LESSON OF THE MONTH

Pneumococcal septicaemia in a patient with systemic lupus erythematosus

A R Mackenzie, R B S Laing, A G MacDonald, C C Smith

Case report

A thirty eight year old woman with insulin dependent diabetes mellitus and systemic lupus erythematosus (SLE) was admitted with a two day history of fever, rigors, and diarrhoea. SLE was diagnosed at the age of 18 years when she presented with joint pain, a positive antinuclear antibody (ANA), and severe autoimmune thrombocytopenia, which was treated with corticosteroids. At no stage of her illness did she have evidence of renal, central nervous system, muscle or skin involvement. She had also suffered four miscarriages in association with anticardiolipin antibodies. There was no history of arterial or venous thrombosis and her disease had been inactive for a number of years.

When reviewed as an outpatient, two months before admission, she was well with no clinical manifestations of SLE. ANA was positive (1:160), extractable nuclear antigen screen negative, C3 141g/l (88–201), C4 23.1g/l (16–47), DNA binding 3I U/l (0–7), anticardiolipin antibody was 30 gpl units (<10) and lupus anticoagulant test was not performed. Full blood count, including lymphocyte count and blood film, was entirely normal. She was not receiving immunosuppressive or corticosteroid therapy.

On admission to the Infection Unit she was febrile at 40°C, with a tachycardia of 130/min, blood pressure 65/38 mm Hg, and tenderness over the frontal sinuses. There was no neck stiffness and she was lucid. She was receiving no immunosuppressive therapy and her only medication was regular subcutaneous insulin injections. Her initial investigations showed a white cell count 30.4×10^9/l (neutrophils 28×10^9/l, lymphocytes 1.8×10^9/l), haemoglobin 104 g/l, platelets 247×10^9/l. The blood film showed prominent Howell - Jolly bodies and giant platelets, consistent with hyposplenism. The XDPs (X fraction of the fibrinogen degradation products) were raised at >200 ng/ml (normal <200) but the clotting screen was normal implying low grade disseminated intravascular coagulation. Urine analysis, blood urea, and electrolytes were normal but the blood glucose was increased at 15.5 mmol/l. C reactive protein was < 1.0 g/l. Immunoglobulin concentration were IgG 11.0 g/l (8–14), IgA 1.1 g/l (0.9–3.5), and IgM 1.9 g/l (0.5–2.5). The IgG subclasses were normal. ANA was positive to 160 (membranous) and the extractable nuclear antigen screen was negative. The DNA binding level was 4.2 IU/l (0–7). The CH50 was 240 (150–250), C3 161 g/l (88–201), and C4 20.6 g/l (16–47). Anticardiolipin antibody 30 gpl units (reference value <10) and the lupus anticoagulant was not assayed. Three sets of blood cultures all grew *Streptococcus pneumoniae*. Stool culture on admission grew no enteric pathogens and her diarrhoea was thought to be secondary to the bacteraemic illness. Chest and sinus *x* rays were normal. An abdominal ultrasound scan revealed that the spleen was too small to visualise.

She was treated for septic shock with oxygen, intravenous colloid expansion, and intravenous cefotaxime pulses with an insulin infusion and made a full recovery over the next five days. She was discharged from hospital while receiving oral amoxycillin and was subsequently started with long term prophylactic phenoxymethyl penicillin and vaccinated against *Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae* type b.

Discussion

Impaired splenic function in SLE patients was first described in 1979[1] and was followed by reports of splenic atrophy.[2 3] The clinical implications of these complications were highlighted by a series of case reports describing fatal or near fatal septicaemia in patients with SLE and hyposplenism.[2 4 5]

Splenic dysfunction is suggested by the presence of Heinz and Howell-Jolly bodies in the red cells, as occurred in our patient, and should be considered in patients with a thrombocytosis or monocytosis on the blood film.[6] The regular examination of peripheral blood films may permit early detection of hyposplenism but the finding of a normal full blood count two months before our patient's admission highlights the comparatively short period over which hyposplenism may develop. Furthermore, this patient's inactive disease (as suggested by her normal DNA binding titre and complement values) did not preclude the development of hyposplenism.

The mechanisms by which hyposplenism develops in SLE are uncertain. Splenic infarction has been described in association with the

The Infection Unit
A R Mackenzie
R B S Laing
C C Smith

Department of Rheumatology
A G MacDonald

Aberdeen Royal Infirmary, Aberdeen

Correspondence to:
Dr A R Mackenzie, The Infection Unit, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZB.

