

Successful Treatment of Familial Mediterranean Fever with Infliximab in a Colchicine Resistant Patient

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Abstract

Familial Mediterranean fever (FMF) is an autosomal recessive disease characterized by recurrent episodes of fever and inflammation. Approximately 10% of patients are reported to be resistant or non-responsive to colchicine. We describe a case of a 30-year-old female patient with familial Mediterranean fever resistant to treatment with colchicine and lack of clinical response to Anakinra, successfully treated with Infliximab. Our case suggests that Infliximab, an anti-TNF antibody, may represent a safe and effective therapy for the treatment of colchicine-resistant FMF.

Keywords: Familial Mediterranean Fever; Infliximab; Colchicine-resistant

Introduction

Familial Mediterranean fever (FMF) is a chronic, autosomal recessive inflammatory disease characterized by periodic self-limiting episodes of high fever, abdominal pain, arthritis and inflammation of the serous. Produced by mutations in the MEFV gene, located on the short arm of chromosome 16, which encodes a protein called marenstrin, with expression on neutrophils, resulting in an alteration of the innate immunity that leads to a dysfunction of the inflammatory response [1].

The main treatment for FMF is Colchicine, which prevents the inflammatory attacks and the deposition of amyloid. However, some individuals appear to be unresponsive to colchicine treatment [2]. Here, we present a case of a colchicine resistant Familial Mediterranean Fever patient.

Case Report

A 30-year-old Spanish female, with a past medical history significant for psoriasis and Hashimoto thyroiditis, presented with recurrent episodes of unfocused fever 39°C, accompanied by polyarthralgias predominating in the shoulders, elbows and knees, and abdominal pain focalized on left hypochondrium, with a duration of 5 days, with a periodicity of 2 weeks.

The patients was visited by different physicians in diversal medical centres. Infectious, malignant and autoimmune diseases were excluded. The laboratory tests revealed high inflammatory markers, with these findings, FMF was suspected. The genetic analysis showed an homozygous mutation present in exons 9 and 2 of the MEFV gene, confirming the diagnosis of FMF.

Once the diagnosis of FMF has been established, treatment with Colchicine was initiated, but the patient continued to present clinical and biological activity of the disease, as well as the intercurrent appearance of an extensive outbreak of psoriasis, which forces corticosteroids to start and stop Colchicine.

Given the lack of response with Colchicine and the associated complications, the treatment with anti-interleukin-1 was proposed. Anakinra was initiated at doses of 1 mg/kg/day subcutaneous route, which triggered a skin reaction, with the appearance of painful granulomatous lesions at the puncture site and absence of clinical response (Figure 1).

Due to the lack of response to Anakinra, Infliximab was initiated at doses of 3 mg/kg every 21 days. After a week of treatment, clinical improvement and normalization of the analytical inflammatory parameters were observed. After six months of treatment, a remarkable improvement of clinical symptoms with a decrease in frequency and intensity of abdominal pain, polyarthralgias and complete remission of fever, were observed and no relevant adverse events were registered.

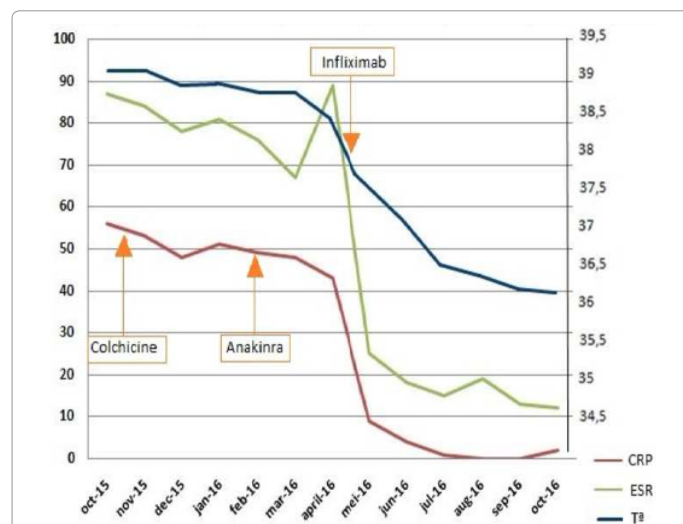


Figure 1: Course of inflammatory parameters in serum: C-reactive protein (CRP mg/l) and erythrocyte sedimentation rate (ESR mm/h) and temperature in Celsius, monitoring the response to treatment with different drugs (Colchicine, Anakinra and Infliximab) in a patient with familial mediterranean fever.

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Discussion

The standard treatment of FMF is oral colchicine, at a dose of 1.5 mg/day, which inhibits neutrophil chemotaxis, preventing recurrence of episodes and avoiding the development of secondary renal amyloidosis, the main prognosis of the disease. However, 10% of patients affected by FMF have no clinical response to colchicine, without clear recommendations on treatment alternatives. However, in recent studies and isolated cases, other therapeutic options, such as anti-interleukin-1 Anakinra and Infliximab are described as effective [3-5].

Although the mechanism of action of TNF- α in the pathogenesis of FMF has not been well defined, in the last decade these drugs have been used in patients with FMF resistant to Colchicine. Infliximab, a chimeric monoclonal anti-TNF antibody, has been effective in controlling FMF attacks, providing an improvement of symptoms in the acute phase [6,7]. Based on series of cases and according to the results of the Eurofever registry, anti-TNF seems to be an option in patients with FMF unresponsive to treatment with Colchicine [8].

In our particular case, the use of Infliximab at a dose of 3 mg/kg was considered opportune, due to the persistence of inflammatory activity and therapeutic failure with other drugs as Colchicine and Anakinra. Infliximab has been used successfully in our patient, who maintains a favorable clinical response after six months, without reported adverse effects. Issues such as the optimal duration of treatment, dosage capable

of maintaining symptom control and long-term safety remain to be resolved.

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