

AN UNUSUAL CASE OF BLOOD DISEASE IN PREGNANCY

BY

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SEVERAL reports have appeared in recent months in the literature of incoagulability of blood associated with severe accidental ante-partum haemorrhage. It has long been realized that certain patients with accidental haemorrhage were prone to severe post-partum haemorrhage, while in others the third stage caused no concern. The first mention of this complication was over fifty years ago when DeLee (1901) postulated a haemophilia-like condition of the blood of a patient dying of severe accidental haemorrhage, and in 1936 Dieckmann associated the condition with a low fibrinogen concentration in the blood. It was not until 1949 that the therapeutic effect of giving fibrinogen by intravenous injection was tried out by Moloney and his colleagues, and in 1950 Weiner and his co-workers showed that there was a definite afibrinogenaemia correctable by the intravenous injection of fibrinogen.

Since then various cases of severe accidental ante-partum haemorrhage associated with afibrinogenaemia have been reported, mostly from America but a few reports have come from the Continent, and very recently three reports have appeared in the British literature (Moore, 1954; Barnett and Cussen, 1954; Feeny, 1954). The case reported by Moore was not recognized until post-partum haemorrhage occurred and in the discussion the comment is made that the diagnosis should be possible before delivery. We present the following case which was diagnosed prior to delivery, in the belief that it shows several interesting features relevant to the early diagnosis of the condition.

The patient, a primigravida of 36 years, had been married for 13 years. She had had no serious illnesses but for the past 5 years she had been taking thyroid gr. i. daily, originally started in an effort to lose weight.

The last menstrual period was in November, 1953 and antenatal care was carried out by the general practitioner. On the 2nd June, 1954 the patient had a wisdom tooth extracted under local anaesthesia. This was followed by fairly severe facial pain but very little haemorrhage. For the pain the patient took aspirin tablets gr. 5 to a total of 6 a day for 6 days, i.e., approximately 180 gr.

On 9th June, the patient awoke about 4 a.m. and found she was bleeding *per vaginam* and also from her tooth socket. She had some right sided abdominal pain. Her blood pressure at 6.20 a.m. was 90/60 mm. Hg. Morphia gr. $\frac{1}{4}$ was given and the patient transferred to hospital.

On admission at 7.15 a.m. the patient was pale, slightly shocked and bleeding orally and vaginally. There were no petechiae but haematomata appeared round each needle puncture. Her pulse was 108/min. B.P. 130/80 mm. Hg. She had no oedema but there was a cloud of albumen in a catheter specimen of urine.

The uterus was the size of a 32-weeks gestation. It was woody hard, but not tender. No foetal parts could be felt and no foetal heart heard. Blood was taken for grouping and cross-matching and a dextrose intravenous drip was commenced soon after admission. At 9 a.m. the patient was vomiting blood and had a fairly heavy vaginal loss. Her B.P. was 110/70 mm. Hg, the pulse 100/min. and the first pint of blood transfusion was started. As it was noted that the blood in a plain tube was not clotted after 2 hours the possibility of fibropenia was entertained and reconstituted fibrinogen 145 mg. in 10 ml. saline was given intravenously.

By 4 p.m. the patient had received 5 pints of blood, 3 being less than 24 hours old and also a further intravenous injection of fibrinogen (145 mg.). Her estimated loss was about 5 pints and the tooth socket had ceased to bleed.

She was complaining of uterine contractions and a vaginal examination was made. The cervix was found to be half dilated and the forewaters were ruptured, a small head descending into the pelvic cavity. Vaginal bleeding ceased and labour progressed normally.

At 6.25 p.m. the cervix was fully dilated and a low forceps delivery of a stillborn foetus weighing 3 pounds was performed under local anaesthesia. Ergometrine 0.5 mg. was given at the time of delivery of the anterior shoulder and the placenta was delivered immediately with about 20 ounces of old and fresh blood. This was followed by a trickle of bright red blood, which was partially due to a vaginal tear. This was sutured with

control of the bleeding. The total loss at delivery was estimated at 40 ounces and the patient's blood pressure was 95/70 mm. Hg. A pint of fresh blood was therefore transfused in 10 minutes.

