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Case report

A case of systemic lupus erythematosus with sideroblastic anaemia terminating in erythroleukaemia

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SUMMARY A case of systemic lupus erythematosus is described in which for 10 years the only significant findings were erythema multiforme and vasculitis. Gross hepatosplenomegaly with persistent pancytopenia developed, and bone marrow examination revealed the presence of sideroblasts. The patient's condition deteriorated, and subsequently she developed a severe bleeding tendency, terminating in erythroleukaemia.

Immunological disturbances, particularly autoimmunity, are frequently associated with chronic lymphoproliferative diseases[1 2] and malignant diseases.[3 4] But a close relationship between a disturbed immunological mechanism and myeloproliferative disorder was not apparent until Finkel *et al.*[5] reported on the frequent occurrence of an autoimmune phenomenon and abnormally high concentrations of immunoglobulins in a study of 49 patients with the Di Guglielmo syndrome.

In this report we describe a patient with systemic lupus erythematosus who developed a refractory normoblastic anaemia with gross hepatosplenomegaly. An initial bone marrow study revealed the presence of sideroblasts. Terminally the marrow showed a picture consistent with erythroleukaemia.

Case report

CLINICAL HISTORY

A 55-year-old Chinese housewife had been seen for recurrent erythema multiforme and erosive lesions in her legs for 10 years by a private skin specialist. Investigations carried out during this period in the Dermatological Hospital did not reveal anything significant.

In February 1976 she developed erythematous lesions over her face and alopecia. Tests for LE cells and antinuclear factor were positive. The erythrocyte sedimentation rate (ESR) was 90 mm/h. Direct immunofluorescence of normal skin showed bands of IgM, IgG, and IgA deposits on the basement membrane. Anti-DNA (double strand) was 32 units/ml (normal less than 25 units/ml). A clinical diagnosis of systemic lupus erythematosus was made.

Physical examination at this time showed a well covered female with no anaemia, raised blood pressure, or visceromegaly. Liver function and renal function were normal. She was treated with low-dose prednisolone. She was followed up regularly at our outpatient department until September 1977, when she failed to come. Then in March 1978 she returned with history of increasing dyspnoea and fatigue. Physical examination now revealed profound anaemia, hepatomegaly of 8 cm, and splenomegaly of 4 cm. She was admitted for investigations.

INVESTIGATIONS

On her first admission in February 1976 haemoglobin was 10·2 g/dl. Urine microscopy revealed mild haematuria and a trace of albumin. Renal biopsy showed mesangial widening and hypercellularity. On electron microscopic examination the mesangium was widened and contained heavy electron deposits (Fig. 1). Virus-like particles were also present in the endothelial cell cytoplasm. Immunofluorescent antibody studies showed moderate (grade 2+) deposits of antihuman IgG, IgM, C3, Clq, and C4 in the mesangium (Fig. 2).

In March 1978 investigations showed haemoglobin 3·7 g/dl, leucocyte count 2×10^9/l, platelets 10×10^9/l, reticulocyte count 2·8%. Peripheral blood film showed normochromic and normocytic cells. The ESR was 160 mm/h, urea 55 mg/dl

