

**Successful treatment with anakinra of refractory pericarditis in systemic lupus erythematosus**

Sirs,

The unpredictability of clinical manifestations of systemic lupus erythematosus (SLE) mirrors the pathophysiology underneath. Indeed, both T and B cell driven immune responses take place simultaneously causing distinctive symptoms, even in the same patient (1). SLE associated pericarditis, often recurrent, has a prevalence ranging from 11 to 50% (2). Little is known about its pathogenesis in SLE, but the high neutrophil count in the pericardial effusion (3) may suggest an involvement of the innate immune system and, therefore, the main cytokine activated by the inflammasome response, namely interleukin-1 (IL-1), might be a therapeutic target (4). Here, we report our experience in a patient with refractory SLE-related pericarditis successfully treated with the IL-1 receptor antagonist anakinra.

In April 2017, a 30-year-old man was referred to our Rheumatology Unit due to fever and thoracic pain. Echocardiography detected pericardial effusion. His laboratory investigations showed increased C-reactive protein (CRP), hypocomplementaemia, and 24-hour urinary protein excretion of 750 mg/day. Anti-nuclear antibody, anti-extractable nuclear antigens (anti-SSa, anti-RNP, anti-Sm) as well as anti-dsDNA antibodies were detected positive. Due to abnormal bleeding time kidney biopsy was not performed. A diagnosis of SLE was made and azathioprine 100 mg/day and prednisone 25 mg/day were started. Three months later, at the dose of prednisone 10 mg/day the patient complained of chest pain due to relapsing pericarditis, which remitted by increasing prednisone dosage at 25 mg/day. Thereafter, the patient underwent different immunosuppressive drugs, including cyclophosphamide 500 mg iv (6 fortnightly pulses), mycophenolate mofetil 2g/day (6 months), and cyclosporine 200 mg/day (4 months), but he experienced several pericarditis relapses with increased CRP levels, always upon the attempt to taper prednisone. In June 2018, belimumab 10 mg/kg monthly and colchicine (1mg/day) were administered but also this strategy was unsuccessful as further pericarditis

flares occurred. In January 2019, anakinra 100 mg/day was started, in combination with prednisone 25 mg/day (the dosage was slowly reduced) and colchicine (1 mg/day). After 12 months, no more pericarditis or fever occurred, CRP levels were persistently normal, but more importantly a dose 2.5 mg/day is being taken from 6 months, along with colchicine and anakinra. Neither systemic nor visceral signs of SLE disease activity were present.

Patients with SLE have a high risk of pericarditis and serositis that are more frequently observed in late-onset SLE patients (5). In our case the patient, despite his young age, developed recurrent pericarditis responsive to prednisone but refractory to the conventional immunosuppressive drugs, including B cell-targeted therapy. As relapsing pericarditis and fever was the prevailing symptom in our patient, based on the evidence showing IL-1 as the driver of inflammation in idiopathic pericarditis (6-8), we reasoned that IL-1 targeting with anakinra could be an effective strategy. In human SLE, IL-1 has been found to be increased in glomerulonephritis and in the serum and cerebrospinal fluid of patients with CNS lupus (9), but never investigated in pericardium involvement. To our knowledge, this is the first case of SLE-associated recalcitrant pericarditis successfully treated with anakinra. For the record, anakinra has been already proven to be effective in SLE-related arthritis (10) and refractory fever (11).

Obviously, this case has an anecdotal meaning and the use of anakinra cannot be generalised to all patients with SLE and pericarditis, but it has a high speculative value as it prompts to hypothesise that SLE is characterised by a dysregulation of either adaptive and innate immune responses and unknown tissue/organ milieu may favour the activation of one or the other. Further studies are needed to explore whether the activation of innate immune system is predominant in pericardium inflammatory disease irrespective of underlying disease.

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