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CASE REPORT

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A case of familial Mediterranean fever presenting with ankylosing spondylitis: A rare case-report

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Key Clinical Message

The association of familial Mediterranean fever and ankylosing spondylitis is rare, but it is essential to consider this diagnosis in patients with a history of FMF who develop symptoms of back pain or other rheumatologic conditions.

Abstract

Familial Mediterranean fever (FMF) is an inherited inflammatory disorder characterized by recurrent fever episodes, abdominal pain, and arthralgia. Ankylosing spondylitis (AS) is a chronic inflammatory disease that affects the spine's joints. The association of FMF and AS is rare. We report the case of a 22-year-old male patient with a history of FMF and a positive family history of FMF in his father, who presented with inflammatory back pain. The patient was found to have sacroiliitis on MRI, which is a characteristic feature of AS. The patient was negative for HLA-B27, a genetic marker often associated with AS. This case report highlights the importance of considering AS in patients with a history of FMF who develop back pain symptoms or other rheumatologic conditions.

KEYWORDS

ankylosing spondylitis, familial Mediterranean fever, HLA-B27, M694V, sacroiliitis

1 | INTRODUCTION

Familial Mediterranean fever (FMF), as a prototypal auto-inflammatory disease, is the most prevalent and the oldest auto-inflammatory disease defined by self-limited episodes of fever and recurrent neutrophilic inflammation bursts.[1,2] In cases with FMF, the second most frequent presentation is musculoskeletal involvement, with sacroiliitis and spondyloarthritis (SpA) being the most prevalent.[3] Additionally, sacroiliitis, which is the SpA hallmark, is indicated to elevate at a higher rate than expected, prevalent in Jewish and Turkish cases with FMF, and has musculoskeletal involvement.[4,5]

Ankylosing spondylitis (AS) is a chronic inflammatory disease and a common type of autoimmune spondyloarthropathy that generally impacts joints of the spine, leading to chronic and severe pain; moreover, it is possible to lead to spine fusion in advanced subjects.[6] In more complex spondyloarthropathy cases, the first presentation is usually sacroiliitis, such as rheumatic disease, psoriasis, inflammatory bowel disease, Crohn's disease, and AS.[7] In this study, we present a case of FMF with the uncommon presentation of AS, a rare manifestation of FMF.

2 | CASE PRESENTATION

A 22-year-old male with a FMF history since childhood (Genetic tests are shown in Figure 1), with a positive

family history of FMF in his father, has been taking colchicine 1 mg daily; he presented to the rheumatology clinic with inflammatory back pain 2 years ago. The patient also noted morning stiffness for about an hour and a half and alternating buttock pain since 2 years ago.

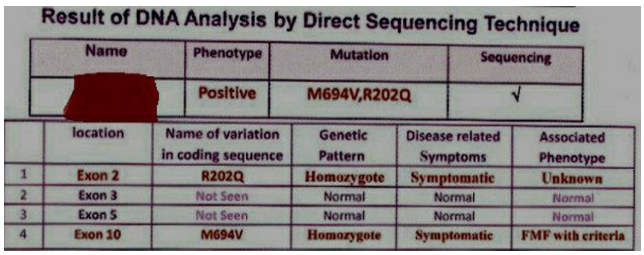
The patient underwent additional examinations, including laboratory tests and physical examinations. The laboratory tests are shown in Table 1. The physical examinations showed limited lumbar flexion, extension, and lateral bending movement. The Schober index was 3.5 cm. The occiput-to-wall test was normal. Faber's test was abnormal, but other examinations were normal. The sacroiliac MRI showed bilateral subchondral bone marrow edema at T2 fat sat and PD sequences and low signal intensity at T1/W, consistent with active sacroiliitis (Figures 2, 3).

According to the comprehensive physical examinations, MRI findings, and laboratory tests, the patient was diagnosed with AS, and the treatment with naproxen 500 mg twice a day was started. Notably, the patient experienced considerable improvement in back pain throughout the subsequent follow-up period, with no significant pathological findings observed. Furthermore, the patient has undergone a 1-year follow-up, with regular three-month assessments to monitor the diseases and kidney and liver function. These consistent evaluations have demonstrated effective disease control and management.

