CONGENITAL THROMBOCYTOPENIC PURPURA
TREATED BY EXCHANGE TRANSFUSION

BY

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The occurrence of thrombocytopenic purpura in
babies born to mothers with idiopathic thrombo-
cytopenia is a well recognized though uncommon
clinical entity. Robson and Walker (1951) were
able to collect from the literature only 19 definite
and nine probable examples of this association.

The suggestion of Epstein, Lozner, Cobbe and
Davidson (1950) that this type of congenital
thrombocytopenic purpura results from the transfer
across the placenta of a maternal factor capable of
causing thrombocytopenia has recently received
support with the demonstration of platelet agglu-
tinins in the serum of both mother and child
(Harrington, Sprague, Minnich, Moore, Aulvin and
Dubach, 1953; Vanderbroucke and Verstraete, 1955;
Tullis, 1956; Schoen, King and Duane, 1956). In
view of these findings it might be expected that
exchange transfusion of affected infants would,
by removing the acquired platelet antibodies,
shorten the period of thrombocytopenia and so
lessen the risk of haemorrhage and death. We
report below observations on a baby with congenital
thrombocytopenic purpura who was treated in this
manner.

Case Report

C.B., now aged 30, had a splenectomy performed when
10 years old for a persistent haemorrhagic disorder
regarded as idiopathic thrombocytopenic purpura.
Since that time she has had no episodes of excessive
bleeding and additionally has had many teeth extracted
without trouble.

In June 1958, after an uneventful antenatal period
and confinement she was delivered of a female child
weighing 6 lb. 3 oz. Shortly after birth the baby was
noticed to have purpura which became more widespread
during the 14 hours of its survival. Necropsy revealed
no haemorrhages other than those in skin; an extensive
pneumonia was present and thought to have been the
cause of death.

The mother’s blood was examined postnatally (August
1958) with the following results: Hb 13.3 g./100 ml.,
packed cell volume 43%, white cell count 7,100/c.mm.,
platelets 124,000/c.mm., bleeding time 7 min., clotting
time 4 min. 45 sec. (ordinary glass), 6 min. (silicone
glass), clot retraction normal in one hour, plasma
prothrombin 11 sec. = 100% (control 11 sec. = 100%),
fibrinogen 137 mg. % and thromboplastin generation
normal. The platelet count was done by the direct
method using Rees Ecker diluting fluid on a venous
sample of blood, as were all platelet counts on the mother;
the normal values for the platelet count as done by this
method, are taken as 200-400,000/c.mm.

Her blood was next examined in July 1959, at which
time she was six months pregnant. On that occasion
the platelets numbered 196,000/c.mm.; all the other
previous blood tests were repeated and found to be
within normal limits. On October 7, when 39 weeks
pregnant, her platelet count was only 84,000/c.mm.;
as before, all the other blood tests showed no abnor-
mality. Although thrombocytopenic there was no
clinical evidence of any bleeding tendency. On Octo-
ber 22, after an uneventful pregnancy and confinement,
she was delivered of a male child weighing 7 lb. 11 oz.
The puerperium was uneventful. On the third postnatal
day the mother’s platelet count was 120,000/c.mm.;
three months later it was 128,000/c.mm.

The baby, when examined shortly after birth, was found
to have a number of purpuric spots on the face and trunk;
no other abnormalities were noted. Examination of
blood obtained from the baby when 2 hours old gave
the following results: Hb 17.2 g./100 ml., platelets
34,000/c.mm., leucocytes 18,200/c.mm. with a differential
white cell count of neutrophils 71%, lymphocytes 27% and
monocytes 2%; the bleeding time was 8 min. 30 sec.
Examination of a stained film confirmed the lack of
platelets; those present showed no morphological
abnormality. Blood samples for these and other studies
on the baby were obtained by heel prick unless otherwise
stated.

When 3 hours old the baby was given an exchange
transfusion with 520 ml. ‘O’ Rhesus negative blood which
had been collected during the preceding 24 hours.
During the transfusion, which was well tolerated, fresh
purpuric spots and ecchymoses appeared mostly on the
face. Further fresh crops of purpura were noted during
the next three days but not thereafter. Following
transfusion he was started on oral cortisone: 25 mg.
were given during the next 24 hours followed by 8 mg.
daily for four days and 4 mg. daily for five weeks; the dose was then gradually reduced, therapy being discontinued after a further six weeks.

