the lesion was not well-demarcated, resulting in longer duration of disappearance. Therefore, the lesion could not be differentiated from infectious-induced erysipelas. In consistent with the literature,<sup>[7]</sup> there was a mild disease phenotype progressing with only myalgia in our case and was able to be diagnosed through genetic testing (M964V homozygote).

Another symptom observed in our case besides rash was myalgia. Myalgia is observed approximately 25% of FMF patients, and three types of myalgia are defined in FMF: exercise-induced myalgia, febrile myalgia syndrome, and spontaneous myalgia.<sup>[8]</sup> Spontaneous myalgia pattern (8% of all myalgia cases) is characterized by mild-to-moderate myalgia without any relevance with exercise or another factor and often not accompanied by fever, and also pain is at mild-to-moderate severity lasting several hours.<sup>[8]</sup> In our case, there was moderate myalgia independent from exercise or another factor and not accompanied by fever. The patient exhibited spontaneous pattern myalgia findings, and the symptoms did not respond to resting or taking NSAIDs, and lasted longer (six to seven days on average), contrary to what is reported in the literature.<sup>[8]</sup> Based on the MEFV mutation analysis showing a homozygous M694V mutation, colchicine treatment was initiated to relieve FMF-induced symptoms, and the patient responded to the treatment well. The diagnostic Tel-Hashomer clinical criteria for FMF were also fulfilled as a probable diagnosis: the positive response to colchicine is a major criterion,

and ELE is a minor criterion for the definite diagnosis according to the Tel-Hashomer criteria.<sup>[9]</sup>

In conclusion, our case report is important as it highlights two important points. First, symptoms observed less frequently in FMF may be the initial and sole manifestation of FMF. Therefore, our case should serve to increase the awareness of practitioners to ELE, which may present as the initial and sole manifestation of FMF. Second, the skin lesions which are unrecognized by the patient, but detected by the treating physician on physical examination may help us with the diagnosis of FMF. Therefore, the value of the inspection during the physical examination should not be ignored, and ELE should be considered in the differential diagnosis in these patient population.

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