RECURRENT BLOOD-COAGULATION FAILURE IN PREGNANCY WITH BIRTH OF A LIVE CHILD

BY

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The following case is remarkable for the occurrence and reoccurrence of coagulation failure in the course of a continuing pregnancy which resulted in the birth of a live child. It also shows that even when a patient has recently had coagulation failure this is not necessarily the cause of post-partum haemorrhage. At the time of the severe post-partum bleeding, blood was clotting adequately. Our experience is that only a few cases of obstetric hypofibrinogenaemia are complicated by post-partum haemorrhage, but when this does occur it is usually due to failure of uterine retraction. When post-partum haemorrhage occurs in association with defective blood clotting it is more important to stimulate uterine contraction than to correct the coagulation defect.

Case History

A married woman aged 33 was pregnant for the tenth time. Her first, third, fourth, and fifth pregnancies had ended in first-trimester abortions; in the second a macerated foetus was delivered at 39 weeks; in the sixth and seventh miscarriage followed intrauterine death at mid-pregnancy. No cause was found for these unsuccessful pregnancies. Two normal pregnancies then occurred, resulting in live children. None of the pregnancies was complicated by abnormal bleeding and at no other time had the patient noted any tendency to bruise easily or bleed excessively. The menses were regular and the loss was normal. The last period began on July 22, 1960. Slight vaginal bleeding occurred at 8 and 12 weeks. The patient first attended Mill Road Maternity Hospital, Liverpool, on December 2. A normal 19 weeks pregnancy was confirmed. (Blood-pressure 110/70 mm. Hg; urine free from albumin, Wassermann reaction negative; haemoglobin 12.4 g./100 ml.)

Six hours after this examination the patient developed lower abdominal pain and fainted at home. She was unconscious for three minutes and vomited blood.

She was referred to Liverpool Royal Infirmary as a case of haematemesis, but on reaching hospital a heavy vaginal

loss of unclotted blood occurred. She was pale, sweating, and appeared moderately shocked. Her blood-pressure was 115/80 mm. Hg, pulse rate 100 a minute, and haemoglobin 10 g./100 ml. Foetal movements had been absent since the onset of her symptoms. The uterus was tense and tender, and unclotted blood trickled from the vagina. During the recording of the blood-pressure petechiae appeared on the forearm and subsequently more appeared spontaneously on the trunk and thighs. Venous blood failed to clot, as did citrated blood to which thrombin had been added (Scott, 1955). Continued oozing occurred from the venepuncture site.

A diagnosis of abruptio placentae with coagulation failure was made. Immediate treatment was by the transfusion of 2 pints (1,140 ml.) of blood. The foetus was presumed dead, and induction of labour was attempted. A tightly closed cervix made amniotomy impracticable and an oxytocin infusion produced no response. Twelve hours later her condition had improved greatly. Bleeding had ceased and clotting was restored. Within 48 hours the fibrinogen level was normal (see Chart) and foetal movements were felt once more.

The clotting-time 12 hours after admission was 13 minutes, bleeding-time 2 minutes, and platelet count 125,000/c.mm. Prothrombin time (Quick, 1942) gave a ratio of twice normal and only a poor clot formed, but the prothrombin concentration (Owren and Aas, 1951) was 100%, suggesting a fibrinogen deficiency, possibly with factor V deficiency. Such a combined deficiency has been described (Johnson *et al.*, 1952; Greenwalt and Triantaphyllopoulos, 1954).

The patient was kept in hospital but no further bleeding occurred; repeated checks on blood coagulation showed no abnormality. She was discharged after 14 days, only to return three days later having had slight vaginal bleeding. This had followed intercourse and was not associated with any evidence of shock or concealed haemorrhage. Coagulation tests all gave normal results. After five days she was allowed home once more, but was admitted yet again three days later. She complained of lower abdominal pain associated with faintness and vaginal loss of unclotted blood. On admission her general condition was good and she was not shocked, but the uterus was again tense and tender, foetal heart sounds were not heard, and foetal movements were not felt. Again there was indefinite prolongation of the clotting-time. Uterine bleeding ceased soon after admission and, as there was no systemic disturbance, no active treatment was undertaken. Within 48 hours the fibrinogen level was restored to normal (see Chart) and all other coagulation tests gave satisfactory results. By this time the patient felt foetal movements once more.

It was decided to terminate pregnancy lest the coagulation failure recur. This was done by oxytocin infusion. On January 6, 1961, a live male foetus weighing 1 lb. 1 oz. (480 g.) was delivered and survived for 24 hours. The placenta, which followed rapidly, was incomplete and showed some pale old blood clot adherent to one portion with some fibrin deposition in this region.

Immediately after expulsion of the placenta there was loss of approximately 1 pint (570 ml.) of clotted blood. Immediate exploration of the uterus produced a piece of placenta 2 in. (5 cm.) in diameter. No tears were evident and the uterus was of normal shape.