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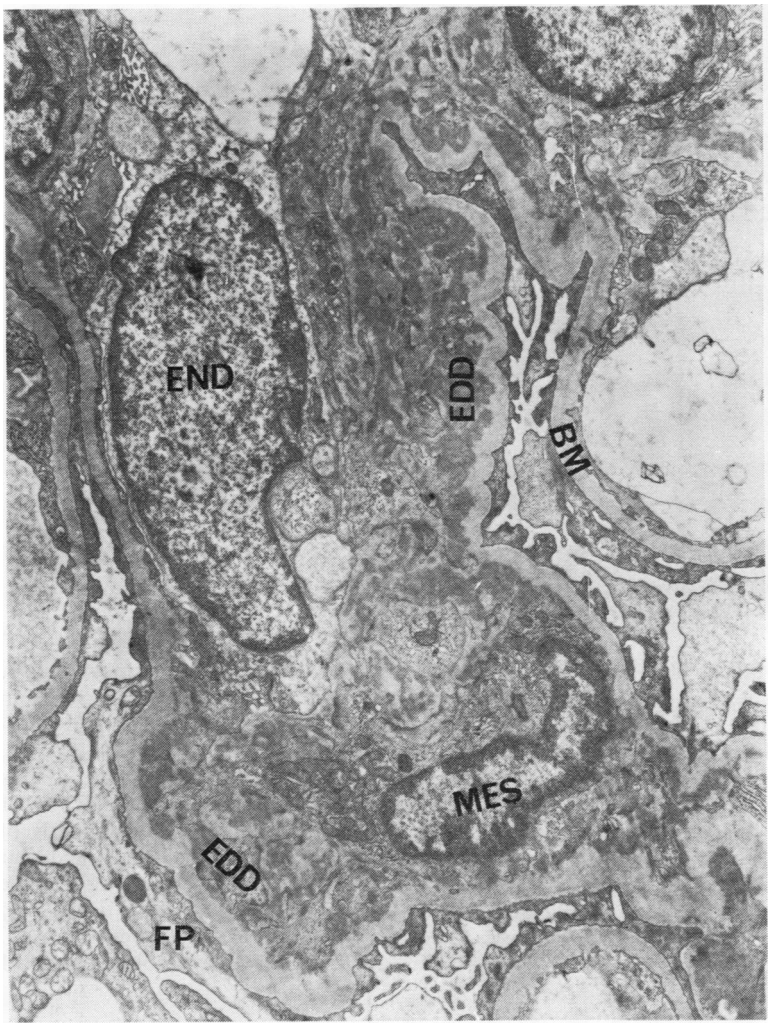

Fig. 1 *Electron micrograph of a portion of a glomerulus. The mesangium is widened and contains electron dense deposits* (EDD). END=*endothelial cell*, MES=*mesangial cell*, BM=*basement membrane*, FP=*foot process*. (×4200).

(9·1 mmol/l). The prothrombin time and partial thromboplastin time were normal. The serum iron was 210 μg/dl (38 μmol/l), total iron binding capacity 260 μg% (47 μmol/l). Serum folate and B12 were normal. The leucocyte alkaline phosphatase score was 160 (normal 52). Direct Coombs test, LE cells, and RA factor were negative. A test for antinuclear factor was positive. Complement studies showed low total complement, Clq, C3, and C4. Immunoglobulins were normal. Liver function tests were normal. A liver scan showed a large liver with no filling defects. A liver biopsy showed no diagnostic features.

A bone marrow aspirate showed small fragments with patchy cellularity. There was evidence of maturation disturbance in the red cell series, with presence of megaloblastoid cells. There was also reduction in granulocyte series with relatively few myeloid forms seen. Prussian blue stains for iron showed markedly increased iron stores, with presence of ring sideroblasts (Fig. 3). A diagnosis of sideroblastic anaemia was made on the basis of the presence of ring sideroblasts. However, the bone marrow features suggested a possible associated preleukaemia.

PROGRESS

The patient was started again on steroids supplement with folic acid. Her haemoglobin rose to 8·6 g/dl and the ESR dropped to 12 mm/h. No blood transfusions were given at this time.

