A CASE OF ACQUIRED HAEMOLYTIC ANAEMIA ASSOCIATED WITH PREGNANCY

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Acquired haemolytic anaemia associated with pregnancy is an uncommon occurrence, although there have been isolated reports of this condition. In the case presented here, an acute haemolytic crisis of a presumably acquired type made its first appearance in a pregnant woman and subsided shortly after delivery.

CASE REPORT

History

A patient, aged 28 years, was admitted to the Beilinson Hospital on 12 October 1958 in the fifth month of her first pregnancy. She complained of extreme weakness, palpitations, and respiratory distress. These symptoms had started a month earlier. A blood examination performed then had shown a haemoglobin of 7 g. per 100 ml. and a red cell count of 2,000,000 per c.mm. Intensive treatment with iron, vitamin B_{12}, and folic acid failed to improve her blood picture.

The patient was already known from 2 previous hospitalizations (1954, 1958) to be suffering from mitral stenosis and aortic insufficiency, proved by X-rays and cardiac catheterization. Blood examinations on both occasions were found to be within normal limits. At that time, conservative treatment produced a fairly good compensation.

On admission to the medical department, the patient displayed a marked pallor with no detectable icteric tinge. She had a severe orthopnoeic dyspnoea. Her blood pressure was 130/70 mm.Hg and her pulse-rate was 130 per minute. Her temperature was normal. There was no glossitis or brittle nails. The liver, spleen and lymph nodes were not palpable. The size of the uterus corresponded to the duration of the amenorrhoea. Auscultation of the heart confirmed the diagnosis of mitral stenosis and mild aortic insufficiency. Delicate râles were heard over the bases of both lungs.

Laboratory Investigations

The blood examination gave the following information: haemoglobin 4·6 g. per 100 ml.; red cell count 1,600,000 per c.mm.; haematocrit 18%; leucocytes 5,000 per c.mm.; platelet count 184,000 per c.mm.; reticulocytes 8·4%. The blood film showed marked anisocytosis with macro- and poikilocytosis,

moderate polychromasia and occasional nucleated red cells. Megalocytes and spherocytes were not found. The differential count was normal.

Bone marrow smears showed a striking proliferation of normoblasts without maturation abnormalities. Numerous haemosiderin-loaded macrophages were seen. The serum iron was 156 μg. per 100 ml. and the serum bilirubin 2·2 mg. per 100 ml. The 24-hour faecal urobilinogen excretion was raised on several occasions (350 - 500 mg.). Repeated examination for occult bleeding was negative. There was 1·2% alkali-resistant haemoglobin, but no electrophoretically abnormal components; osmotic and mechanical fragility of the erythrocytes was normal. The antiglobulin test (with the aid of papin-, fycin- and trypsin-treated cells), the Ham test and the Crosby test, cold agglutinins, and haemolysins, were all found to be negative. The urine and blood biochemistry was normal. Blood cultures remained persistently sterile. Haematological investigations of family members did not disclose any hereditary blood disorder.

Treatment and Follow-up

Conventional anti-anaemic treatment failed to prevent a rapid deterioration in the patient's condition. She was therefore given 3 transfusions of packed red blood cells (350 c.c. each) at short intervals. The haemoglobin went up to 8 g. for 2 days, then dropped rapidly and remained low despite 2 additional blood transfusions. It was then decided to attempt steroid therapy. The patient received 30 mg. meticorten daily for 3 weeks. At the end of that period, her haemoglobin rose to 8 g. per 100 ml. An increase of the daily dose of meticorten to 40 mg. resulted in an even more rapid and convincing response as the haemoglobin reached 11 g. per 100 ml. and the erythrocyte count 4,000,000 per c.mm. The faecal urobilinogen output and the reticulocyte count returned to normal. The general condition of the patient improved markedly. However, any attempt to maintain these therapeutic results with a smaller dose of meticorten caused a recurrence of the anaemia and an immediate increase in the faecal urobilinogen.

In the eighth month of her pregnancy, the patient gave birth by spontaneous delivery to a healthy and haematologically normal baby. Her haemoglobin dropped once more to 9 g. per 100 ml., due to loss of blood during the third stage of labour. She was given a transfusion of packed red cells and continued to receive meticorten in decreasing amounts. Two-and-a-half months after delivery her haemoglobin was again 12 g. per 100 ml. and the red cell count 4,000,000 per c.mm., allowing the ultimate withdrawal of the steroids with no further deterioration.

For a period of 9 months since this time the patient was under constant haematological supervision. Her blood picture remained normal, and she underwent a successful cardiac operation with no adverse effect on her blood condition.

