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Case Report

Familial Mediterranean fever and scleroderma: a rare case report from Syria

Lujain Nahas[1,*], Rawan Al Khudari[2] and Basheer Khalil[3]

[1]Faculty of Medicine, Damascus University, Damascus, Syria
[2]Department of Pediatrics, Children's University Hospital, Faculty of Medicine, Damascus University, Damascus, Syria
[3]Division of Rheumatology, Department of Pediatrics, Children's University Hospital, Faculty of Medicine, Damascus University, Damascus, Syria
*Correspondence address. Faculty of Medicine, Damascus University, Fares Al Khouri St., Damascus, Syria. Tel: +00963 938453789;
E-mail: lujainnahas28@gmail.com

Abstract

Familial Mediterranean fever (FMF) is an inherited autoinflammatory disease that affects the skin, joints, serous membranes and other various organs. Presentation of FMF can be solely but it can coexist with other conditions. It has been shown that it can be accompanied by various different disorders. Scleroderma is an autoimmune dermatologic condition that can present with systemic manifestations. No previous cases about the coexistence of FMF and scleroderma were previously documented, therefore we report the first case in Syria of a 10-year-old female that presented with clinically clear signs of both conditions (periodic fever and serous chest pain in addition to skin hyperpigmentation). The patient's symptoms required full genetic testing along with the proper antibody detection and The diagnosis of FMF and scleroderma was confirmed by genetic testing and treatment was started.

INTRODUCTION

Familial Mediterranean Fever (FMF) is a genetic autoinflammatory disorder that usually presents as recurrent attacks that last 1–3 days and include fever, abdominal pain, swollen joints and a red rash [1]. This illness mostly affects habitants of the Mediterranean areas like Turkey, Greece and -in our case- Syria. Often discovered in childhood, FMF is mostly diagnosed on a clinical basis based on the nature of the recurrent attacks and the accompanying symptoms [1]. The gene responsible for FMF is located on chromosome 16p and is designated MEFV. Scleroderma, a rare disease that generally presents as one of two forms: systematic sclerosis (triad of autoimmunity, noninflammatory vasculopathy and collagen deposition with fibrosis) or localized scleroderma. Both tend to be chronic and have variable presentations [2]. Upon research, FMF has been stated to be accompanied by and coexist with rheumatic diseases, inflammatory bowel diseases, systemic vasculitis and other autoimmune illnesses [3]. No cases associated with scleroderma were found therefore we present this case.

CASE REPORT

On June 13th of 2022, a 10-year-old female was admitted to the children's hospital of Damascus complaining of pain in her left chest for the last 4 years, the pain was recurrent every one and a half to two months and was partially alleviated by regular painkillers and was always accompanied by a fever partially responsive to simple medication. FMF was suspected clinically six months prior by another doctor and she was started on colchicine but was stopped by the parents. Hyperpigmentated skin lesions started to evolve around that time initially on the posterior right thigh and gradually grew in size and the mother noted retraced skin over the affected area (see Fig. 1), similar lesions soon appeared on her other limbs (see Figs 2 and 3). The child has no past medical or surgical history and there is a case of vitiligo and G6PD deficiency in the girl's cousins and a demise due to presumable pemphigus vulgaris. Physical examination of the respiratory, cardiovascular, intestinal and the central nervous system showed no anomalies. No musculoskeletal deformities were present and examination of the joints showed no swelling or pain or limitation in movement except limited flexion in the right leg along with greater skin retraction in the right leg (see Fig. 4) and a stiffness in palpitation. Scleroderma was also suspected. Negative Anti-Scl70 and Anti Centromere Antibody and the absence of systemic presentations suggested a localized morphea affecting the stated limbs. ESR (Erythrocyte sedimentation Rate) was tested multiple times all in which it showed elevation, other lab findings were within the normal range (including liver and renal function tests). Testing was positive (homogenous) for ANA-HEP-2(Anti-Nuclear Antibody) at 1/60 dilution. The symptoms which the patient presented with suggested a co-existing case of FMF. The main 26 FMF genes (MEFV) were investigated and she tested positive for V726A and M680I mutations and heterozygosity confirming the diagnosis. The patient was put on prednisolone (5 mg), omeprazole, methotrexate and Folic acid.

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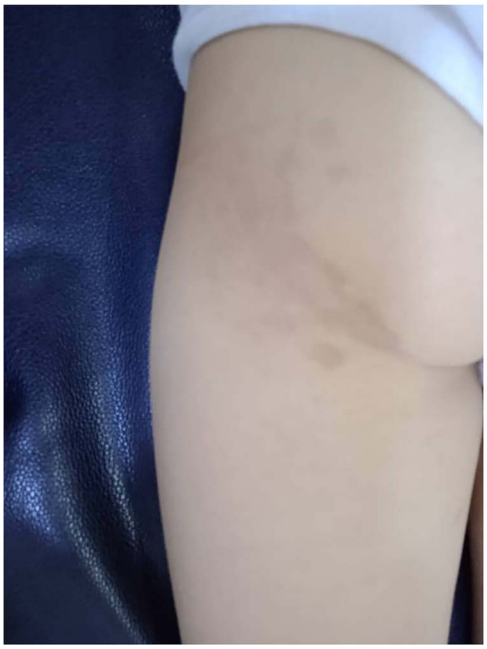

Figure 1. The initial hyperpigmentation located in the gluteal area of the left leg.

