A CASE OF PLACENTA PRAEVIA COMPLICATED BY AFIBRINOGENAEMIA

BY

I. ROCKER, M.B., M.R.C.S., M.R.C.O.G.

Late S.H.O., United Cambridge Hospitals

IN view of the interest shown in the occurrence of afibrinogenaemia in pregnancy, and as there does not appear to be a reference in the British literature associating this complication with placenta praevia, the following case record is reported.

Mrs. E.W., a secundigravida aged 32, was admitted to hospital because of a sudden painless ante-partum haemorrhage of about half a pint. The pregnancy was of 34-weeks duration. Her first pregnancy, 4 years previously, had resulted in the spontaneous delivery of a live male infant at term.

On admission the patient's general condition was good, the blood pressure was 120/80 mm. Hg and a catheter specimen of urine contained no albumen. The foetus was lying transversely, the foetal heart rate was regular and there was no uterine tenderness.

On the morning following admission one pint of whole blood was transfused as the haemoglobin was 9·7 grams per cent.

The patient remained in hospital and no further bleeding occurred until the thirty-eighth week of pregnancy. Profuse bleeding commenced in the early hours of morning of the day chosen for examination under anaesthesia. An intravenous drip was commenced immediately with normal saline solution, and at this stage the patient's pulse rate was 90/min. and the blood pressure was 140/90 mm. Hg. Twenty minutes later, at the onset of anaesthesia, the patient was collapsed and the blood pressure had fallen to 100/70 mm. Hg. Blood transfusion was commenced, a lower segment Caesarean section was performed and a live female infant was extracted without difficulty. The placenta was attached to the posterior lower uterine surface and also extended to cover the internal cervical os completely. There was profuse bleeding during the early part of the operation but haemostasis was effected without undue difficulty and blood clots were forming normally. At the termination of the operation the blood pressure was 90/60 mm. Hg. Two pints of blood had already been transfused and transfusion was maintained with Dextran whilst more blood was crossmatched. The clinical estimate of the patient's blood loss was 4 pints. During the next hour there was steady improvement and the blood pressure slowly rose to 110/70 mm. Hg. Then, suddenly, profuse vaginal bleeding occurred. Ergometrine 0·25 mg. was given intravenously and the same dose was also given intramuscularly and the bleeding was arrested. The measured loss was one pint. Ten minutes later vaginal bleeding recommenced and it was also noted that the abdominal dressing was soaked with blood. On removal of the dressing blood was seen to be spurting from the centre of the wound. The clips and sutures were removed from this area but no single bleeding point was seen. The wound surfaces were just oozing blood freely. Under local anaesthesia six silk sutures were inserted into the skin and tied firmly over a large gauze roll. This arrested the haemorrhage from the abdominal wound but a trickle of blood continued to emerge from the vagina. By this time the pulse rate had risen to 132 per minute and the blood pressure was 84/50 mm. Hg. Neither ergometrine nor intravenous pitocin had any effect in controlling the bleeding. Blood transfusion was just maintaining the patient's poor general condition.

At the onset of bleeding after the operation 20 ml. of blood had been taken from the patient in order to have a reserve supply of serum. It

was noted that one hour after the collection of this blood no clot had formed. The clotting time was in fact in excess of 12 hours as by that time the blood had been used for laboratory investigation. The plasma fibrinogen level was later reported to be 90 mg. per cent. (Normal 250 mg. –350 mg. per cent.)

In view of the continued oozing and the failure of clot formation a presumptive diagnosis of acquired afibrinogenaemia was made. The following quick tests were performed, protamine sulphate, tested active solutions of thrombin and human fibrinogen were added in turn to separate specimens of the patient's unclotted blood. Only the addition of human fibrinogen resulted in the formation of a firm clot. (Two minutes.) This finding supported the presumptive diagnosis and arrangements were made for the supply of whole blood and human fibrinogen. By this time a total of 10 pints (6 litres) of stored whole blood and one pint of Dextran had been transfused and the clotting time was 10 minutes (Lee and White) though only a poor clot was formed. An intravenous injection of 420 mg. of human fibrinogen brought the clotting time down to 3 minutes. A further 1,008 mg. of human fibrinogen and 6 pints of blood (3,500 ml.) were given, 4 pints (2,300 ml.) of blood being fresh donor's blood. Bleeding had ceased after the first injection of fibrinogen and the plasma fibrinogen level was later reported as being within normal limits.

The extent of intra-peritoneal bleeding was difficult to decide, but fullness and tenderness in the flanks persisted for 7 days. The patient made a slow recovery. The urinary output steadily increased after the initial oliguria whilst hypotension existed, and partial breast feeding was also accomplished. A *Bacterium coli* urinary infection responded to a course of streptomycin. A deep calf vein thrombosis developed on the 11th post-operative day and this was treated with intramuscular heparin. Wound healing was delayed by infection and the lower half of the wound healed by secondary intention. The patient was discharged from hospital 7 weeks after her operation fit and well. The abdominal scar was unsightly and pelvic examination revealed a normally involuted, mobile anteverted uterus.