On a routine follow-up in July 1978, 7% blast

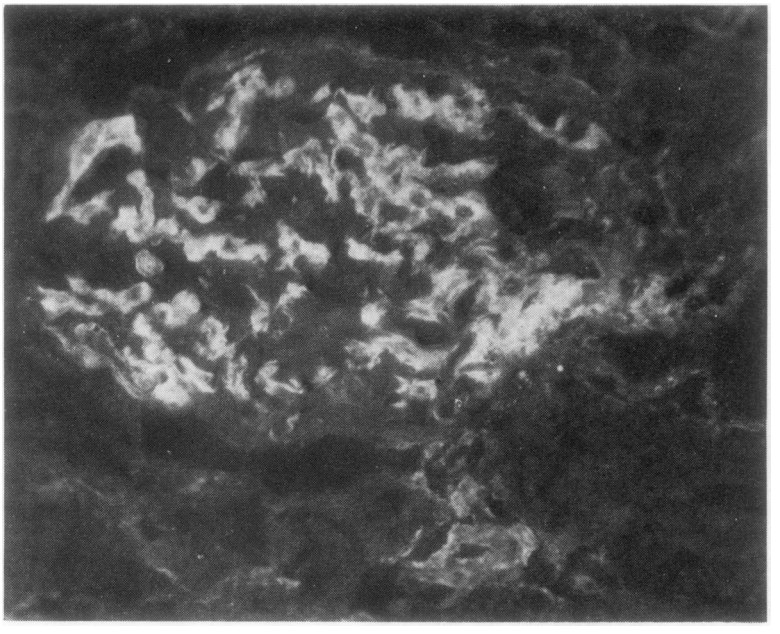

Fig. 2 *Immunofluorescent antibody study showing moderate (grade 2+) fluorescent deposits of anti-Hu-IgG predominently in the glomerular mesangium (125 ASA 60 sec, × 300).*

cells were seen in the peripheral blood. The blood film now showed marked variation in size and shape of the red cells, with presence of macrocytes and punctate basophilic normoblasts. Blasts, myelocytes, and metamyelocytes were also present. Giant platelets were also seen (Fig. 4).

Bone marrow examination at this time showed intense and abnormal activity, with megaloblastoid changes and increase in proerythroblasts and binucleated and multinucleated erythroblasts (Figs. 5 and 6). There was still depression of the granulocytic series, with few mature forms present. The megakaryocytes were also abnormal in morphology. The periodic acid Schiff stain for normoblasts in the marrow was positive. A diagnosis of erythroleukaemia was made.

Although the patient was asymptomatic at this time her condition began to deteriorate by October 1978. By December she had gross splenomegaly of 10 cm and liver span was 16 cm at the midclavicular line. Her haemoglobin dropped to 4·9 g/dl. The total white cell count was 30×10^9/l with 23% blast cells. The other investigations showed: platelets 10×10^9/l, ESR 34 mm/h, blood urea 191

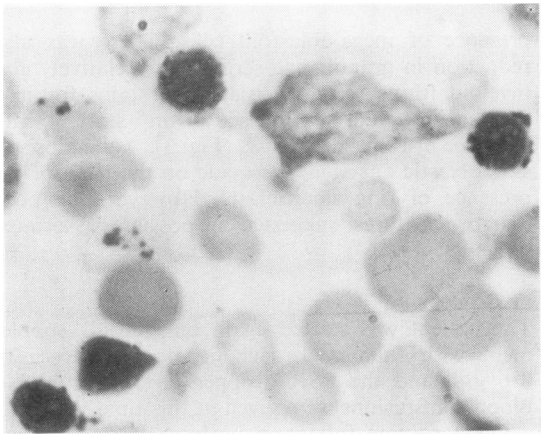

Fig. 3 *Bone marrow, with markedly increased iron stores and ring sideroblasts. (Prussian blue).*

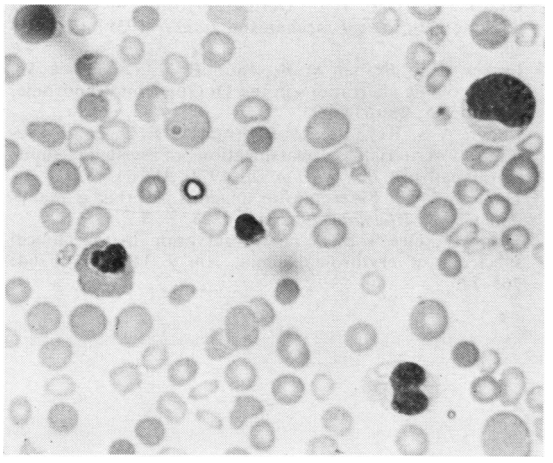

Fig. 4 *Peripheral blood film: marked variation in size and shape of the red cells, with normoblasts, blasts, myelocytes, and metamyelocytes.*

