SKIN

BRIEF ARTICLE

Cyclic Flares of Fever, Rash, and Swelling: A Case Report of FMF in Adulthood

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ABSTRACT

Familial Mediterranean Fever (FMF) is an inherited condition characterized by recurrent bouts of fever and serosal inflammation that most commonly presents in individuals before 10 years of age. Although onset of the disease can occur at an older age, such a presentation is rare, especially after 40 years. This case report aims to highlight the rare manifestation of this disorder in a 63-year-old patient with recurrent bouts of fever and rash. With limited findings and a cure for this disorder, this case delves into the presentation and treatment regimen that provided symptomatic relief to this patient.

INTRODUCTION

Familial Mediterranean Fever (FMF) is an inherited condition characterized by recurrent bouts of fever and serosal inflammation that most commonly presents in individuals before 10 years of age. Although onset of the disease could occur at an older age, such a presentation is rare, especially after 40 years of age. Febrile and inflammatory episodes typically last from 24 to 72 hours but can vary amongst different individuals. With no direct cure for this disorder, different treatment plans for those affected continue to be a point of interest and area of exploration.

CASE REPORT

A 63-year-old white woman with a history of cervical cancer in remission presented to dermatology clinic with a ten-year history of annual flares of fever and erythematous rash on the circumferential upper limb (**Figure 1**) which gradually increased in severity and frequency over the past year. Over the past year, frequency of febrile episodes increased from approximately 3 times a year to monthly, with extension of rash from lateral thighs to posterior buttocks (**Figures 2, 3**).

The patient endorsed tenderness to palpation and progressive pruritus in areas of rash involvement. Right lower extremity (RLE) swelling had accompanied the most recent flare that was initially painless but became painful and red with chronicity. She denied oral ulcers, genital ulcers, abdominal pain, chest pain, joint pain, or sore throat.

Labs demonstrated CRP 157 mg/L (0-10 mg/L), ESR 108 mm/hr (0-30 mmh/hr), C3 209 mg/dL (82-167 mg/dL), C4 52 mg/dL (12-38 mg/dL), and RF 14.2 IU/mL (<14