On the day after exchange transfusion the bleeding time had fallen to 6 min. 30 sec., 10 days later it was 5 min. and on all subsequent occasions was less than 4 min. There was, however, no commensurate increase in the platelet count which during the first month never exceeded 80,000/c.mm. Between the first and third months the platelet count varied between 80,000 and 120,000/c.mm. At 4 months the baby's platelet count was still only 106,000/c.mm., but at 5 months this had risen to 166,000 (Fig. 1).

Specimens of venous blood obtained from the baby immediately before and after exchange transfusion and from the mother on the day following delivery were examined for platelet agglutinins by the method described by Kissmeyer-Nielsen (1955). The mother's serum and the baby's pre-transfusion serum both gave a strong positive result whereas the post-transfusion serum from the baby gave only a doubtful positive result. Twenty-six days after birth when the baby's platelet count was still only 59,000/c.mm. both the mother's and baby's sera were again examined for platelet agglutinins. On this occasion the mother's serum gave a strong positive result as previously whereas the baby's was definitely negative.

From a post-transfusion level of 13.7 g./100 ml. the baby's Hb fell steadily to 7.2 g./100 ml. with 1% reticulocytes by the 26th day. Two weeks later the Hb was still only 7.4 g./100 ml. but the reticulocytes had increased to 7%. Thereafter there was a gradual rise in Hb to 13.3 g./100 ml. at 5 months (Fig. 1).

A sample of bone marrow was aspirated from the iliac crest on the 27th day. Though the sample was diluted with sinusoidal blood the relative number of normoblasts appeared somewhat reduced; otherwise no abnormality was noted and, in particular, appreciable numbers of morphologically normal megakaryocytes were seen.

Except for the development of purpura during the first three days the baby showed no other signs of bleeding. His clinical progress was wholly uneventful, he was bottle-fed throughout and at 3 months weighed 13 lb. 12 oz.

**Discussion**

It is now established that neonatal thrombocytopenic purpura is a clinical disorder of multiple aetiology (Kaplan, 1959). One form is that which occurs in babies born to mothers suffering from idiopathic thrombocytopenic purpura. Platelet agglutinins have now been demonstrated in both the serum of the mother and of her thrombocytopenic infant on at least five occasions (Harrington *et al.*, 1953; Vanderbroucke and Verstraete, 1955; Tullis, 1956; Schoen *et al.*, 1956, and the present case) thereby providing good reason for believing the disorder to be due to the passive transfer of maternal antibodies.

This type of congenital thrombocytopenic purpura is a self-limiting condition. Complete recovery can be expected provided affected infants survive the hazards of haemorrhage during the early neonatal period. Robson and Walker (1951) and Morris (1954) found that of those infants reported in the literature 15-20% had died within the first
week. The severity of the disease in the mother and
the sex of the child are two factors which appear
to affect the chances of survival. In general, the
more active the disease in the mother the more
likely is the baby to be badly affected. There have,
however, been reports of affected infants being born
to mothers who were either in spontaneous remission
or, as in the present case, were clinically well
following splenectomy (Robson and Davidson,
1950; Epstein et al., 1950). Secondly, Robson and
Walker (1951) in their review of published cases,
noted that although slightly more female children
were affected all fatalities had occurred in males.

Although fresh purpuric lesions usually cease to
appear between the third and 10th day the bleeding
time in most cases remains prolonged for some 10
to 28 days. Thrombocytopenia usually persists
even longer commonly up to six but rarely beyond
15 weeks with an average duration of the order
of 10 weeks (Harrington et al., 1953; Morris, 1954;
Vanderbroucke and Verstraete, 1955; Stefanini and
Dameshek, 1955).

Only the reports of Schoen et al. (1956) and
Vanderbroucke and Verstraete (1955) mention the
length of time the platelet agglutinins persist in the
foetal circulation and only in the latter is this cor-
related with the platelet count and bleeding time.
Schoen et al. found platelet agglutinins to be present
at 38 but absent at 80 days. Vanderbroucke and
Verstraete record a positive result for platelet
agglutinins at 39 days with a negative result at
78 days. The platelet count in their patient at
these times was 100,000 and 110,000/c.mm.; four
weeks later when the baby was 15 weeks old the
platelets numbered 260,000/c.mm. The bleeding
time which on the first day was 22 min. had fallen
to 1½ min. by the 11th day. On the basis of these
findings it seems that thrombocytopenia is likely
to persist for some time after the disappearance of
the platelet agglutinins. This is contrary to the view
of Kaplan (1959) who without reference to specific
elements records that platelet antibodies may persist
after restoration of the platelet count to normal.