Discussion

In 1901 De Lee mentioned a haemophilic tendency in a case of "utero-placental apoplexy". Since that time many cases of prolonged bleeding due to a reduced plasma fibrinogen level have been described in association with accidental haemorrhage, amniotic fluid emboli and in cases of intra-uterine death of the foetus associated with Rhesus immunization. In 1919 Obata found that the infusion of placental extracts into mice caused blood defibrination and Sakurai (1929) confirmed this finding in dogs. Howell (1941) found that, in dogs, rapid injection of thromboplastin caused extreme intravascular clotting and death of the animal whereas sub-lethal doses produced defibrination. Schneider (1947) concluded, after extensive experiments in dogs, that thromboplastin was the toxic element contained in placental extracts which when liberated in the blood stream resulted in afibrinogenaemia. Page, Fulton and Glendenning (1951) showed that the injection of placental extracts caused a fall in the plasma fibrinogen level and that the critical level for bleeding was 200 mg. per cent.

Weiner and his colleagues (1950, 1953) studied several hundred cases of abortion, hydatidiform mole, placenta praevia and "premature separation of the placenta" and found that the plasma fibrinogen level fell after the bleeding in severe degrees of placental separation. They describe 34 cases in which they treated this complication with blood transfusion and intravenous fibrinogen. They do not, however, describe a case of placenta praevia amongst their treated cases.

It is argued that the release of thromboplastin can cause a severe depletion of the circulating fibrinogen, the liver being unable to correct the deficiency in time to prevent severe haemorrhage. Prolonged hypotension may in turn cause liver damage and so adversely affect the ability of the liver to produce fibrinogen. Page and his colleagues also describe that the injection of placental extracts in dogs caused liver necrosis.

The problem remains, however, as to the portal of entry of thromboplastin into the maternal circulation. Weiner postulates that the coagulant containing liquor is forced into the open venous sinusoids at the side of placental separation by the increasing intra-uterine pressure in labour and that the liquor is further

enriched with thromboplastin released from the decidua.

In the case described above, the amniotic cavity was intact. It is, therefore, suggested that massive blood loss alone may be a cause of acquired afibrinogenaemia. The normal plasma fibrinogen level is between 250 mg. to 350 mg. per cent. A loss of six pints of blood will severely deplete the circulating fibrinogen level even though the circulating fluid volume may be nearly normal due to transfusion. Stored blood has little fibrinogen content and Dextran in excess may further disturb the coagulation mechanism. The concurrent shock will impair liver function and so delay restoration of the plasma fibrinogen level above 100 mg. per cent. This figure is believed to be the critical level in the human. In cases of accidental haemorrhage the blood-loss associated with a sudden increase of the circulating thromboplastin level may result in defective coagulation due to defibrination. However, Crichton's (1950) figures show that, in cases of accidental haemorrhage, rupture of the membranes when labour is established as opposed to rupture of the membranes before the onset markedly reduces the maternal mortality. This is in opposition to the results expected if Weiner's postulate is correct. Afibrinogenaemia associated with Rhesus isoimmunization may be the result of defective placental permeability.

Summary

A case of severe haemorrhage due to placenta praevia is described. Recurrence of bleeding was thought to be due to a lack of circulating fibrinogen and treatment consisted of blood transfusion and the available human fibrinogen. Treatment with fresh blood and fibrinogen should be instituted on the result of simple laboratory tests and not delayed until more elaborate investigations can be performed. All cases of severe haemorrhage in pregnancy should have simple clotting tests and such tests as the addition of fibrinogen and thrombin to samples of blood if the clotting time is abnormal. Thirty ml. of blood should be reserved for fibrinogen content examination and electrophoretic patterns.

It is suggested that severe haemorrhage alone even in the absence of thromboplastin release may deplete the circulating plasma fibrinogen level sufficiently to prevent blood coagulation. This is a factor of importance in cases of abortion, placenta praevia and post-partum haemorrhage as the circulating blood volume may be maintained with stored blood and plasma substitutes.

My thanks are due to Mr. O. Lloyd for permission to publish this case report. I am indebted to Dr. J. Marks and Dr. N. R. Lawrie of the John Bonnett Clinical Laboratories, Cambridge, for the laboratory investigations. I should also like to acknowledge the assistance of Dr. J. Walker of the Regional Transfusion Service who organized the supply of fibrinogen and of Group B blood.

References

Crichton, D. (1950): *Brit. med. J.*, **1**, 401.
De Lee, J. B. (1901): *Amer. J. Obstet. Gynec.*, **44**, 785.
Howell, W. H. (1941): *J. Amer. med. Ass.*, **117**, 1059.
Obata, I. (1919): *J. Immunol.*, **4**, 111.
Page, E. W., Fulton, L. D., and Glendenning, M. B. (1951): *Amer. J. Obstet. Gynec.*, **61**, 1116.
Sakurai, K. (1929): *Sei-i-Kwai med. J.*, **48**, 4.
Schneider, C. L. (1947): *Surg. Gynec. Obstet.*, **90**, 613.
Weiner, A. E., Reid, D. E., and Roby, C. C. (1953): *Amer. J. Obstet. Gynec.*, **66**, 465, 475.
Weiner, A. E., Reid, D. E., Roby, C. C., and Diamond, L. K. (1950): *Amer. J. Obstet. Gynec.*, **60**, 1015.