**Occurrence of Behcet's disease** **in a patient with a history of FMF since childhood , Rare Case Report**

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# **Occurrence of Behcet's disease in a patient with a history of Familial Mediterranean fever since childhood, Rare Case Report**

**Introduction**

Familial Mediterranean fever (FMF) is known as an autosomal recessive genetic disorder. The distinguishing criteria of this disorder are recurring periods of fever and inflammation of the peritoneum, erysipelas, pleura, or some skin conditions that resemble erysipelas.[1]

Behcet’s disease (BD) is a multisystemic inflammatory/autoimmune disease with uncertain pathogenesis that affects eyes, skin, joints, large and small blood vessels, the gastrointestinal system, and so on. Despite the fact that the etiology of BD is still unknown, like other autoinflammatory and autoimmune diseases, it has been supposed to cause by dysfunctions in the immune system [2].

It is very unusual for Behcet's disease (BD) and Familial Mediterranean fever (FMF) to coexist, yet it has been recorded. The autoimmune diseases FMF and BD have many symptoms. Mutations in the MEFV gene have been associated with FMF, while BD has been related to other HLA genes, including HLA-B51.[3] The presence of both FMF and BD in a single person is possible due to the fact that both genetic factors often coexist and share similar symptoms.[4]

**Method**

In this study, we investigated the relationship between FMF and Behcet disease in a 39-year-old patient. Our research shows that although the combination of these two diseases is rare, it is not impossible. The case that we studied had symptoms related to FMF, which were controlled with an appropriate dose of colchicine. The genetic test performed on the patient clearly confirms the presence of FMF. Considering the similarity of the symptoms of this disease with Behcet and also the recurrence of symptoms in the patient, the presence of Behcet was also investigated. And the answer was positive . Both diseases were controlled by prescribing the appropriate dose of colchicine and the patient is doing well.

**Key words:** Familial Mediterranean fever (FMF), Behcet’s disease (BD),Inflammation

**Case report**

The patient is a 39-year-old woman with a history of FMF since the age of 8years old, with symptoms of fever (39-40 degrees of centigrade) and abdominal pain and myalgia, which symptoms last for 2-3 days and were improved spontaneously, and in the intervals between attacks, there were no symptoms. In the genetic test conducted, FMF was confirmed by identifying the homozygous mutation in exon E148Q and was treated with colchicine. About 2 years ago, she suffered frequent and painful oral and genital aphthous ulcer, which was accompanied by arthralgia in small joints of hands and skin lesions in the form of pseudo folliculitis. The Pathergy test performed for the patient was positive. Other examinations, including the eye examination, were normal. During the last 2 years, the patient's clinical symptoms were under control with colchicine 1 mg daily, but since about a month ago, due to the worsening of the oral and genital aphthous, the dose of colchicine was increased to 2 mg daily, and now the symptoms are under control.  
Due to frequent and typical oral and genital ulcers, pseudofolliculitis, and positive patergy, the diagnosis of Behcet's disease was proposed along with FMF, and the patient is under regular follow-up in terms of FMF and Behcet's complications, including amyloidosis and eye involvement.

**Discussion**

We reported a 39 year-old-person who had a history of FMF from childhood and symptoms of Behçet’s disease had started recently . [5] The trend is that genotypes including two mutations located within mutational ‘hot-spots’ (codons 680 or 694) of the gene are associated with severe phenotypes, whereas mild phenotypes are associated with some other mutations, E148Q being the mildest and least penetrant that our patient was of this type.[6]. Patients are usually free of symptoms between attacks[3]. Colchicine is the primary treatment used to inhibit inflammation and avoid episodes and consequences in FMF [7]. Colchicine resistance, which is characterized by the occurrence of multiple attacks per month over three months or the presence of ongoing systemic inflammation between episodes, is seen in around 5% of patients.[7].

The condition referred to as BD is characterized by a variety of clinical symptoms. Almost all patients with BD have recurring oral ulcers; between 87% and 98% of them first develop these symptoms with the onset of the disease.[8] The painful lesions are circular or oval-shaped ulcers seen on the lips, tongue, cheeks, or palate, characterized by red borders. Although solitary ulcers are few, numerous ulcers are more prevalent. Genital ulcers are seen in 55-83% of patients, making them the second most prevalent characteristic of BD. Genital lesions often exhibit greater depth, irregular edges and subsequent scarring throughout the healing process. Behcet disease (BD) may affect the central nervous system either by directly involving the brain tissue (parenchymal) or by affecting the surrounding structures (nonparenchymal).[9] A worse prognosis is linked to parenchymal involvement and abnormal cerebrospinal fluid results. It has been suggested that HLA B51 has a self-antigenic function in the pathophysiology of BD. The FMF phenotype typically manifests in early childhood, whereas BD onset occurs later in life. The primary symptoms of FMF, fever and recurring serosal inflammation, are not common in BD. Conversely, BD is more specifically associated with uveitis, vasculitis, and neurological dysfunction. Colchicine and topical corticosteroids are frequently chosen for the treatment of mucocutaneous findings. Research has documented the co-occurrence of FMF and BD in certain patients. Consequently, the convergence of some disease features has prompted suggestions of a shared genetic vulnerability between BD and FMF, and perhaps the notion that both diseases represent contrasting extremes of the same spectrum.[10].

