

Interpretation of C-reactive protein values in systemic lupus erythematosus

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A significant rise in C-reactive protein (CRP) levels in patients with systemic lupus erythematosus (SLE) often reflects a co-existent infection or associated serositis. A number of investigators have proposed that the level of CRP can differentiate between infected and non-infected SLE patients. However, there have been conflicting views as to the usefulness of CRP measurement in SLE. Hind *et al.*^[1] showed modest elevations in serum CRP with an acute flare, but substantially higher levels of CRP with intercurrent infection. Becker *et al.*^[2] investigating a series of 41 patients showed that, even in the presence of florid disease activity, in the absence of infection the CRP value did not exceed 60 mg/l. This was further supported by Pepys *et al.*^[3] in a prospective study of 124 Caucasian patients with SLE; a serum CRP level greater than 60 mg/l in a febrile patient strongly suggested the presence of infection. Borg *et al.*^[4] in a study of 71 SLE patients found that CRP levels exceeding 60 mg/l during exacerbations without serositis indicated infection in all cases; however, the investigators also found that during exacerbations of SLE accompanied by serositis CRP levels up to 375 mg/l (median 76 mg/l) were recorded.

We report a challenging case of an SLE patient presenting with fever and high CRP. A 37-year-old Afro-Caribbean female with a known diagnosis of SLE, presented with a 5-day history of generalised malaise, arthralgia and persistent fever similar to her original presentation 12 years previously. She had been treated with steroids and cyclophosphamide 10 years previously for biopsy-proven lupus nephritis but currently took only hydroxychloroquine 200 mg twice a day. She was pyrexial at 39°C, normotensive, with widespread tender joints but no swelling. Examination of the cutaneous, cardiovascular, respiratory, abdominal and neurological systems was normal.

Investigations showed a haemoglobin 11.2 g/dl, white cell count $15.2 \times 10^9/l$ with predominant neutrophilia ($13.1 \times 10^9/l$), platelets $462 \times 10^9/l$, eosinophil sedimentation rate 116 mm/h and CRP 328 mg/l. Complement levels were reduced and dsDNA antibody was negative. Five sets of blood cultures were negative. Electrocardiography showed sinus tachycardia but was otherwise normal. An echocardiogram revealed an anterior pericardial effusion (0.5 cm) but no valvular lesions and a chest X-ray was unremarkable. Urinalysis was positive for protein (3+) and blood (1+) but was culture-negative with no casts. A subsequent renal biopsy showed scar tissue with no features of active lupus nephritis. Computed tomography (CT) scan of the chest/abdomen/pelvis revealed no infective focus but the presence of mild ascites consistent with serosal involvement.

The patient continued to have high fevers up to 39.5°C during the initial days of her admission, with a persistently raised CRP between 300 and 328 mg/l. In the absence of an obvious septic focus, she was treated for an acute SLE flare, initially with intravenous methylprednisolone 500 mg, followed by oral corticosteroids (prednisolone 30 mg/day). She had an excellent clinical response with the fever normalising within days and the CRP normalising within 4 weeks.

In the majority of cases of SLE, unlike most other systemic inflammatory conditions, a significantly lower CRP response has been observed, which may be accounted for by underlying immunoregulatory mechanisms such as CRP consumption by immune complexes.^[5] Genetic factors,^[6] as well as concomitant use of corticosteroids may also play a role in the unresponsiveness of CRP. However, as our case indicates, patients with SLE are still capable of producing high levels of CRP even in the absence of infection, an observation also noted by other investigators.^[7-9] This is particularly the case in the presence of serositis^[4] but, as our case highlights, the rise of CRP in association with serositis in lupus flares is not always apparent clinically. Thus, symptomatic pericarditis has an incidence of 20-30% in most large series but echocardiography reveals pericardial involvement in up to 50% of cases^[10].

This case illustrates the significant rise in CRP that can occur in lupus flares in the presence of subclinical serositis and warns against the use of cut-off values of CRP to differentiate flare from infection.

Teaching points

1. Using cut-off values for CRP to distinguish infection from disease flares in SLE may be misleading.
2. Although CRP often rises in lupus serositis the latter may not always be clinically apparent.

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