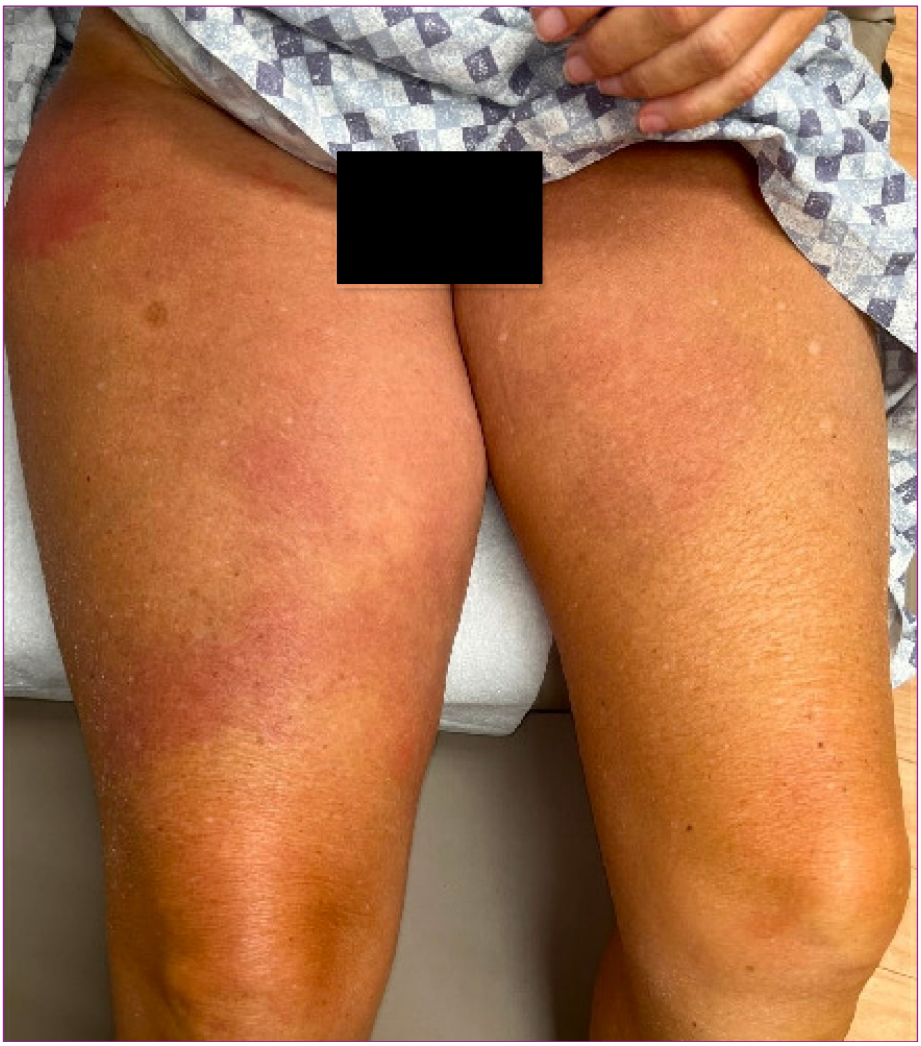

Figure 1. Ill-defined erythematous rash on bilateral thighs.

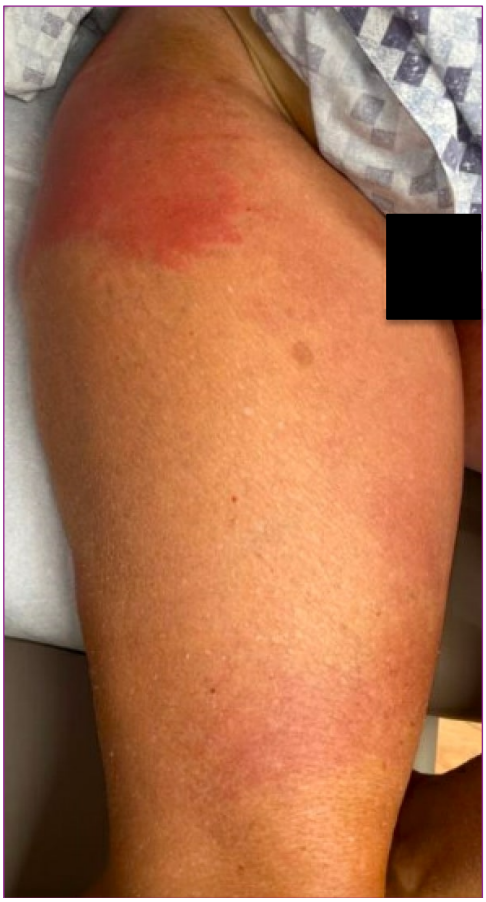

Figure 2. Ill-defined rash form lateral thighs to buttocks.

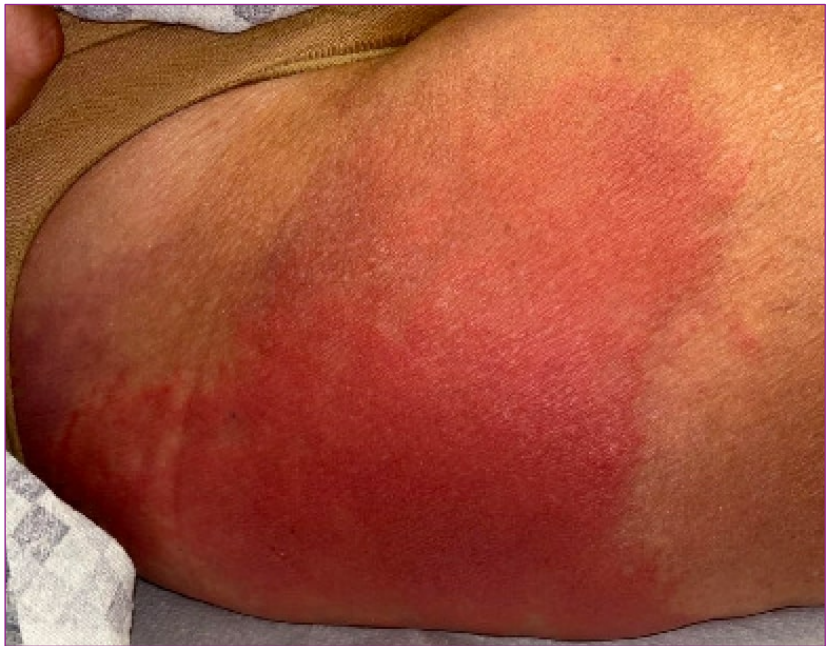

Figure 3. Ill-defined rash form lateral thighs to buttocks.