Accepted for publication
22 April 1997

antiphospholipid syndrome[7] and thrombosis has been suggested as a possible mechanism for hyposplenism in SLE.[2]

A recent review of published reports revealed 13 SLE patients with functional asplenia, seven of whom developed sepsis with pneumococcal sepsis in six and a salmonella septicaemia in one.[8] All of these patients were female, nine had hypocomplementaemia and only two of the septicaemic patients survived. The duration of SLE ranged from two months to 14 years.

This patient's SLE activity was thought to be low because of normal values of complement, DNA binding, and lymphocytes. The C reactive protein is often normal in SLE but would be expected to rise in bacterial sepsis. Our patient's clinical presentation, coupled with her positive blood cultures, put the diagnosis of sepsis beyond doubt and her normal C reactive protein might be explained by the fact that this acute phase reactant can take 48 hours to rise in response to infection.[9]

Loose stools or frank diarrhoea are common in septicaemia but the clinical features of this case suggested that sinusitis was the primary focus of infection. Enteric infection such as Salmonellosis must always be excluded in such patients.

Recent British guidelines for patients with an absent or dysfunctional spleen have not included patients with SLE.[10] In view of the potentially fatal complications, we would suggest that patients with SLE who have any features of hyposplenism on blood film should be actively considered for pneumococcal prophylaxis—that is, pneumococcal vaccination and long term therapy with phenoxymethyl penicillin. The *Haemophilus influenzae* type b vaccine should also be given and vaccination against *Neiserria meningitidis* should be considered. As the response to pneumococcal vaccination may be better in patients with normal splenic function than in those with hyposplenism or asplenism[10 11] and as this case shows the difficulty in identifying those most at risk of hyposplenism, it might be argued that all patients with SLE, 5% of whom are likely to develop hyposplenism,[2 12] receive pneumococcal vaccination.

The lesson

- Hyposplenism is a predisposing factor to septicaemia in patients with SLE.
- Hyposplenism is frequently found in clinically inactive SLE.
- Regular monitoring of the blood film is required to detect early hyposplenism and start appropriate prophylaxis against infection.

1 Lockwood CM, Worlledge S, Nicholas A, Cotton C, Peters DK. Reversal of impaired splenic function in patients with nephritis or vasculitis (or both) by plasma exchange. N Engl J Med 1979;300:524–34.
2 Dillon AM, Stein HB, English RA. Splenic atrophy in systemic lupus erythematosus. Ann Intern Med 1982; 96:40–3.
3 Pines A, Kaplinsky N, Olchevsky D, Holtzman E, Frankl O. Hyposplenism in systemic lupus erythematosus. Br J Rheumatol 1983;22:176-8.
4 Foster PN, Hardy GJ, Losowsky MS. Fatal salmonella septicaemia in a patient with systemic lupus erythematosus and splenic atrophy. Br J Clin Pract 1984;38:434-5.
5 Kamdar N, Zanzi I, Kroop S, Furie R, Margouleff D. Reversible functional asplenia in systemic lupus erythematosus. Clin Nucl Med 1991;16:760-2.
6 Hoffbrand AV, Lewis SM. *Postgraduate haematology*. 3rd ed. Oxford: Blackwell Scientific, 1989:20.
7 Obarski TP, Stoller JK, Weinstein C, Hayden S. Splenic infarction. A new thrombotic manifestation of the circulating lupus anticoagulant. Cleve Clin J Med 1989;56:174-6.
8 Scerpella EG. Functional asplenia and pneumococcal sepsis in patients with systemic lupus erythematosus. Clin Infect Dis 1995;20:194-5.
9 Dinarello CA, Wolff SM. Pathogenesis of fever and acute phase response. In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and practice of infectious diseases*. New York: Churchill Livingstone, 1995:535.
10 Working party of the British Committee for standards in Haematology Clinical Haematology Task Force. Guidelines for the prevention and treatment of infection in patients with an absent or dysfunctional spleen. BMJ 1996;312:430-4.
11 Liote F, Angle J, Gilmore N, Osterland CK. Asplenism and systemic lupus erythematosus. Clin Rheumatol 1995; 14:220-3.
12 Valles R, Rivero I, Moran D, Diumenjo MS. Spontaneous splenic hypofunction in systemic lupus erythematosus and primary Sjogren syndrome. Medicina 1993;53:397-400.