By 9 p.m. the transfusion of the 9th pint of blood was commenced. The patient had lost a further 40 ounces despite the fact that the uterus was firmly contracted. In view of this a general anaesthetic was given and the vagina explored. No laceration was found and the uterus was packed with difficulty owing to the firm contraction which was maintained throughout the manipulation. The bleeding was controlled by the pack. Transfusion was continued overnight and a further fibrinogen injection given after packing the uterus. The pack was removed 12 hours later without further loss. Total blood given was 11 pints and the total loss was approximately 9 pints.

The patient's subsequent progress was complicated by pelvic sepsis and venous thrombosis, but no further bleeding occurred.

Pathological Investigations

9th June, 1954. On admission. Haemoglobin 94 per cent. Platelets abundant. Fibrinogen present. Bleeding time 4 minutes 30 seconds. Blood collected in a dry tube failed to clot. 9 p.m. Clotting time 9 minutes.

10th June, 1954. Haemoglobin 72 per cent. Clotting time 5 minutes.

11th June, 1954. Blood collected in a dry tube clotted immediately but after 30 minutes the clot had partially fragmented.

18th June, 1954. Haemoglobin 70 per cent. W.B.C.'s 18,400 per c.mm. Reticulocytes 5 per cent. Platelets abundant. Plasma fibrinogen 0.35 g./100 ml. Prothrombin Index 100 per cent.

DISCUSSION

It is surprising that so little notice of this complication of accidental ante-partum haemorrhage has been taken in this country until so very recently. Since Weiner and his co-workers (1950) reported the results of their investigation into the cause of this condition a number of case reports have been published in America and a few on the Continent, and now 4 cases have been reported in Great Britain. The condition is also given brief mention by Biggs and Macfarlane in their recent book on blood coagulation (1953).

The first serious effort to find the cause of this condition was made by Weiner and his co-workers and the results were published in 1950. They found that in certain cases of accidental ante-partum haemorrhage there was a defect in the coagulation mechanism and that the changes were characterized primarily by a decrease in

fibrinogen concentration, but that there was also some decrease in prothrombin activity and in some cases a circulating fibrinolysin was present. They noted that these changes only occurred in severe cases of accidental ante-partum haemorrhage but that the condition could be diagnosed by the repeated observation of the clot formed by the patient's blood. In 2 of the patients studied the blood coagulating mechanism was normal prior to the accidental ante-partum haemorrhage suggesting that the fibrinogen-aemia was secondary to the accidental ante-partum haemorrhage and not the cause.

About the same time Schneider (1950) showed that in rabbits placental extracts produced first a hastening of coagulation and later a delay and he was able to identify the toxic principle as thromboplastin. He produced similar results by traumatizing the placental site. Page, Fulton and Glendenning (1951) published their results of the effect of the intravenous injection of placental thromboplastin in dogs and the study of 6 cases of accidental ante-partum haemorrhage. They concluded that defibrination is probably due to the escape of placental or decidual thromboplastin into the maternal circulation. This converts the prothrombin to thrombin which in turn converts the fibrinogen to fibrin and the latter is deposited over a very large vascular area, but may sometimes be the cause of severe visceral lesions. The rate of the fibrinogen depletion was measured in minutes, whereas if it were due to a fibrinolysin it would be a much slower process. The presence of a fibrinolysin in some cases was due, they postulated, to a repair mechanism developing after the initial injury, for the purpose of removing deposited fibrin and repairing the damage done by the action of the thromboplastic proteins. In 1953, in a further communication, they showed by means of radioactive extracts that most of the thrombin was deposited in the liver, lungs and spleen.

In 1952 Schneider published a method for the rapid evaluation of fibrinopenia which he claimed aided in the diagnosis of the condition, but the simple observation of a sample of venous blood incubated at 37° C. seems to give adequate information. If the freshly drawn venous blood fails to clot or form a normal

sized stable clot it indicates a critical level of circulating blood fibrinogen and if the clot dissolves within an hour the haemostasis is inadequate. This dissolution of the clot which was originally thought to be due to a fibrinolysis Weiner, Reid and Roby (1953) now believe to be due solely to low blood fibrinogen (100–150 mg. per cent).