In view of the risk to life from haemorrhage
during the first week, treatment of these infants
must be directed primarily at preventing such
catastrophes. No treatment has yet proved effective
(Killander, 1959). If one accepts that the thrombo-
cytopenia in the infant is due to the passive transfer
of maternal platelet agglutinins then it seems logical
to treat these infants by exchange transfusion with
the object of washing out the transmitted maternal
antibodies. In our patient, no new purpuric
lesions appeared after three days, the bleeding time
fell to less than 4 min. from the 10th day onwards
and the platelet count, initially 34,000/c.mm.,
remained below 80,000/c.mm. until the 29th day
and was still only 166,000/c.mm. at 5 months.
Platelet agglutinins present before the start of the
exchange transfusion could no longer be identified
with certainty immediately after the transfusion and
were definitely absent on re-examination of the
baby's serum at 26 days. The wide variation in the
natural history and the paucity of data relating to
the persistence of platelet antibodies make it
impossible to assess accurately the value of such
therapy by reference to only a single case. Com-
parison with the reports of Vanderbroucke and
Verstraete and Schoen et al. suggests that we
did succeed in accelerating the elimination of anti-
bodies from the baby's serum. However, there is
nothing to indicate that this had any effect in shorten-
ing the duration of purpura, prolonged bleeding
time and thrombocytopenia. These observations
are similar to those of Killander (1959) who alone
has treated a similar case by exchange transfusion.
In this author's patient bleeding episodes occurred
up to 4 weeks and the platelets still numbered only
60,000/c.mm. at 7 weeks.

It is of interest that in both our patient and that of
Killander exchange transfusion was followed by a
period of anaemia. In the present case there was
no evidence to suggest a haemolytic process as the
cause of the anaemia; generalized marrow failure
can also be excluded as an aetiological factor on the
basis of the essentially normal marrow picture.
Thus it appears likely that the anaemia was of
similar origin to that which not uncommonly
occurs after exchange transfusion for haemolytic
disease especially when the immediate post-trans-
fusion haemoglobin level is less than 15 g./100 ml.
(Gairdner, 1958) as was the case with our patient.

This apparent lack of response to exchange
transfusion in congenital thrombocytopenia is in
marked contrast to that recorded by Stefanini,
Mednicoff and Plitman (1954) on a baby with
erythroblastosis foetalis and associated thrombo-
cytopenia. Maternal platelet iso-agglutinins were
detected in the baby's serum. After the second of
two exchange transfusions performed within 48
hours of birth the purpura disappeared and the
platelet count rose promptly from 60,000 to 250,000/
c.mm. subsequently remaining above this figure.
This type of response is what one might expect if
the baby's low platelet count was due solely to the
destruction of platelets by circulating antibody.
Is the lack of a similar response in babies born to
mothers with idiopathic thrombocytopenic purpura
indicative of a more complex mechanism? Some
support for this view is provided by the observation
that the thrombocytopenia may persist for a considerable time after the disappearance of antibodies (Vanderbroucke and Verstraete, 1955; and the present case).

Corticosteroids are of acknowledged value in the treatment of patients suffering from idiopathic thrombocytopenic purpura and it therefore seems logical to use these drugs on babies with congenital thrombocytopenic purpura. As judged by the rate of improvement in the bleeding time and platelet count cortisone did not appear to hasten the recovery of our patient nor that of Schoen et al. (1956). This is not to say that corticosteroids may not be beneficial in this condition for in idiopathic thrombocytopenic purpura it is recognized that cortisone lessens the risk of hemorrhage often without producing any effect on the platelet count. In view of the not inconsiderable risks of hemorrhage during the first week of life it seems desirable to treat these infant patients with corticosteroids.

The result of exchange transfusion in our patient is disappointing and suggests that this procedure may not materially alter the natural course of the disease. A final assessment of the therapeutic value of both exchange transfusion and corticosteroids must, however, await the publication of detailed studies on more patients.

Summary

A case report of a baby with congenital thrombocytopenic purpura is presented. The baby's mother had had a splenectomy for idiopathic thrombocytopenic purpura 20 years previously. The infant was treated by exchange transfusion and corticosteroids.

Platelet agglutinins which were demonstrated in the serum of mother and baby shortly after birth could not be identified in the baby's serum at 26 days. The thrombocytopenia, however, persisted and during the first three months the platelet count never rose above 120,000/c.mm.

Although the baby made an uneventful clinical recovery it is doubtful if therapy materially altered the natural course of the condition.

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REFERENCES