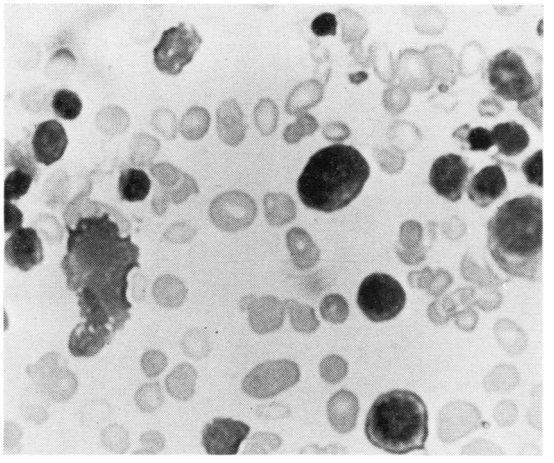

Fig. 5 *Bone marrow: intense and abnormal erythroid hyperplasia and multinucleated erythroblast.*

mg/dl (31·7 mol/l), serum creatinine 3·6 mg/dl (318·2 μmol/l). She eventually developed a bleeding tendency and died in spite of intensive supportive treatment. A formal necropsy was refused. A post-mortem liver biopsy showed heavy periportal and sinusoidal cellular infiltrate consisting of both primitive red and white blood cell series and megakaryocytes. The spleen also showed diffuse infiltration by cells of the erythroid and myeloid series. These changes were consistent with infiltration by erythroleukaemia.

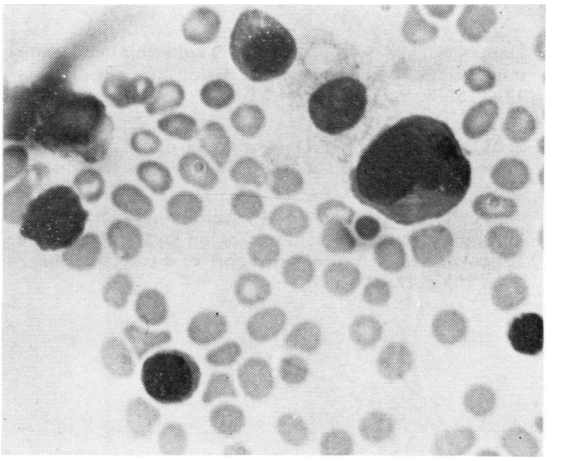

Fig. 6 *Bone marrow: intense and abnormal erythroid hyperplasia and multinucleated erythroblast.*

Discussion

This patient presented with classical systmic lupus erythematosus having fulfilled the diagnostic criteria of the American Rheumatism Association.[6] Erythroleukaemia was eventually confirmed by bone marrow examination. In the early stage of the disease, i.e., the stage of erythraemic myelosis, sideroblasts are commonly seen in this condition as well as in many other myeloproliferative syndromes.[7]

In one large review of 49 patients with erythroleukaemia 17 patients showed at least one distinctly unusual immunological feature.[5] The majority had only in-vitro signs of autoimmunity without overt signs of the disease. Only 1 patient had definite systemic lupus erythematosus before signs of primary bone marrow dysfunction and erythroleukaemia developed. Our patient is the second such patient to be reported.

Similarly in a more recent report of 46 patients with erythroleukaemia multiple abnormalities of the immune system were also noted.[8] 30% of these patients have nonspecific rheumatic complaints, including chest, joint, and abdominal pain. None of these patients had specific collagen or collagen vascular disease. Hence, although an association of erythroleukaemia with symptomatic rheumatic disease and numerous immunological aberrations has been established, the immunopathogenetic mechanisms have yet to be established. In conclusion this clinical complex should be sought in all cases of erythroleukaemia and in cases of rheumatic disease presenting with refractory normoblastic anaemia.

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