



Adult Familial Mediterranean Fever Treated with Canakinumab

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Abstract

Familial mediterranean fever (FMF), the most common form of hereditary auto inflammatory disorders, characterized by recurrent attacks of fever with serosal or synovial inflammation. Colchicine, the standard of care for patients with FMF, considered as safe, cheap and effective remedy in the majority of the patients for reducing both the frequency of the inflammatory episodes and the risk of developing amyloidosis. Several reports of patients with FMF being successfully treated with agents blocking IL-1 activity, initially with daily injections of the recombinant form of IL-1 receptor antagonist (IL-1Ra), Anakinra and more recently with canakinumab which is a fully human immunoglobulin G (IgG) antibody directed against IL-1 β . This is a case report for an adult male patient with FMF treated successfully with canakinumab.

Keywords: Familial mediterranean fever (FMF); Interleukin-1 (IL-1)

Case Report

A 53-year-old Jordanian male living in Dubai was diagnosed in 2008 as to have FMF. His initial symptoms started in childhood when he used to get infrequent but mild chest, back and abdominal pain attacks. His condition worsened in adult hood she developed more frequent and severe attacks which became associated with fever. He was diagnosed initially on different occasions as to have pleurisy, pericarditis, and acute abdomen until 2008 when a diagnosis of FMF was established based on clinical presentation and genetic studies.

His symptoms much improved on treatment with Colchicine that he used to receive in Jordan and later here after moving to UAE. However, he gradually became intolerant to Colchicine side effects developing loose motions with colicky abdominal pain and even diarrhea on low doses as 500 mcg tablets daily. Thus on few occasions he needed admission to emergency unit to receive parenteral analgesia and anti-inflammatory medications. Milder attacks at home were relieved with short courses of oral steroids. Relevant laboratory investigations were normal apart from elevated ESR, neutrophils and C-reactive protein during the attacks. Urinalysis show microscopic hematuria but no albuminuria. Abdominal CT scan show no renal abnormalities. He has one sister who suffers from the same disorder.

Previously, he received treatment with anakinra daily injections for four weeks; but he developed troublesome injection site reactions to that biologic agent and was discontinued. Later, he became increasingly intolerant to Colchicine even to small doses equivalent to 250 mcg daily.

Accordingly, there was a need to start him on an alternative approved biologic therapy, thus canakinumab therapy was initiated. A total of five injections 150 mg each subcutaneous canakinumab were administered as once every two months until current date (monthly dose regime was not feasible due to insurance restrictions).

The response to canakinumab therapy was described as highly effective by the patient himself with marked reduction of the FMF attacks frequency and severity from around three attacks per month on average to almost nil. The laboratory inflammatory markers levels remained low throughout the treatment period.

Discussion

Familial Mediterranean fever (FMF), the most common form of hereditary auto inflammatory disorders, characterized by recurrent attacks of fever with serosal or synovial inflammation, generally lasting 12 to 72 hours. It has also been associated with increased risk of secondary amyloidosis, mainly affecting renal and vascular function in untreated or insufficiently treated patients [1].

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Colchicine, the standard of care for patients with FMF, considered as safe, cheap and effective remedy in the majority of the patients for reducing both the frequency of the inflammatory episodes and the risk of developing amyloidosis. However, until recently there has been no effective and approved alternative for FMF patients who are intolerant to colchicine, and dose reductions due to adverse effects may result in diminished efficacy. In addition, approximately 5% to 10% patients with FMF continue to have frequent inflammatory episodes despite receiving the highest tolerable doses (1.5 mg/day to 2.0 mg/day) of colchicine [2].

The majority of FMF patients have autosomal recessive inheritance associated with mutations in the MEFV gene, which encodes pyrin protein. FMF-related MEFV mutations, which affect pyrin-mediated regulation of caspase 1 activity in the inflammatory process, are associated with increased IL-1 β production in mice and humans. Therefore, inhibition of IL-1 activity may decrease both frequency and severity of acute attacks in patients with FMF [3].

Several reports of patients with FMF being successfully treated with agents blocking IL-1 activity, initially with daily injections of the recombinant form of IL-1 receptor antagonist (IL-1Ra), anakinra and more recently with canakinumab which is a fully human immunoglobulin G (IgG) antibody directed against IL-1 β . This has confirmed the critical role of IL-1 in the pathogenesis FMF [3].

Complete response to therapy without a single attack during treatment has been reported in 76.5% of patients on anakinra and in 67.5% of patients during canakinumab [4].

In patients with established type AA amyloidosis, anti-IL-1 treatment can reverse proteinuria [4].

The US Food and Drug Administration (FDA) had approved in September 2016 three new indications for canakinumab; 1) Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS); 2) Hyper immunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD); and 3) Familial Mediterranean Fever (FMF).

Up to the author's best knowledge, this is the first case of adult FMF being treated with canakinumab in the United Arab Emirates.

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