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Case report

Overwhelming pneumococcal bacteraemia in systemic lupus erythematosus*

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SUMMARY An 18 year old woman presented with fulminant pneumococcal bacteraemia and subsequently died with multisystem organ failure. A search for diseases predisposing to overwhelming encapsulated bacterial infections was negative except for previously undiagnosed systemic lupus erythematosus (SLE). This case emphasises the severity of immune system dysfunction in some patients with SLE, regardless of immunosuppressive treatment. The possible relation between Fc receptor dysfunction and pneumococcal bacteraemia in SLE is discussed.

Key words: septicaemia, infection susceptibility, splenic dysfunction.

Infection occurs at an increased rate in patients with systemic lupus erythematosus (SLE) and is a principal cause of death.1,2 This increased infection rate has previously been attributed to the increased use of immunosuppressive agents.3 Regardless of immunosuppressive treatment, however, there appears to be an increased risk of infection intrinsic to SLE,4 possibly secondary to defects in the immune surveillance system.

We present a young, previously healthy patient, who died of overwhelming pneumococcal bacteraemia as the initial presentation of SLE.

Case report

An 18 year old black woman was admitted to Fitzsimons army medical centre in respiratory failure. She was in excellent health until two weeks before admission. During these two weeks she complained of malaise, intermittent lower extremity arthritis, and chest pain compatible with pericarditis. In the 24 hours preceding admission the patient experienced rigors, high fever, and rapidly progressive respiratory distress.

Past medical and surgical histories were unremarkable. Her mother had died of overwhelming bacterial infection while receiving immunosuppressive drugs for SLE several years earlier.

On examination the patient was in severe respiratory distress. Her pulse was 150 beats a minute, blood pressure 105/70 mmHg, temperature 39.5°C, and respirations shallow and laboured at 40 breaths a minute. Auscultation of the chest showed diffuse crackles in both lung fields and an intermittent pericardial rub. The left knee was warm and tender with a demonstrable effusion. The remainder of the examination was unremarkable.

Laboratory investigation showed a packed cell volume of 0.333 and a white cell count of 9.5×10⁹ cells/l with 35% neutrophils and 47% band forms. Intracellular cocci were seen on a peripheral blood smear. An arterial blood sample drawn while the patient was breathing room air showed a partial pressure of oxygen (Pao₂) of 5.2 kPa, a partial pressure of carbon dioxide (Paco₂) of 5.2 kPa, and pH 7.22. The chest roentgenograph showed bilateral lobar infiltrates, cardiomegaly, and a small pleural effusion. An echocardiogram confirmed a small pericardial effusion without evidence of cardiac tamponade. Surgical consultation resulted in the administration of broad spectrum antibiotics. Despite a positive blood culture, improved over the subsequent 24 hours but was breathing room air showed a partial pressure of oxygen (Pao₂) of 5.2 kPa, a partial pressure of carbon dioxide (Paco₂) of 5.2 kPa, and pH 7.22. 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compromise. A left knee arthrocentesis showed 1.8x10^9 cells/l, 100% lymphocytes, with negative Gram stain and culture. Sheets of polymorphonuclear cells and abundant Gram positive diplococci were seen on Gram stains of sputum.

On admission to the medical intensive care unit the patient required ventilatory support. Treatment with penicillin and cefotaxime was initiated for presumed bacteraemia. Severe lactic acidosis and recurrent bouts of hypotension necessitated continuous intravenous infusions of sodium bicarbonate and dopamine respectively. Her course was complicated by the development of clinical and laboratory evidence for disseminated intravascular coagulation. By the second hospital day there was progressive renal, cardiac, hepatic, and respiratory failure. Blood and sputum cultures were positive for Streptococcus pneumoniae. Despite aggressive medical management the patient's condition continued to deteriorate, and she died on the third hospital day.

While in hospital the patient was evaluted for diseases predisposing to overwhelming pneumococcal bacteraemia. A haemoglobin electrophoresis, serum protein electrophoresis, and immunoglobulins measured quantitatively were normal. At necropsy bilateral pneumonia and serosal haemorrhage consistent with disseminated intravascular coagulation were noted. The spleen was normal, except for minimal germinal centre atrophy and mild periartrial fibrosis.