In July 2016, Abdulla Watad and his colleagues reported the finding that a diagnosis of BD was associated with a greater occurrence of FMF, especially in females and those with additional genetic disorders. Based on their study findings, there is a lack of discernible distinction between FMF and BD in a real-world sample of BD patients.[10]

A significant discovery regarding the genetic relationship between these two conditions concerns the clinical presentation of FMF in individuals who carry a single mutant MEFV allele and also manifest BD. Ten of eleven patients with clinical manifestations of FMF and a single mutated MEFV allele also had BD, according to Livneh et al..[11] This result implies that BD might cause carriers' FMF expression to increase. Granulocytes, the effector cells in both circumstances, and the cells where Pyrin is almost exclusively expressed could be a potential underlying mechanism for this. These patients with this comorbidity may be at risk for FMF attacks due to a decreased level of functional Pyrin, which is likely indicative of heterozygotes, and an increased demand for Pyrin by active granulocytes.

Talia Schwartz and et al studied a population of 4000 patients with FMF and examined the association of FMF and Behcet in terms of family relationships.

The study incorporated two control groups: 1. The FMF control group comprised one hundred consecutive FMF patients who were unrelated and visited the FMF clinic for a routine follow-up examination. Patients with FMF who came from families with FMF-BD were not admitted. The BD-control group, consisting of 29 patients, was representative of all BD patients under observation at the Rheumatology Clinic in Israel. None of these patients were members of an FMF-BD family or satisfied the eligibility requirements of the FMF. With the exception of two sets of siblings, every BD control was unrelated. All control patients were subjected to both an examination and an interview. Additionally, the overlapping phenomenology of BD and FMF was investigated.[12]

Both FMF and BD are characterized by fever, arthritis, stomach pain, acute scrotum, kidney dysfunction, and constitutional signs.[13] However, according to the definition, FMF was characterized by short-term periods of fever and abdominal pain, monoarthritic, or acute scrotum. On the other hand, BD was associated with prolonged fever and abdominal pain, occasionally accompanied by diarrhea, insensitivity to colchicine injection or withdrawal, arthritis affecting multiple joints simultaneously, and prolonged abdominal pain. Among the roughly 4,000 patients who underwent follow-up at their FMF clinic, 39 instances were identified as having FMF-BD.[12]. claimed that there were 39 patients with both FMF and BD, and that the individuals with both conditions responded less well to colchicine treatment than the patients with FMF alone. [14]

**Conclusion**

In conclusion, our article presented a female with a history of FMF, developed, Behcet’s disease which is a rare complication of FMF.

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**Author contributions**

All authors approved the final manuscript.

**Competing interests**

The authors declare that they have no competing interests.

**Availability of data and material**

Considering that this study is about a rare disease availability to patients and data may hard to some extent.

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| --- | --- | --- | --- |
| Test | Result | Normal range | Unit |
| ESR | 9 | For males: 0-15 mm/hr  For females: 0-20 mm/hr | mm/hr |
| CRP | Negative | Less than 10 mg/L | mg/L |
| LFT | NL | - | - |
| TSH | NL | - | - |
| Urea | 20 | 8-20 | mg/dL |
| Creatinine | 0.9 | adult males: 0.6 - 1  adult females: 1.3 0.5 - 1.1 | mg/dL |
| WBC | 7180 | 4,500 to 11,000 | cells/μL |
| HB | 13.3 g/dl | males: 13.8 to 17.2 g/dL  females: 12.1 to 15.1 g/dL | g/dL |
| PLT | 287000 | 150,000 to 450,000 | platelets/μL |
| Urine protein | Negative | - | - |
| Urine RBC | Negative | - | - |

**Table 1:** Laboratory parameters of the patient

ESR: Erythrocyte Sedimentation Rate, CRP: C-Reactive Protein, WBC: White Blood Cell Count, HB: Hemoglobin, PLT: Platelet Count, .TSH :Thyroid-stimulating hormone , LFT: Liver Function tests

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