3 | DISCUSSION

AS or SpA is less common in the general population compared to FMF patients. SpA prevalence in 3000 FMF cases is 0.4%, with an 11 in 3000 frequency.[8] The sacroiliitis prevalence in FMF subjects was mentioned more in Turkish subjects. The sacroiliitis prevalent was 7%–10.5%.[9,10]

MEFV gene is responsible for FMF and is found on the chromosome 16 short arm and codes for an immunoregulatory protein recognized as marenostrin or pyrin.[11,12] The main variation of the MEFV gene among Sephardic Jews and Turkish people is M694V polymorphism, and it has been shown that M694V presence is related to arthritis.[13,14]


Result of DNA Analysis by Direct Sequencing Technique

Name	Phenotype	Mutation	Sequencing
[redacted]	Positive	M694V,R202Q	√

	location	Name of variation in coding sequence	Genetic Pattern	Disease related Symptoms	Associated Phenotype
1	Exon 2	R202Q	Homozygote	Symptomatic	Unknown
2	Exon 3	Not Seen	Normal	Normal	Normal
3	Exon 5	Not Seen	Normal	Normal	Normal
4	Exon 10	M694V	Homozygote	Symptomatic	FMF with criteria

FIGURE 1 Genetic test results, confirming the familial Mediterranean fever diagnosis.

In addition, some studies revealed that in FMF patients with sacroiliitis, M694V variation could be more prevalent.[5] FMF is generally expected in Arabs, Armenians, Turks, and Jews. In these populations, the carrier MEFV variation frequency has been demonstrated to be as high as 39%.[15,16] M694V mutation and/or the HLA-B27 may function in the development of sacroiliitis and the SpA severity in patients with FMF.[5] In our case, HLA-B27 was negative, and the M694V mutation was positive.

A study showed a 34-year-old female subject with a 14-year history of FMF. She mentioned a two-year inflammatory lower back pain and morning stiffness of more than one-hour history. The patient was found to have sacroiliitis on MRI, which is a common feature of seronegative SpA. She also had a dry mouth and eyes, characteristic of Sjogren's syndrome. The patient was negative for HLA-B27, which is a genetic marker that is often associated with SpA. However, she was positive for the M694V mutation, a genetic variant associated with FMF. The coexistence of FMF, AS, and Sjogren's syndrome is rare. This case report highlights the importance of considering this diagnosis in patients with a history of FMF who develop symptoms of SpA or Sjogren's syndrome.[17] However, our patient had only AS and FMF with negative HLA-B27; no related diseases were found.

In addition, another study revealed that a Tunisian man presented with a 10-year history of Behçet's disease (BD), a 5-year history of FMF, and a 2-year history of AS. The patient had a classic presentation of BD, with skin lesions, uveitis, genital ulcers, and oral ulcers. He also had a dry mouth and eyes, characteristic of Sjogren's syndrome. Additionally, he had recurrent episodes of fever, abdominal pain, and arthralgia, characteristic of FMF.

TABLE 1 Laboratory parameters of the patient.

Laboratory parameters	Patient's values	Normal range
Leukocyte count, per μL	8.5×10^3	4–10×103
Hemoglobin, g/dL	15.6	12.3–15.3
MCV	90	80–100
Platelet count, per μL	387,000	150,000–450,000
ESR, mm/h	13	0–30
CRP, mg/L	18	<6
Creatinine, mg/dL	0.7	0.7–1.3
SGOT, g/dL	26	8–35
SGPT, g/dL	21	8–35
Alk.P, U per L	294	64–306
Urine analysis	Normal	–
Wright test	Negative	–
Coombs Wright	Negative	–
HLA-B27	Negative	–