Figure 2. Other lesion shown on the forearm.

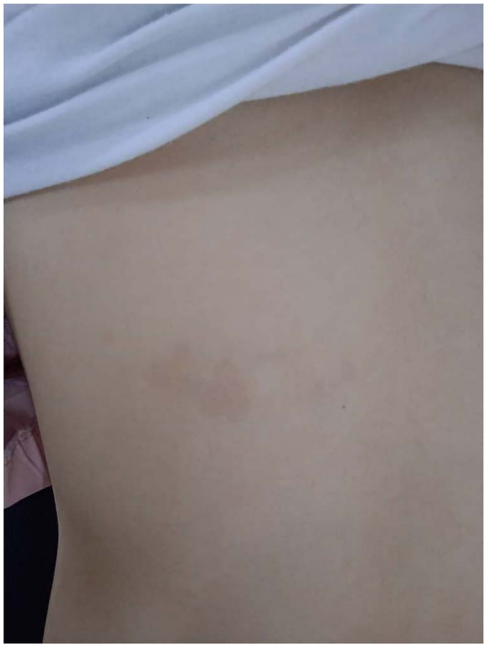

Figure 3. Another lesion presenting on the back.

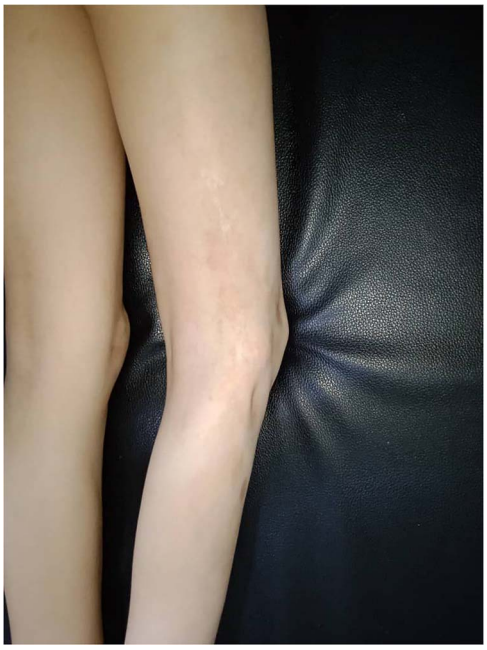

Figure 4. The lesion on the right leg that caused the most limitation in the patient's mobility.

DISCUSSION

FMF was first described in 1945 and genetically characterized in 1992 [3]. Since then, many cases have been reported of co-existing conditions, the most common related to FMF being spondyloarthropathies, systemic vasculitis and inflammatory bowel disease (IBD) [3]. More common associations include multiple sclerosis, juvenile idiopathic arthritis and non-alcoholic fatty liver disease [3]. The relationship between FMF and scleroderma is yet to be determined and proved as no similar cases were diagnosed yet. According to research, if there is a detectable MEFV mutation, the patient is more prone to develop other inflammatory conditions [4]. Although our patient exhibited the positivity of ANAs, a study suggested that this positivity or that of ENA or other markers such as anti-CCP and RF is not clinically correlated with the status of FMF patients. [5] So this presence only concerned the accompanying condition and doesn't affect FMF prognosis.

Morphea has variable presentations as stated and occurs mostly in children aged 2–14 years and tends to affect females [6]. Another study suggests that is affects adults and children equally but women are more susceptible and that children aged 7–11 years are the most common age group [7]. Symptoms in

morphea are usually limited to the skin and in rare cases causes defects in limb growth and joints.

Pathophysiology is unclear as a number of factors are involved in its manifestation. The most common form of morphea presentation is circumscribed. Traditionally it requires a skin biopsy to confirm the diagnosis but morphea is usually diagnosed clinically and can be assured by examination, thus the absence of positive specific antibodies in our patient does not rule out the diagnosis (although generally there are none) [7]. Given the diversity in presentation, other organ involvement and how that affects the prognosis of scleroderma. There have been recent studies pointing out the importance of AntiNuclear Antibodies for the diagnosis and further ANA subtyping that aids in understanding the molecular differences of scleroderma and this subtyping might be used in future classifications [8].

To conclude: Further observations must be made to decide the nature of this case as a true association or just a coincidence.

ACKNOWLEDGEMENTS

None to mention.

CONFLICT OF INTEREST STATEMENT

None declared.

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ETHICAL APPROVAL

Patient information has been de-identified and consent for publication has been obtained.

CONSENT

This case report has been published with the written consent of the patient's parents present.

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