Owing to the patient's family history and suggestive symptoms during the two weeks preceding admission, a diagnosis of SLE was considered. An antinuclear antibody determination was positive at a titre of ≥1/256 in a speckled pattern. Analysis for specific antibodies showed a positive anti-SSA, positive anti-Sm at a titre of ≥1/128 by counterimmunoelectrophoresis, and raised anti-double-stranded DNA antibody of 29% binding by Millipore filter assay (normal <10%). The positive anti-Sm antibody and raised DNA binding coupled with the clinical evidence of arthritis and serositis supported a diagnosis of SLE. Other studies showed a C3 of 120 mg/l (normal 830-1770), C4 of 20 mg/l (normal 150-450), CH50 of 8 units (normal 32-128), and circulating immune complexes raised at 64% (normal 0-13%) by the C1q assay. Complement levels of a twin sister were normal, ruling out a congenital complement deficiency.

Discussion

Our patient's course of fulminant pneumococcal bacteraemia, disseminated intravascular coagulation, and multisystem organ failure is identical with the syndrome of infection after splenectomy previously reported. A search for other diseases associated with this syndrome, including thalassemia, sickle cell disease, immunoglobulin deficiency, congenital complement deficiency, and splenic abnormalities, was negative. This is the first reported case of overwhelming pneumococcal bacteraemia occurring as the presenting manifestation of SLE. The absence of immunosuppressive treatment highlights the intrinsic risk of immune system dysfunction in some patients with SLE.

The immune system abnormality predisposing this patient to develop overwhelming pneumococcal sepsis is probably due to a defect in bacterial clearance by the patient's reticuloendothelial system. Previous reports have suggested an increased risk of infection with encapsulated bacteria, especially salmonella and the pneumococcus, in patients with SLE. To be cleared from the blood stream encapsulated organisms require opsonisation with specific immunoglobulin and complement facilitating attachment to splenic macrophages via Fc and complement receptors. Internalisation and killing can then occur. Thus the defect in some patients with SLE could relate to a defect in opsonisation, Fc receptor function, or tissue macrophages.

There have been no studies evaluating the ability of sera from patients with SLE to opsonise encapsulated bacteria. One recent report found a decreased ability of sera from patients with SLE to opsonise other bacteria, including certain strains of staphylococci, owing to interference by circulating immune complexes. The possibility that circulating immune complexes interfere with the ability to opsonise encapsulated bacteria has not been similarly investigated. The role of hypocomplementaemia in this patient's clinical course is unclear as we do not know the complement levels before the development of bacteraemia, and thus the contributions of her bacteraemia and SLE in inducing hypocomplementaemia cannot be discerned.

A defect in Fc receptor function and the reticuloendothelial system has been recorded in some patients with SLE. A few patients had irreversible defects with splenic atrophy and marked lymphocyte depletion found at necropsy. In others the defect has been at least partially reversible and correlated best with disease activity and titre of circulating immune complexes. This led early investigators to suggest circulating immune complexes were saturating Fc receptors, thereby blocking attachment and clearance of opsonised antigens. According to this theory the number of available Fc receptors on the surface of mononuclear phagocytes in patients with SLE should be reduced. Fries et al, however, showed a 40% increase in the number of available...
Fc receptors on the cell surface of blood monocytes of patients with SLE. This finding suggested a primary defect in Fc receptor function in SLE and not an acquired blockade by circulating immune complexes. In fact this defect may allow both opsonised particles and circulating immune complexes to accumulate in the circulation. This may explain the increased risk of infection and the ability of immune complexes to be deposited in various tissues, causing the diverse clinical manifestations of SLE.

Further investigation has shed some light on the conflicting reports of decreased Fc receptor function associated with increased Fc receptor number. Salmon et al demonstrated significantly decreased Fc receptor mediated internalisation of opsonised particles in patients with SLE despite increased Fc fragment-Fc receptor binding. Although the extent to which this internalisation defect is involved in SLE remains unknown, it may explain several aspects of disease activity and the intrinsic increased risk of severe infections by encapsulated organisms.

Owing to our patient’s rapid demise, it was impossible to delineate a specific defect in the reticuloendothelial system or the Fc receptor. The marked degree of bacteraemia (organisms seen on the peripheral blood smear) and increased circulating immune complexes, however, point to a defect in the immunological clearance pathway. As previously mentioned there are few data to support an opsonisation defect, and at necropsy the spleen showed no significant atrophic changes, suggesting our patient’s dysfunction may have been at the level of the Fc receptor. We therefore present this case as a possible clinical correlate to the in vitro studies documenting a defect in the Fc receptor. This case highlights the increased risk of overwhelming pneumococcal infection in some patients with SLE. If the defect is at the level of the Fc receptor the use of the pneumococcal vaccine may be of little or no help in preventing this often fatal complication.

References
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