Interferon alfa in protracted arthritis of familial Mediterranean fever: a robust alternative for synovectomy

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A 17 year old girl was admitted to our rheumatology clinic with right knee pain and swelling for the past 3 months. A diagnosis of familial Mediterranean fever (FMF) had been made 8 years previously; she had recurrent attacks of fever, abdominal pain, and knee arthritis. She had been using colchicine 1.5 mg/day regularly since then. Although her abdominal attacks and fever had subsided with colchicine treatment, recurrent mild knee attacks occurred almost every month. Two years ago she was found to have the homozygous M694V gene mutation for FMF. Three months ago, she was admitted to hospital owing to monarthritis in her right knee—but this time with a prolonged and severe episode. She was given antibiotics, and a suspected diagnosis of septic arthritis was made. As the cultures did not yield any bacterial growth and her symptoms persisted, she applied to our department.

A physical examination disclosed painful and limited movement, swelling and warmth in the right knee joint. Laboratory findings were as follows: erythrocyte sedimentation rate: 96 mm/1st h, C reactive protein: 165 mg/l (0–8), fibrinogen: 8.5 g/l (1.4–4.3). Protracted arthritis of FMF was diagnosed and the dose of colchicine was increased to 2 mg/day. Ten days later, she was seen on a control visit with complaints of abdominal pain, diarrhoea, skin rash—probably due to colchicine—and persistent knee arthritis, which did not respond to colchicine treatment. Accordingly, interferon alfa 4.5 million IU (twice a week) was started and the colchicine dose was decreased to 1.5 mg/day.

Thereafter, she has been followed up every 10 days for 3 months and her knee arthritis has disappeared and the laboratory measures have improved (table 1). She is still being routinely followed up and is completely normal with the above mentioned regimen of interferon alfa and colchicine together with a protocol of isometric quadriceps strengthening exercises.

Table 1 The changes in the laboratory variables of the patient with interferon alfa treatment

Interferon treatment	ESR (mm/1st h)	CRP (mg/l)	Fibrinogen (g/l)
Immediately before	61	106	8.8
Two weeks after	35	11	4.9
Six weeks after	30	4	4.8
Twelve weeks after	25	4	4.5

DISCUSSION

Arthritis in FMF usually comprises acute attacks, with complete resolution within a few days or 2 weeks. It is more common in patients with the homozygous M694V gene mutation. Occasionally, the attacks are protracted, lasting for several months, and chronic joint disease has been estimated to contribute about 5–10% to the joint manifestations in FMF.[1 2] However, once degenerative or necrotic changes ensue, the recurrent attacks of arthritis are no longer punctuated by symptom-free intervals. Additionally, the irreversible morphological changes in the joints become non-responsive to colchicine, corticosteroids, or non-steroidal anti-inflammatory drug treatment. Although ruling out a coexisting chronic inflammatory arthritis should remain a prerequisite,[3] surgery is usually warranted in such cases.[1 4 5] To the best of our knowledge, a medical treatment alternative for these patients that would make synovectomy unnecessary has not been reported. Only one report, by Tunca *et al,* has described favourable effects of interferon alfa on the abdominal attacks of seven patients with FMF.[6] As recent studies have disclosed up regulation of the MEFV gene by interferon,[7] the mechanism—which could not have been substantiated previously—has become evident. Thus, overall, we advocate the use of inteferon alfa as an adjunct for the treatment of colchicine resistant arthritis attacks in FMF.

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