IU/mL). Antinuclear antibody testing via indirect immunofluorescence, CCP, p-ANCA, c-ANCA, and MPO antibodies negative. Periodic fever syndrome panel with single MEFV variant (2177T>C (Val726Ala)).

Pathology demonstrated a perivascular dermatitis with a neutrophil-predominant inflammatory infiltrate around the superficial vascular plexus with vessels predominantly intact. PAS was negative for fungi or a thickened basement membrane. Alcian blue was negative for increased dermal mucin. Immunofluorescence was negative for IgG, IgM, IgA, C3 and fibrinogen.

Upon presentation to rheumatology clinic, physical examination revealed multiple violaceous patches with ill-defined borders over the right outer thigh, right buttock, and RLE. The patient's right ankle was cool to touch with significant soft tissue swelling and absence of discoloration. Diagnosis of FMF was made based on the Tel-Hashomer clinical criteria, which includes two or more major symptoms or one major symptom with two minor symptoms. Major symptoms include (1) febrile, paroxysmal attacks of pleuritis, peritonitis, synovitis, and/or dermatitis, (2) amyloidosis of AA type without a predisposing condition, and (3) an adequate response to colchicine treatment.[3] Minor criteria consist of (1) recurrent febrile attacks, (2) erysipelas-like erythema, and (3) FMF in a first-degree relative.[3] This patient exhibited major criteria 1 and 3, and minor criteria 1 and 2.

She was started on colchicine 1.2 mg and prednisone 60 mg daily which had mitigated rash extension and RLE swelling although pain in her extremity persisted.

DISCUSSION

Familial Mediterranean fever (FMF) is a hereditary autoinflammatory condition characterized by episodes of fever and inflammation, typically affecting the abdomen, chest, or joints.[1] Many patients also present with an erythematous rash on the lower extremities, specifically the ankles or feet that can be accompanied with swelling.[1] Flares are often preceded by a mild cutaneous prodrome in the area where rash appears.[1] Episodes typically last 24 to 72 hours and range in frequency as well as severity.[3]

FMF is caused by mutations in the Mediterranean fever (*MEFV*) gene which encodes *pyrin*, a protein produced by erythrocytes to modulate inflammation.[2] Although carrier children are often asymptomatic, literature has shown that a single MEFV mutation may confer heightened inflammation in typical sites, namely the joints and the peritoneum. Carriers also have an increased risk of more than four febrile episodes per year, arthralgia, and rheumatoid arthritis.[2]

Historically, the diagnosis of FMF is based on Tel-Hashomer clinical criteria. Aside from these criteria, molecular diagnostic testing can also detect select variations in the *MEFV* gene, the one gene known to be associated with FMF.[4]

While FMF is typically detected in childhood, there are cases, such as in this patient, where the inflammatory disorder persists in adulthood.[5] There may be several reasons as to why this could occur. One of the primary reasons include improved diagnosis and treatment in childhood: since many individuals' FMF symptoms present early, they are typically treated early as well.[6] However, if physicians do not have access to family history, they may not consider FMF as a diagnosis in adults, especially if symptoms

present vaguely.[6] While early diagnosis and treatment can help to manage symptoms and prevent complications, a lack of awareness of the diagnosis or family history can contribute to under- or misdiagnosis.

Treatment largely targets symptomatic management along with colchicine, prednisone, and canakinumab for prevention of attack recurrence.[7] In our patient's case, ankle swelling, and rash resolved with prednisone, but joint pain was persistent. The patient exhibited minimal responsiveness to a daily 1.2 mg of colchicine and dose increases to 1.8 mg were limited by gastrointestinal side effects. Therefore, she was started on 45 mg prednisone daily and 150 mg SC monthly canakinumab injections, an effective alternative or adjunctive therapy.[8] Around a week after starting treatment, the patient began to see noticeable improvement in her inflammation. Although RLE swelling slightly increased when upright, symptoms improved rapidly upon elevation.

CONCLUSION

Rare occurrence of FMF in late adulthood can potentially go unrecognized in patients due to the lack of systematic laboratory tests and definite treatment to diagnose and cure the cutaneous disease. This case aims to highlight the process through which a diagnosis of FMF was made in order to explore how to provide symptomatic and long-term relief for such patients.

Conflict of Interest Disclosures: None

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