It was the absence of clotting in blood taken for cross matching and the presence of oral bleeding that made us suspect a blood dyscrasia and realize we were not dealing with a simple ante-partum haemorrhage in our case. It was also noted that each venepuncture wound and injection site continued to ooze for many minutes. Owing to the kind help of Dr. Tovey of the South Western Regional Blood Transfusion Service we were able to obtain human fibrinogen for intravenous injection and the first ampoule was given with the first pint of blood. Not having had previous experience in the use of therapeutic fibrinogen we failed to give an adequate dose early on, and, although 290 mg. of fibrinogen and 4 pints of blood controlled the oral bleeding, it did not prevent a severe post-partum haemorrhage. It seems probable that the further injection of fibrinogen did more in stopping the bleeding than did packing the uterus.

The sudden onset of bleeding from a tooth socket that had not bled for 6 days was one of the interesting features of our case. That the oral bleeding occurred almost simultaneously with the vaginal bleeding seems to confirm the view that the incoagulability of the blood follows the accidental ante-partum haemorrhage and is not the cause of the condition. Weiner suggests that artificial rupture of the membranes by decreasing intra-uterine pressure, may prevent the further dissemination of placental thromboplastin and thus arrest the defibrination. We certainly found that our patient's condition improved after the membranes were ruptured but the subsequent post-partum haemorrhage showed that the fibropenia was still uncorrected.

In reviewing the case the role of aspirin was considered. This drug is known to be capable of reducing prothrombin to a level sufficient to cause abnormal bleeding and the amount this patient had taken during the week prior to

admission may possibly have been a complicating factor in this case. However, the pathological findings fitted in much better with an afibrinogenaemia than with a reduction of prothrombin.

In spite of the relative infrequency of this complication of accidental ante-partum haemorrhage it must have been the cause of death in numerous cases which were attributed solely to haemorrhage and shock. If this possibility is kept in mind in all cases of severe accidental ante-partum haemorrhage an early diagnosis can be made. The freshly drawn venous blood should be examined for clot formation and for clot fragmentation when incubated at 37° C. If the first sample clots normally fresh samples should be examined at hourly intervals as the defibrination occasionally does not occur for several hours after the initial haemorrhage.

In order to arrest the haemorrhagic tendency rapidly, human fibrinogen should be administered intravenously at the earliest possible opportunity, while of course the blood loss is replaced by adequate blood transfusion. Unfortunately fibrinogen is still in short supply. Multiple transfusions, however, do not supply adequate amounts of fibrinogen, one pint only raising the blood fibrinogen concentration 5–10 mg. per cent. Moore (1954) suggests that at least 2 grammes is necessary and Weiner and his colleagues (1953) advise that 10 grammes of fibrinogen should be kept available as they consider that this amount will be sufficient to treat one patient adequately. Our patient received a total of 435 mg. of fibrinogen. Barnett and Cussen (1954) consider that the amount of fibrinogen required is much less than that advised by Weiner, and their 2 patients received 404 mg. and 390 mg. respectively, which is approximately the same amount as we found necessary. This is a most gratifying finding in view of the small supplies of fibrinogen at present available.

Where fibrinogen is not available fresh blood offers the next best treatment. It must also be remembered that a similar condition of afibrinogenaemia is sometimes associated with intra-uterine death due to Rh incompatibility, but it seems only to occur when labour is delayed for many weeks. Amniotic fluid emboli may also

produce an afibrinogenaemia but this condition is fortunately uncommon, so that the combination must be extremely rare.

Although the condition described is relatively rare, it is none the less important that all obstetricians should be aware of this complication of accidental ante-partum haemorrhage, particularly as the diagnosis can be so readily made by the "clot observation" test. Also, although fibrinogen is still scarce, it is now stocked at all the regional headquarters of the Blood Transfusion Service and will be immediately supplied on request.

SUMMARY

A case of severe accidental ante-partum haemorrhage associated with acquired afibrinogenaemia is presented. The aetiology, diagnosis and treatment are discussed. A plea is made for the early recognition of this condition and a mode of treatment is outlined.

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