HEMOPHILIA B (CHRISTMAS DISEASE) IN THE NEWBORN

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There are several conditions manifested by abnormal bleeding during the newborn period. Certainly the single most common entity among these is hemorrhagic disease of the newborn. In these patients, bleeding usually occurs between the first two to five days of postnatal life. Generally, bleeding is from the gastrointestinal tract, the umbilicus and into the cranial cavity.[1] It is more commonly seen in premature babies and is known to be more serious in such cases. Aside from prematurity however, there do seem to be other factors which influence the severity of the disease. These include ingestion of salicylates, cumarin, reserpine, and sulphanamid by the mother toward the end of the period of gestation. Anticonvulsive drugs, such as Dilantin [R] and phenobarbitol may also produce much the same effect. It is thought that these medications probably increase the physiological hypoprothrombinemia of the newborn because of liver damage.[2] Antibiotics (chloramphenicol, streptomycin) and anticonvulsive drugs, when given to newborn babies themselves, also seem to result in hemorrhagic tendencies, caused either by a change in the intestinal flora or a change in liver function.

Generally in hemorrhagic disease of the newborn, the plasma levels of vitamin K-dependent factors, such as prothrombin, PTC, stable and Stuart-Prower, are decreased. Usually the factor V level is normal in these patients. However, in premature babies with neonatal anoxia, the factor V level may also be decreased.[1] In normal newborns, vitamin K-dependent coagulation factors are at their lowest levels on the second or third day of life, and increase gradually after the fifth postnatal day. It takes weeks for the Stuart-Prower factor, and months for prothrombin to reach low adult levels.[3]

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Anoxia, thrombocytopenia, and different infections in the neonatal period might be other causes of abnormal bleeding. On rare occasions, cytomegalic inclusion disease and deficiency of coagulation factors are the causes of hemorrhage in this period of life. Circulating anticoagulants are reported in newborns as a cause of hemorrhage.[4] It is rather surprising that bleeding is not more common in newborns with these diseases and the various kinds of hemophilia.

In the literature we could find only one case of a hemophiliac baby in which a cord blood AHG assay had been done, the results of which were zero.[5] Although it is a single case, it shows at least that AHG is not transferred from the mother to the baby. Mothers of babies with hemorrhagic disease do not usually show any abnormal bleeding during delivery, indicating that they themselves carry clotting factors in normal quantities and that these factors are not transfered from the mother to the baby.

For more than ten years it has been known that hemophilia, characterized by poor thromboplastin formation, includes at least four different entities. Of these, hemophilia A and B are inherited through the mother's X chromosome. For this reason the disease is symptomatic in males only. Although it is rare, there are proven cases of hemophilia A in girls whose chromosome pattern is XX.[6,7] Recently a family was described in which both the male and female members were hemophiliacs.[8]

Usually, the patients with hemophilia B are less prone to excessive bleeding than those with hemophilia A. Hemophilia A,B, and vascular hemophilia are not infrequently seen in this country, but PTC deficiency is rarely a cause of hemorrhage in the neonatal period anywhere. For this reason we thought it would be of interest to report such a case.

Case Report

A 13 day old boy was admitted to Hacettepe Children's Hospital with complaints of umbilical bleeding. From the past history it was learned that the baby was brought to the hospital at 4 days of age with the same complaint. At that time the cord was sutured and vitamin K (5 mg i.m.) was given with the possible diagnosis of hemorrhagic disease of the newborn. The parents stated that in spite of this treatment oozing from the umbilicus continued and he was brought back for additional treatment.

On admission his weight was 2,900 gm., length 51 cm., sucking and Moro reflexes were present. Over the right gluteal area there was an area of echymosis 6 by 8 cm, and just above this area, as well as in the deltoid region, there were two hemotomas, about one cen-

timeter square in size. The liver was just palpable. Except for a mild jaundice (8 mg %, indirect bilirubin) other findings were within normal limits.

The patient was the second child of the family, the first male child having died at the age of one month with umbilical bleeding.

Laboratory examination: Hb was 6.95 gm per 100 cc; RBC was 2,080,000 per cmm; WBC was 2,400 per cmm. Platelets were abundant in the peripheral smear. Initial coagulation work-up is summarized in Table 1.

TABLE 1
RESULTS OF INITIAL COAGULATION TESTS

Bleeding time	8 minutes
Quick prothrombin time Quick, A.J.: J. Biol.Chem. 109: 73, 1935	14 seconds (control 12 seconds)
Partial thromboplastin time (PTT) Rodman, N.F. Jr., Barrow, E.M., and Graham, J.B.: Amer. J. J. Clin. Path. 29: 525, 1958.	More than 120 seconds (Normal time: 45 to 90 seconds)

TABLE 2
RESULTS OF THROMBOPLASTIN GENERATION TEST

	Normal serum and normal adsorbed plasma	Normal serum and patient adsorbed plasma	patient serum and normal adsorbed plasma	patient serum and patient adsorbed plasma
1	36 sec.	30 sec.	over 60 sec.	over 60 sec.
2	16 "	17 sec.	over 60 sec.	over 60 sec.
3	14 "	12.5 sec.	over 60 sec.	over 60 sec.
4	12 "	———	48 sec.	over 60 sec.
5	—	———	40 sec.	43 sec.