DISCUSSION

The name 'haemolytic anaemia of pregnancy'[1] has not gained universal acceptance as describing a separate clinical and aetiological entity. This is probably due to the fact that various factors might be held responsible for an increased red-cell destruction in pregnant women. It is known that megaloblastic anaemia is associated with diminished viability of erythrocytes[2] which, in isolated cases, might be so pronounced as to simulate a primary haemolytic syndrome. Acute haemolytic episodes have been described in late pregnancy or early in the puerperium.[3] A sudden onset with fever, leucocytosis, reticulocytosis and a megaloblastic type of anaemia are their main features. These cases have been identified as haemolytic anaemia of the Lederer type, a controversial entity, frequently mentioned in the literature. They respond promptly to single blood transfusions and liver therapy. These cases might very well be megaloblastic anaemias with exaggerated haemolysis resulting from some intercurrent infection.

Still more confusing are cases of primary haemolytic anaemia in pregnant women with megaloblastic transformation due to secondary vitamin B_{12} or folic acid depletion.[5] This variety of anaemia is not improved by the administration of the deficient haemopoietic factors, although a return to normocytosis has been observed.[6]

Difficulties may also arise when trying to distinguish between congenital and acquired types of haemolytic anaemia in pregnancy. It is usually accepted that the diagnosis of the congenital type requires the presence of familial features and signs of corpuscular defect, such as spherocytosis, sickling, increased fragility of the erythrocytes, abnormal haemoglobins, etc. Yet, this is not always the rule. Cases of latent congenital haemolytic anaemia are known to appear for the first time in adult life, and in the absence of a positive family history.[7] Association of such instances with pregnancy have also been described.[8] Isolated spherocytes or a mildly-increased osmotic fragility may be encountered in acquired haemolytic anaemia, whereas the antiglobulin test has been reported positive in definite cases of the congenital type.[9]

The recognition of the acquired mechanism of a haemolytic anaemia usually rests on positive serological evidence. In cases in which no immune factors are detected, survival studies of transfused normal red cells have been used, and decreased viability, whenever found, has been taken as proof of an extracorpuscular mechanism of the haemolysis.[6]

The clinical approach might be useful in discerning haemolytic anaemia secondary to some underlying disease such as leukaemia, malignant lymphoma, systemic or infectious disease or exposure to injurious agents, whose association with pregnancy is a potential possibility. Haemolytic anaemia may accompany complications due to the pregnancy proper, such as eclampsia or toxaemia of pregnancy.[10-13] A case of haemolysis associated with toxaemia in 2 consecutive pregnancies has been reported.[14]

When all these considerations are taken into account, only a few cases of an acquired anaemia appearing in a normally proceeding gestation with no detectable signs of some concomitant disease may be found in the literature. In these rare cases, the anaemia completely subsided[15] or was greatly improved after delivery.[6,16]

In the case presented here, we find all the necessary criteria of an acute haemolytic syndrome of the acquired type. There was a sudden and rapidly-progressing anaemia in a woman whose personal and familial haematological background, confirmed by the appropriate investigations, could not disclose any hereditary disorder. Neither could evidence of toxaemia or exposure to injurious agents be detected. No underlying disease liable to promote haemolysis could be found. The anaemia was associated with definite signs of increased red-cell destruction, such as elevated serum-iron and bilirubin levels, increased excretion of faecal urobilinogen, peripheral reticulocytosis, and normoblastic proliferation in the bone marrow. Furthermore, repeated apparently compatible transfusions failed to achieve any lasting improvement of the anaemic condition, and an immediate increase of the faecal urobilinogen output resulted. This pointed to an indiscriminate destruction of the donor's as well as the patient's red cells,

hence to an extracorpuscular reason for the haemolysis. The anaemia responded favourably to steroid therapy, as anaemias of auto-immune origin usually do, although repeated serological investigations failed to disclose the presence of immune haemolytic factors of any type. The negative serological results in this particular type of acquired haemolytic anaemia in pregnant women have been recognized in all the abovementioned reports. The observation of the favourable effect of steroid therapy has been confirmed.[6]

An interesting feature of this anaemia was its association with gestation and its rapid subsidence after delivery. The relationship between haemolysis and pregnancy, whether incidental or precipitating, has been frequently debated.[17,18] However, no one has been able to advance any definite proof of a possible immunological or hormonal mechanism,[19] and the problem still awaits further elucidation.

SUMMARY

A case of acquired haemolytic anaemia associated with pregnancy is described. The use of meticorten brought the haemolysis under control. Only after delivery did the blood picture return to normal without steroid treatment. Aspects of the diagnostic problem of acquired haemolytic anaemia during pregnancy are discussed.

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