

LETTERS TO THE EDITOR

Adult-onset Still's disease: an uncommon differential diagnosis of urticaria and treatment with anakinra

Editor

Still's disease is a chronic, systemic inflammatory childhood disorder. Adult-onset Still's disease (AOSD), first described in 1971, is rare and may pose a diagnostic and therapeutic challenge.¹

A 50-year-old woman reported a 1-year history of mild recurrent urticaria. She presented with a disseminated urticarial rash (fig. 1) in combination with a painfully sore throat, fever and arthralgia of the big joints. The admission diagnosis was infection-associated urticaria. Systemic antihistamines (dimethindenmaleate, 5 mg intravenously twice daily), antibiotics (clarithromycin, 250 mg twice daily) and prednisolone (up to 100 mg/day) for 5 days did not alleviate her symptoms, although continuation of prednisolone (50 mg/day) for three more days led to partial remission. However, after discontinuation of the steroid, the patient developed spiking fever (up to 40.5 °C), general rheumatic pain, lethargy, nausea, diarrhoea and, again, a painfully sore throat. The urticarial rash regularly exacerbated along with the fever.

Laboratory examinations revealed leukocytosis (15 000 cells/ μ L), neutrophilia (86%), accelerated erythrocyte sedimentation rate (44 mm/h) and elevated C-reactive protein (CRP; 35.9 mg/dL). Lactate dehydrogenase (560 U/L) and aspartate aminotransferase (80.8 U/L) were increased. Ferritin was extremely high (20 800 μ g/L). Antinuclear antibodies were mildly increased (1 : 80). All other laboratory

parameters were unremarkable. Blood cultures, throat smear, serum and faeces revealed no viral, bacterial, fungal or parasitic cause for the symptoms. Abdominal and cardiac ultrasound, gastroscopy, chest X-ray and computed tomography were largely normal.

A skin biopsy showed a normal epidermis, a moderately oedematous and mucinous upper dermis with a perivascular and interstitial infiltrate composed of lymphocytes and abundant neutrophils, but no vasculitis (fig. 2). Direct immunofluorescence was unremarkable.

The conspicuous triad of high spiking fever of unknown origin, arthralgias and evanescent rash as well as defined additional criteria gave rise to the diagnosis of AOSD.² The patient was put on prednisolone [initial intravenous pulse (250 mg) followed by oral medication (1 mg/kg/d)] in combination with pantoprazol (40 mg/day) and ranitidin (150 mg/day). Antihistamines were continued, and ibuprofen was initiated. However, the quotidian fever (as high as 40°C) and elevated CRP remained for 6 days, although a gradual attenuation occurred. In addition, arthralgia and the intermittent urticarial rash persisted. Overall, this treatment resulted in slow but consistent alleviation of the symptoms. Ibuprofen was finished, the systemic corticosteroid was tapered, and the patient was treated with the interleukin-1 receptor (IL-1r) antagonist, anakinra (100 mg/d subcutaneously) combined with oral methotrexate (20 mg/week).³ Within the next weeks, the corticosteroid dosis was reduced to 7.5 mg prednisolone per day. The symptoms resolved under this therapy, and the patient is now symptom-free for 10 months.

The diagnosis of AOSD may pose considerable challenges and is often established via exclusion of other disorders.⁴ The clinical triad of intermittent or quotidian fever spikes,



fig. 1 Disseminated urticarial rash of a 50-year-old woman suffering from AOSD.

