Striking Effect of the IL-1 Receptor Antagonist Anakinra in Chronic Urticarial Rash with Polyclonal Increase in IgA and IgG

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Accepted November 24, 2006.

Sir,
Schnitzler’s syndrome (SS) is characterized by chronic urticarial rash, (monoclonal) gammopathy (IgM) and at least two of the following: intermittent unexplained fever, arthralgia, bone pain, lymphadenopathy, hepatosplenomegaly, elevated erythrocyte sedimentation rate (ESR), leukocytosis and abnormal findings on bone morphological investigations (1, 2).

CASE REPORT
A 58-year-old woman presented with an erythematous macular and partly urticarial rash (Fig. 1) without lymphadenopathy. She had a 13-year history of this rash, together with anaemia, fatigue, arthralgias and an elevated ESR. The symptoms were resistant to therapy with different antihistamines and non-steroidal anti-inflammatory drugs (NSAIDs), but responded in part to weekly injections of betamethasone, given for 6 months 8 years prior to consultation. Five years prior to presentation, an elevated IgA was documented, but not correlated to the rash and other symptoms. Nine months prior to presentation, an elevated ESR was noted, but not correlated to the rash and other symptoms. After 14 weeks on anakinra therapy the patient showed complete recovery. There were no side-effects except erythematous macules at the injection sites. The ESR (20 mm/h) and haemoglobin level (14.4 g/dl) had improved markedly, and within the normal range were leukocytes, globular volume, CRP, IgA, IgG.

Fig. 1. Erythematous macular and partly urticarial lesions on the patient’s arm in July 2006. The rash disappeared within 6h of the first application of the interleukin-1 antagonist, anakinra.

DISCUSSION
As in this case, SS is frequently resistant to therapy. Previous therapeutic approaches have included glucocorticoids, NSAIDs, colchicine, dapsone, thalidomide, interferon-α, rituximab, immunoglobulins, methotrexate, cyclophosphamide, purine analogues, plasma exchange and psoralen ultraviolet A (PUVA) therapy (1, 2).

To our knowledge, this is the first report of anakinra treatment in a sine IgM variant of SS with polyclonal immunoglobulin increase (1, 3, 4). Adult-onset Still’s disease was considered to be the differential diagnosis, but the patient showed no increase in serum ferritin levels, which is a major diagnostic criterion (1). There was no evidence for other autoimmune diseases.

Anakinra is an interleukin-1α and -1β antagonist (IL1Ra) that competitively blocks the action of this cytokine at the receptor level. The efficacy of anakinra in SS was reported for the first time in a patient who became asymptomatic within one week on 100 µg/day of anakinra plus methotrexate (5 mg/week) (5). Another study described the resolution of the rash and fever in three patients with the classical variant of SS (with monoclonal IgM or IgG) within one day on monotherapy with anakinra at 100 g/day (6).
IL-1 has been suggested to be pathogenetically important in SS, and an IgG auto-antibody mediated prolongation of the half-life of IL-1 has been suggested to account for symptoms of the disease (7). As IL-1 may limit the availability of iron for erythrocytes, our patient’s anaemia was attributed to the chronic inflammatory process (8).

The successful treatment of SS with anakinra, including a clear improvement in anaemia, supports the theory that IL-1 has an important role in the pathogenesis of this disease.

REFERENCES