Case Report

Systemic lupus erythematosus, repeated abortions, and thrombocytopenia

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SUMMARY A case is described of severe thrombocytopenia in a pregnant patient with mild SLE. Three previous pregnancies had ended in abortion. Attempts to reverse the thrombocytopenia with steroids, plasmapheresis, and splenectomy failed, the platelet count returning to normal immediately after the death of the fetus at 20 weeks gestation.

It is known that patients suffering from systemic lupus erythematosus (SLE) may show a deterioration in their disease during pregnancy, and that spontaneous abortions are frequent (Grigor et al., 1977). This report describes a case in which for several years the only significant symptom of SLE was mild thrombocytopenia; however, during this time 4 pregnancies ended in spontaneous abortion, and 2 of these were complicated by severe, potentially life threatening thrombocytopenia.

History

The patient is a 31-year old woman. She gave a history of 3 previous pregnancies in 1970, 1971, and 1975 all of which ended in spontaneous abortion between 18 and 24 weeks. The second pregnancy was complicated by episodes of purpura and thrombocytopenia with platelet counts of around 20 x 10^9/l. These responded to oral prednisone. The platelet counts did not fall significantly during the first and third pregnancies.

When first seen in Cardiff in December 1973, SLE had already been diagnosed on the basis of a positive anti-nuclear factor and a DNA binding of 70%. She had been prescribed 10 mg prednisone on alternate days with 100 mg azathioprine daily. The latter was stopped without any ill effects, and her only symptoms were occasional attacks of arthralgia. Her platelet count varied between 70 and 140 x 10^9/l with occasional episodes of mild purpura.

She was admitted to hospital in January 1977, during the 14th week of her fourth pregnancy, at the request of her obstetrician, because of a steadily deteriorating thrombocytopenia, which had failed to respond to raising the prednisone dose to 80 mg daily. On admission she was found to be in excellent physical health, there was no bruising, purpura, bleeding from any source in spite of a platelet count of 20 x 10^9/l. It appeared from her notes that the platelet count 3 weeks earlier had been in the region of 200 x 10^9/l, but had shown a steady decline since then, in spite of massive increases in steroid dosage. The fetus was alive, according to the Sonicaid findings.

Investigations and management

Investigations showed a haemoglobin (Hb) of 15 g/dl, normal urea, electrolytes and liver function tests, ESR 13 mm/h, DAT 1/32 and an active bone marrow with abundant megakaryocytes. Complement studies showed low CH50, C3 and C4 but normal factor B. Complement fixing platelet and red cell antibodies were also found (Fig. 1) although, no cryoprecipitate or anticomplementary activity could be detected at any time.

The chances of a successful pregnancy in the presence of severe thrombocytopenia and high steroid dosage were considered to be very small. Two further methods were therefore proposed to reverse the thrombocytopenia; plasmapheresis to remove the platelet autoantibodies and splenectomy. Plasmapheresis was tried first, as it has been successfully used in pregnancy for the removal of antibodies. Rhesus antibodies with no ill effects on the fetus.
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(Fraser et al., 1976). The procedure was carried out 3 times at 4-day intervals, each exchange consisting of 41. Platelet counts, complement factors, and platelet antibodies were monitored before and after each exchange but apart from a slight improvement in the platelet count after the first episode, there was no change whatsoever in any of the other parameters, and it was abandoned (Fig. 1).

Although splenectomy carried a high risk of spontaneous abortion during or immediately after the operation, it was felt that this now offered the only chance of a successful outcome to the pregnancy. The patient was kept fully informed of the situation throughout, and agreed to splenectomy. This was carried out on February 9, 1977. For the next 5 days there was no change in any haematological or biochemical parameter, except for a slight rise in platelets due to transfusion during the operation. The fetal heart remained audible. Thereafter, however, the fetal heart sounds could no longer be heard and simultaneously a rise in the platelet count was observed. This continued and reached 250 x 10⁹/l after a week (Fig. 2). The complement and anti-platelet antibody levels also returned to normal during this time, and within 10 days of splenectomy the Gravindex test had become negative. The pregnancy was considered to be non viable, and a therapeutic abortion was performed. The fetus was small and macerated.

The platelet count remained at around 250 x 10⁹/l for the remainder of her stay in hospital, but fell to 160 x 10⁹/l on discharge on March 1. Since then, it has fluctuated between 90 and 200 x 10⁹/l. She remains in good health, taking only 7.5 mg of prednisone daily.

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Fig. 1 Composite graph showing values of the complement components C₃, C₄, and factor B, before, during and after plasmapheresis, together with the platelet antibody titre and total platelet count.

Fig. 2 The changes in platelet count and prednisone dosage in the time interval described in the report.
Discussion

Apart from minor improvements all 3 methods used to reverse the thrombocytopenia, ie, high dose steroids, plasmapheresis, and finally splenectomy were without effect. Since the platelet autoantibodies that had been detected during pregnancy on several occasions were shown to fix complement, it was concluded that their destruction was occurring primarily within the circulation—a hypothesis supported by the findings of a normal sized spleen at splenectomy, and reduced levels of complement in the serum. It was also assumed that the mild thrombocytopenia that existed in the non pregnant state was due to the same antibodies at a much lower titre.

In 25% of samples from their patients with SLE, Stastry and Ziff (1971) reported that, platelets were capable of fixing complement even in the absence of serum, suggesting that the platelets were already coated with antibody. This did not occur in normal controls.

The failure of plasmapheresis to remove these antibodies implies a high rate of synthesis. This procedure is often disappointing in the treatment of SLE, possible for this very reason, but it has been used with success in acute life threatening situations when there is good evidence of circulating immune complexes (Verrier Jones et al., 1976; Moran et al., 1977).

Assuming the platelet count inversely reflected autoantibody activity, the effect of the pregnancy on the rate of autoantibody production could be closely monitored. The platelet count was seen to fall steadily over a period of about 5 weeks between the ninth and 14th week of the pregnancy, and to rise rapidly at a time coincident with the apparent demise of the fetus. Presumably, therefore, the autoantibody production increased steadily from its non pregnant level to its maximum over this period and stopped suddenly when the pregnancy ended (Fig. 2).

The cause of the repeated abortions, during the trimester generally considered to be the safest is unclear.

Lymphocytotoxic antibodies which have been shown to be present in 80% of patients with SLE are also present in the majority of patients suffering repeated miscarriages. They are however usually absent in patients with SLE who have successful pregnancies (Bresnihan et al., 1977). Our patient, in spite of her history, had only slightly raised levels of lymphocytotoxic antibodies.

In cerebral lupus, lymphocytotoxic antibodies have been shown to cross react with brain tissue (Blue- stein and Zvaifler, 1976, Bresnihan et al., 1977), but it is not yet clear whether a similar cross reactivity between such antibodies and placental tissue exists in patients who suffer repeated abortions.

Lymphocytotoxic antibody tests were carried out by Dr G. R. V. Hughes, Royal Postgraduate Medical School, London.

References