The obvious prolongation of minimal substrate clotting time with normal adsorbed plasma and patient serum, indicates a deficiency of a factor effective in thromboplastin formation, i.e., PTC.

The possibility of the presence of an anticoagulant effective on the PTC level [13] was ruled out by the studies summarized in Table 3. As can be seen from this table, when the patient's serum was mixed with normal serum in varying amounts, the minimal substrate clotting times were not prolonged. These studies ruled out the possibility of circulating excessive anticoagulant against factor IX as being the cause of the coagulation defect in this case.

The partial thromboplastin time test is a simple and quite reliable screening test for the detection of abnormalities in thromboplastin

* Since the PTC was abnormal, thromboplastin generation test was performed. The results are given in Table 2.

TABLE 3

RESULTS OF TESTS FOR CIRCULATING ANTICOAGULANT EFFECTIVE ON THROMBOPLASTIN GENERATION (NORMAL ADSORBED PLASMA WAS USED)

	0.1 cc. patient serum and 0.1 cc normal serum	0.1 cc. patient serum and 0.3 cc normal serum	0.1 cc. patient serum and 0.9 cc normal serum
1	23 sec.	26 sec.	27 sec.
2	18 sec.	15 sec.	15 sec.
3	16 sec.	14 sec.	13 sec.
4	15 sec.	13 sec.	13 sec.
5	15 sec.	13 sec.	—

generation. In this test, using mixtures of patient's plasma with normal adsorbed plasma (1 to 1) and diluted normal serum (1 to 20) respectively, it is possible to diagnose hemophilia A and B. In our case the thromboplastin generation test, more sensitive than the PTC, was performed.

Because of the patient's severe anemia he was given fresh blood (10 cc per kg) after obtaining blood for the coagulation studies. When diagnosis was established, he was transfused with bank blood (10 cc per kg) twice at 24-hour intervals for correction of anemia and control of bleeding. After the bleeding was under control, and he was observed for another day, he was discharged.

To correct the coagulation defect in Christmas disease, bank blood or plasma are usually used. Sterile blood serum could also be used for the same purpose.

PTC is activated in the serum and for that reason much less is needed than when plasma is used, in order to control bleeding in these patients. The half-life of Christmas factor is much longer (24 to 48 hours) than that of factor VIII, hence the plasma needed for the control of bleeding in this disease is much less than is required for cases of Hemophilia A.

Summary

The case of a newborn with Christmas disease is presented. The causes of abnormal hemorrhage and its treatment during this period of life are briefly discussed.

REFERENCES

1. Ehling, L.R.: Hemorrhagic disease of the newborn, AMA J. Dis. Child. **101**: 241, 1961.
2. Creveld, S. Van: Coagulation disorders in the newborn period, J. Pediat. **54**: 633, 1959.
3. Dyggve, H.: Prothrombin and proconvertin in the newborn and during the first year of life, Acta paediat. (Upps) **47**: 251, 1958.
4. Frick, P.G.: Hemophilia-like disease following pregnancy with transplacental transfer of acquired circulating anticoagulant, Blood **8**: 598, 1953.
5. Didisheim, P., and Lewis, J.H.: Congenital disorders of the mechanism for coagulation of blood, Pediatrics **22**: 478, 1958.
6. Chapelle, A. de la, Ikkala, E., and Nevanlinna, H.R.: Haemophilia A in a girl. A probable exception from sex-linked recessive inheritance, Lancet **2**: 578, 1961.
7. Mellman, W.J., Wolman, I.J., Wurzel, H.A., Moorhead, P.S., and Qualls, D.H.: A A chromosomal female with hemophilia A, Blood **17**: 719, 1961.
8. Bond, T.P., Levin, W.C., Celander, D.R., and Guest, M.M.: "Mild hemophilia" affecting both males and females, New Engl. J. Med. **266**: 220, 1962.
9. McMillan, C.W., Diamond, L.K., and Surgenor, D.M.: Treatment of classic hemophilia: the use of fibrinogen rich in factor VIII for hemorrhage and for surgery, New Engl. J. Med. **265**: 224, 1961.
10. Welsh, J.F.: Serum transfusion in the treatment of deficiency of plasma thromboplastin component, Amer. J. Clin. Path. **33**: 118, 1960.
11. Özsoylu, S.: Bir kız çocuğunda geçici hemofili B, Çocuk Sağlığı ve Hastalıkları Dergisi **7**: 101, 1964.