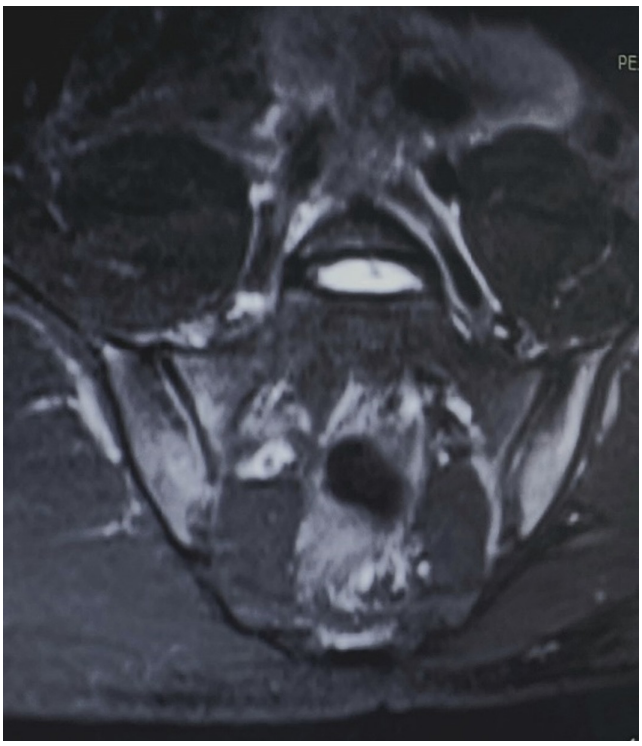


FIGURE 2 T2-weighted fat-saturated MRI of the sacroiliac joints.

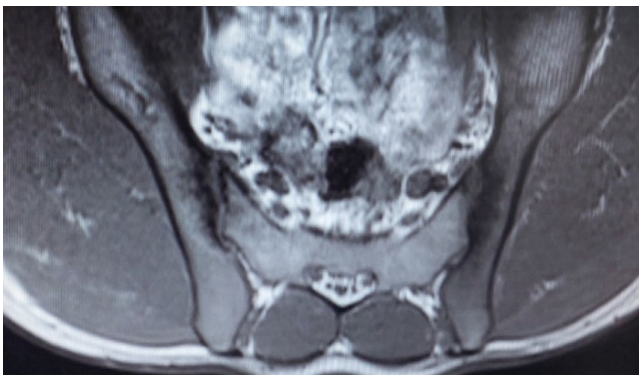


FIGURE 3 T1-weighted MRI of the sacroiliac joints.

The patient was positive for HLA-B27, a genetic marker associated with AS. He also had sacroiliitis on MRI, a common AS feature. The coexistence of BD, FMF, and AS is a rare occurrence. This study highlights the importance of considering this diagnosis in patients with a history of BD or FMF who develop symptoms of AS.[18] This case report documents the coexistence of AS, FMF, and another rheumatologic disease.

4 | CONCLUSION

This study presents a rare case of an FMF patient with an uncommon presentation of AS. It is notable for highlighting the rarity of AS manifestation in FMF cases and the fact that the patient in this particular case tested negative for HLA-B27. This study underscores the importance of considering as a differential diagnosis in patients with a history of FMF who present with back pain symptoms or other rheumatologic conditions.

AUTHOR CONTRIBUTIONS

Amirreza Khalaji: Data curation; project administration; writing – original draft; writing – review and editing. **Mehdi Jafarpour:** Investigation; resources; supervision; validation; writing – review and editing.

FUNDING INFORMATION

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DATA AVAILABILITY STATEMENT

The data supporting the findings of this research are available upon reasonable request from the corresponding author.

ETHICS STATEMENT

This study was performed according to the principles outlined by the World Medical Association's Declaration of Helsinki on experimentation involving human subjects, as revised in 2000, and has been approved by the ethics committee of the Tabriz University of Medical Sciences.

CONSENT

Written informed consent was obtained from the patient to publish this report and clinical images. Consent has been signed and collected in accordance with the journal's patient consent policy.

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