Approximately 5 oz. (140 ml.) of clotted blood was lost during this operation. Shortly afterwards, despite intravenous infusion of oxytocin and ergometrine, a massive post-partum haemorrhage occurred and the patient became pulseless. Blood transfusion was started. Uterine bleeding continued and it was noted that the blood was clotting adequately and the loss appeared to be entirely due to uterine relaxation.

Despite all measures, bleeding continued at a rate equal to or greater than blood could be replaced, and the woman's death seemed imminent. Eventually, after three and a half hours, the uterine retraction became more sustained. This

Results of serial fibrinogen estimations with episodes of coagulation failure indicated.

may have been encouraged by a hot intrauterine douche. Adequate blood coagulation was again demonstrated by the douche nozzle becoming blocked by clots. During the fifth hour after delivery only 1 pint (570 ml.) of blood was lost, and after this the loss gradually ceased. The patient had by this time received a total of 17 pints (9.7 litres) of blood and 1½ pints (850 ml.) of plasma, together with 5 mg. of ergometrine, 30 units of oxytocin, and 30 ml. of 10% calcium gluconate solution.

The haemoglobin level, which had been 10.3 g./100 ml. prior to delivery, was only 8.4 g./100 ml. on the day after. All coagulation tests done after delivery were entirely normal. The patient was discharged well 14 days after delivery.

Discussion

Blood-coagulation failure is now accepted as an uncommon but by no means rare hazard of pregnancy, and the circumstances in which it may occur have been detailed (Reid *et al.*, 1956; Hodgkinson, 1956; Jeffcoate and Scott, 1956; and Sharp *et al.*, 1958). Usually it is associated with foetal death, either in severe placental abruption or after prolonged retention of a dead foetus *in utero*. Amniotic fluid embolism, however, is a rare cause of coagulation failure which occurs when labour is tumultuous and the clotting defect may then present after the birth of a live child.

It is not surprising that coagulation failure sometimes affects the same patient in different pregnancies. Fyfe and Grant (1960) recorded such a case and we have experience of a similar happening. In the case recorded here, however, coagulation failure not only recurred 24 days later in the same pregnancy but a live foetus was eventually delivered. The cause is not certain, but inspection of the placenta suggested that a minor degree of abruption had occurred some weeks before delivery.

This case also illustrates how rapidly fibrinogen can be replenished from the natural sources (see Chart). This is important, as fibrinogen administration carries risks. If given during a period of thromboplastin release it may act as "fuel to the flames of the fibrinolytic process" and lead to a deterioration in the patient's condition (Jeffcoate and Scott, 1959), while it also may cause homologous serum hepatitis. Pritchard (1958) quotes a minimum figure of 5% based on the finding that 37 out of 727 patients treated with fibrinogen were known by the obstetrician concerned to have developed jaundice. It is likely that the true incidence was higher. Longo *et al.* (1959) record 2 cases in 38 patients (5.3%), while Skinner (1957) found that 6 out of 17 patients developed hepatitis. It is known that the homologous serum hepatitis virus is transferred in the fibrinogen fraction of plasma and the relatively large pools of plasma needed for fibrinogen preparation must increase the hazard.*

Hodgkinson (1956) recommended that patients treated with fibrinogen should receive gamma-globulin to prevent hepatitis. There seems, however, much to be said for Pritchard's (1958) advice to withhold fibrinogen in obstetric defibrinogenation except if (a) an operation becomes necessary, (b) genital-tract lacerations are present, or (c) there is post-partum failure of uterine retraction.

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*The fibrinogen available in this country is prepared from a 300-donor pool (Maycock, 1961, personal communication). Plasma is normally prepared from a 10-donor pool.

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CHRISTMAS DISEASE ASSOCIATED WITH PRIMARY CAPILLARY ABNORMALITIES

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A number of patients with capillary defects of the von Willebrand type have been shown to have antihæmophilic globulin (factor VIII) deficiency. Biggs and Macfarlane (1958), Horler and Witts (1958), and Blackburn (1961) are some of the authors who have described such cases and who have reviewed the literature on the subject. The object of the present paper is to record a demonstrable deficiency of Christmas factor (factor IX) associated with a primary capillary defect in two unrelated females. Care was taken to exclude in both patients the existence of hypertension, renal disease, diabetes mellitus, thrombo-embolic diseases, scurvy, and ovarian deficiency, all known causes of capillary abnormalities.

Case Reports

Case 1.—A confectioner's assistant aged 16 had always bruised more readily than her blood relatives and had always bled excessively after cuts and abrasions. On the single occasion when a permanent premolar tooth had been extracted, abnormal hæmorrhage had continued for three days. Incision of a small abscess in the region of the right ankle had been followed by persistent oozing of blood for 48 hours. Recurrent crops of purpura had been noticed on the feet, legs, and arms for many years. Treatment for a tuberculous right knee-joint had been completed at the age of 12; hæmarthrosis of this joint having been mistaken for