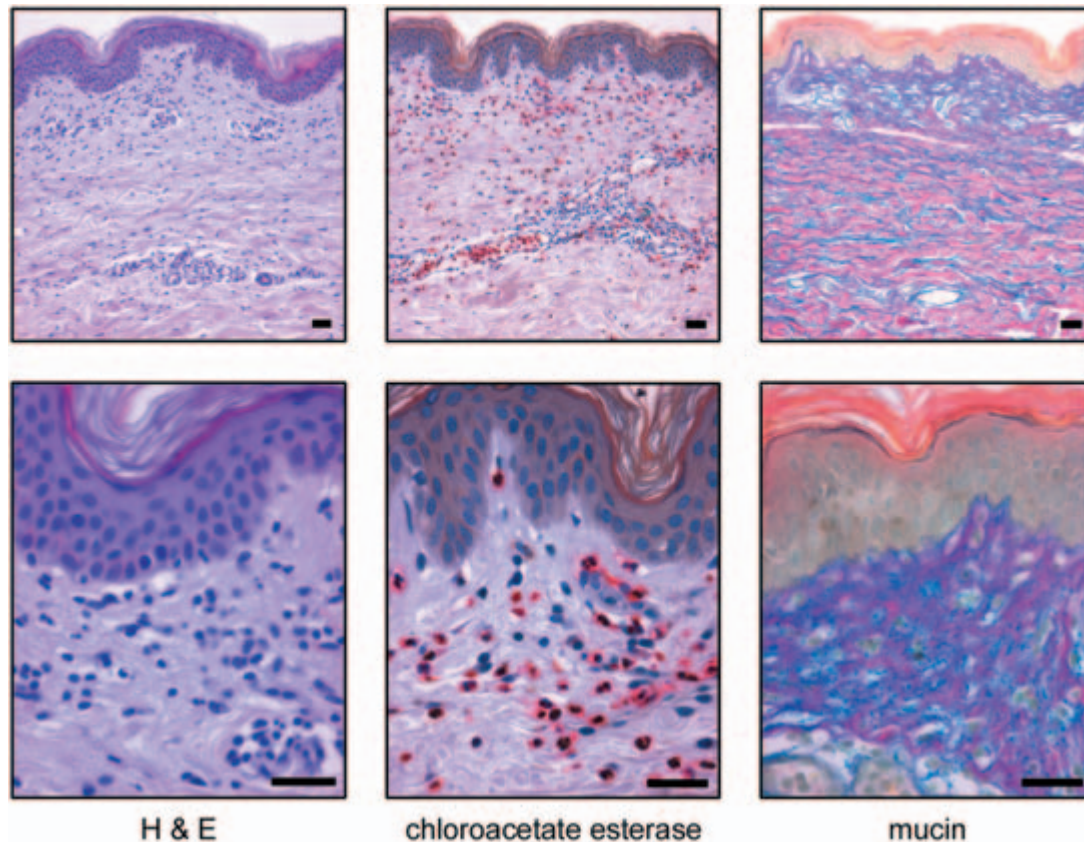


fig. 2 A biopsy was taken from a skin lesion on the patient's forearm. Haematoxylin and eosin staining showed perivascular and interstitial inflammatory infiltrate and moderate oedema of the upper dermis (left). The identity of many of the infiltrating leucocytes as neutrophilic granulocytes is confirmed by chloroacetate esterase staining (middle). Deposition of mucin within the upper dermis is depicted in the right-hand panels. Scale bar, 20 µm.

evanescent rash and arthralgia is regarded as a hallmark constellation. Neutrophilic leukocytosis, hepatosplenomegaly, sore throat, high ferritin and other acute phase proteins are often found, giving rise to the definition of major and minor criteria.² Our patient fulfilled almost all of these criteria. Urticarial manifestations, as seen in our patient, are occasionally described in the literature and usually respond poorly to conventional antihistaminic therapy.^{5–7}

AOSD is regarded as a rheumatic, multisystem inflammatory disorder, whose pathogenesis is still unclear. An infectious aetiology has been postulated, but a specific agent has not been identified. Inflammatory cytokines are elevated in some AOSD patients in a circadian fashion, possibly explaining the quotidian fever spikes.⁸

Owed to the rarity of the disease, evidence-based guidelines for the treatment of AOSD are not available. Treatment options include nonsteroidal anti-inflammatory drugs, glucocorticosteroids and disease-modifying anti-rheumatic drugs.⁸ In some cases, AOSD was successfully treated with tumour necrosis factor antagonists, anti-IL-6 or anti-IL-1r (anakinra), often in combination with traditional immuno-

suppressants.^{8–10} The efficacy of such novel treatments is evidenced by our patient, whose symptoms responded well to anakinra in combination with methotrexate.

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