VON WILLEBRAND'S DISEASE IN THE BANTU*

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Von Willebrand's disease, an autosomal-dominant inherited bleeding disorder, is characterized by a prolonged bleeding time and a low antihaemophilic factor (factor VIII) level. The disease was first described in 1926 by Von Willebrand when investigating a bleeding diathesis among the Aaland Islanders.8 Although well described in White populations, the disease appears to be a rarity among the Asiatic and Negro races.8 We have been unable to find documented cases of Von Willebrand's disease in the Bantu.

This paper presents the first report of Von Willebrand's disease in the South African Bantu. The family is of the Tswana ethnic group. Three members presented with severe clinical bleeding and a fourth died of haemorrhage in infancy.

MATERIALS AND METHODS

Platelet count, bleeding time (Ivy), prothrombin time and factor VIII assay were carried out by standard procedures.9 Kaolin partial thromboplastin time was measured by the method of Langdell et al., plasma fibrinogen by the method of Ellis and Stransky, and euglobulin lysis time by the method of Nilsson and Olow.1 Platelet adhesiveness in vivo was measured by the method of Borchgrevink, and in vitro by the method of Hellem.2 ADP-induced clumping and platelet factor 3 availability (platelet thromboplastic activity) were assayed by the method of Hardisty and Ingram.3

'Fibrinogen concentrate' (human fibrinogen dried—South African Blood Transfusion Service) corresponded to Cohn's fraction 1. It was prepared by the ethanol extraction method from time-expired plasma, and the factor VIII content, although variable, was consistently low.

Clinical and Laboratory Data of Affected Family Members

IIIC, mother of the propositus, is the probable carrier of the Von Willebrand gene. She was clinically unaffected, and the factor VIII level was 80% on 2 occasions, but the bleeding time was prolonged to 8½ min.

IIII and IIIJ, female cousins of the propositus, were both clinically unaffected. Coagulation studies showed normal factor VIII levels (75% and 95% respectively), but the bleeding times of both were prolonged (7½ and 8 min. respectively).

IIIB, the propositus, a Bantu female aged 21 years, was admitted to hospital 4 days postpartum because of persistent vaginal bleeding. Clinical examination was otherwise normal. Therapy consisted of antibiotics, blood transfusions and curettage, following which the vaginal bleeding diminished. Five days later vaginal bleeding again became severe, and continued despite a further 3 curettages and numerous blood transfusions (Fig. 2). A bleeding diathesis was suspected and coagulation studies showed a factor VIII level of 8% with a bleeding time of 18½ min. (Table I). A provisional diagnosis of Von Willebrand's disease was made. Further therapy consisted of transfusions of whole blood, fresh frozen plasma, vitamin K and calcium. This therapy failed to control the haemorrhage adequately (Fig. 2). Four units of 'fibrinogen concentrate' were then administered daily for 3 consecutive days. Before use, each unit was reconstituted to

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*Date received: 9 January 1969.
TABLE I. LABORATORY DATA ON THREE SEVERELY AFFECTED CASES OF VON WILLEBRAND’S DISEASE

<table>
<thead>
<tr>
<th>Case</th>
<th>Bleeding time (min.)</th>
<th>Partial thromboplastin time (sec.)</th>
<th>Factor VIII level (%)</th>
<th>Platelet count/cu. mm.</th>
<th>ADP aggregation Stickiness in vivo (%)</th>
<th>Stickiness in vitro (%)</th>
<th>Factor 3 availability (%)</th>
<th>Prothrombin time (sec.)</th>
<th>Fibrinogen (mg/100 ml.)</th>
<th>Euglobulin lysis time (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIIB</td>
<td>15</td>
<td>65</td>
<td>8</td>
<td>235,000</td>
<td>Normal</td>
<td>84</td>
<td>68</td>
<td>40</td>
<td>11:3</td>
<td>237</td>
</tr>
<tr>
<td>IIIG</td>
<td>9</td>
<td>350,000</td>
<td>Normal</td>
<td>Adequate on film</td>
<td>370</td>
<td>350</td>
<td>140,000</td>
<td>370</td>
<td>350</td>
<td>140,000</td>
</tr>
<tr>
<td>IVB</td>
<td>73</td>
<td>3</td>
<td>2</td>
<td>400,000</td>
<td>Normal</td>
<td>65</td>
<td>50</td>
<td>25-75</td>
<td>10-12</td>
<td>210</td>
</tr>
<tr>
<td>Normal range</td>
<td>2-7</td>
<td>35-45</td>
<td>50-150</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

For hyperbilirubinaemia, possibly due to absorption of blood from an occipital cephalhaematoma sustained at

On careful questioning, the patient admitted to severe menorrhagia for many years. A tooth extraction some years previously had been followed by severe haemorrhage, necessitating blood transfusion.

Further coagulation studies were subsequently carried out (Table I). Platelet number, morphology and function were normal. The factor VIII level was less than 10% and the bleeding time markedly prolonged on numerous occasions. The final confirmation of Von Willebrand’s disease was made with infusion studies. The factor VIII level rose rapidly after infusions of both fresh frozen plasma and the ‘fibrinogen concentrate’ and subsequently fell slowly (Fig. 3). The factor VIII concentration of the fresh frozen plasma was 45% and of the ‘fibrinogen concentrate’, infused in this study, under 1%.

IVA, the infant son of the propositus, was admitted to hospital at the age of 2 weeks for exchange transfusion for hyperbilirubinaemia, possibly due to absorption of blood from an occipital cephalhaematoma sustained at...
tions were available for testing. The variability of ex-
pressivity of the coagulation defects necessitates repeated
evaluation of the apparently unaffected subject.6

The therapy of Von Willebrand's disease differs from
that of classical haemophilia. The bleeding diathesis in
both diseases is related directly to the factor VIII level.
In haemophilic correction of the low factor VIII concen-
tration achieved passive correction by transfusing blood products
containing high concentrations of factor VIII such as cryoprecipitate, fresh and fresh frozen plasma and
'haemophilic factor concentrates' prepared by pharmaceu-
tical manufacturers. In Von Willebrand's disease the correction
can be either active or passive, using fresh or
fresh frozen plasma. Cohn's fraction 1 or 'fibrinogen
concentrate'.4,6 These plasma or plasma derivatives with
a high factor VIII content will result in an immediate
rise in the recipient's factor VIII level, followed in many
instances by 'complementation' and a further increment in
the factor VIII level, and a slow fall over 24 hours. A
'fibrinogen concentrate' with low factor VIII activity
will cause a slow rise in the factor VIII level to a maxi-
mum about 4 hours after infusion, corresponding to
intrinsic factor VIII synthesis, with a slow fall over the
next 24 hours. The propositus aptly demonstrates these
features when both fresh frozen plasma and a 'fibrinogen
concentrate' were administered. In the control of the
vaginal bleeding in the propositus, a response was noted
with both fresh frozen plasma and 'fibrinogen
concentrate'. It appeared that the response to the 'fibrinogen
concentrate' was better, but this may be dose related.

SUMMARY

A bleeding disease in a Bantu family has been investigated. The
disease is transmitted in the family in an autosomal-dominant
pattern. The affected members of the family show low plasma
levels of antihaemophilic globulin (factor VIII) and/or a
prolonged bleeding time. The low factor VIII level was shown to
rise following infusion of plasma fractions low in factor VIII.
These features are diagnostic of Von Willebrand's disease,
which has to our knowledge not been previously described in
the Bantu.

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Medical Research, for facilities to carry out this study; and
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principal paediatrician, Baragwanath Hospital, for permission
to publish these cases.

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