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Treatment of Schnitzler's syndrome with anakinra

Sirs,

Schnitzler's syndrome is a rare disorder characterized by chronic urticaria, bone pain, monoclonal immunoglobulin M gammopathy and intermittent fever (1). Treatment is usually very disappointing, and only high-dose corticosteroids can improve the skin lesions, but they rapidly induce adverse effects. Recently, an interleukin 1 receptor antagonist (IL1Ra), anakinra, has demonstrated prolonged efficacy in some case reports (2, 3).

We report on a new case of a patient with Schnitzler's syndrome treated with anakinra, which was able to achieve a rapid and persistent remission of clinical and laboratory abnormalities.

This patient was a 72-year-old man without any particular medical history. He had been chronically ill for over a year, suffering from fever reaching 39°C, fatigue, weight loss and lower back pain. Examination revealed chronic urticaria affecting the back, chest and abdomen. This was associated with elevated C-reactive protein (180 mg/l), and leukocytosis (25x10⁹/l). Serum protein electrophoresis revealed a monoclonal IgM kappa component (total IgM 2.55 g/L). A skin biopsy identified urticarial changes. Bone radiographs and CT-scan films evidenced condensations on the iliac bone and L4 vertebrae.

This led us to make a diagnosis of Schnitzler's syndrome (1). First-line therapy was based on full-dose corticosteroids (prednisone 1 mg/kg/day), but steroid dependency was observed when the daily dosage was tapered to 30 mg. Adding methotrexate did not ameliorate his dependency on prednisone.

A course of subcutaneous anakinra at a dose of 100 mg/day was then considered. Following the first injection, the urticaria immediately resolved and laboratory features of inflammation normalized over a few days. Remission still persisted after 6 months of follow-up, at which point, the injections of anakinra were maintained but reduced to 100 mg every two days. This change was followed by a relapse of urticaria, fever, leukocytosis and inflammatory syndrome. Reintroduction of the initial dosage of 100 mg/day enabled a complete regression of clinical and biological abnormalities. At the time of writing (12 months of follow-up), CRP and leukocytes remain normal, and urticaria and fever have not recurred. The concentration of the monoclonal component remains unchanged. Anakinra injections are well-tolerated, with only moderate skin dryness and pain at the injection sites.

Schnitzler's syndrome is a rare disease consisting chiefly of chronic urticaria, together

with monoclonal IgM. Other symptoms include fever, joint and bone pain, enlarged lymph nodes, bone condensations, leukocytosis, and elevated CRP levels.

Dependency on high doses of corticosteroids is the rule, entailing steroid toxicity. Immunosuppressive drugs are mostly ineffective. The disease evolves to chronicity and affects the patient's quality of life (1). The pathophysiology of Schnitzler's syndrome remains unclear. Anakinra is an interleukin 1 (IL-1) receptor antagonist. Its effectiveness in this syndrome evokes a key role for IL-1 (2, 3). It has been suggested that anti-IL1 α IgA antibodies are more frequent in Schnitzler's syndrome than in controls (4).

In previous case-reports, the clinical benefits of anakinra were very rapid, observed within a few hours on urticaria, and within a few days on CPR and leukocytosis (2). We observed the same response, and showed that a reduction in dosage was followed immediately by a clinical and biological relapse of symptoms. However, anakinra only "suspends" the symptoms of this syndrome. It could perhaps be proposed as a diagnostic test. Nonetheless, the use of anakinra should be studied at a larger scale in order to confirm its efficacy and to evaluate the benefit/risk ratio in Schnitzler's syndrome (5).

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