Intracranial ventricular haemorrhage as a first presentation of haemophilia

A case of successful surgical management

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Between 1957 and 1968, six cases of haemophilia were encountered at the University College Hospital (U.C.H.), Ibadan, Nigeria, of which the last (which forms the subject of this report) was the only one which presented first with intracranial haemorrhage. Haemorrhage of the central nervous system in haemophilia was first described in 1819 (Lane, 1840) and was once regarded as a rare occurrence. Bulloch and Fildes (1911) in their extensive review of the literature found only 13 cases; Aggeler and Lucia (1944) reported 32 cases; Sköld (1944) cited another five cases from Scandinavian literature; and Jones and Knighton (1956) found that the total documented cases (including three of their own) of this complication numbered 64 by 1945. However, in the last decade or so, the reported incidence of intracranial bleeding in haemophilia included the 7.2% of Hartmann and Diamond (1957); 6.3% of Silverstein (1960); 13.8% of Kerr (1964); 1.6% of Fessey and Meynell (1966); and the 3.4% of Davies, Turner, Cumming, Gillingham, Girdwood, and Darg (1966).

While the bulk of evidence in recent years would indicate that intracranial haemorrhage is not as uncommon as suggested by earlier reviewers, haemorrhage into the ventricular system in haemophilia remains a rarity. Up to 1945 Jones and Knighton (1956) in their review of the literature found no single case of this complication. The present paper describes a patient whose first significant manifestation of a haemophilic state was ventricular haemorrhage which was successfully treated by surgical and medical measures.

CASE REPORT

R. O. (No. 203575) a Nigerian Yoruba male aged 3 months and the first child of his parents was first seen at the General Out-patient Department of University College Hospital (U.C.H.), Ibadan, on 19 September 1968, with two days history of productive cough and convulsions

and extreme pallor of his skin. On examination, he was afebrile, anaemic, and had bilateral fine basal crepitations. He was neurologically normal. His packed cell volume (PCV) was 18% and chest radiographs showed no specific abnormality. He was admitted on that day into the Children's Emergency Room as suffering from early bronchopneumonia and anaemia and was treated with antibiotics (penicillin and streptomycin) and transfused with 60 ml. of packed cells. He was discharged home four days later.

When he was seen on 8 October 1968, at the Children's Out-patient Department, his mother complained that he had suffered from a stiff neck and insomnia for three days. Clinically, he was ill-looking with a low grade pyrexia 100.8°F (38.2°C). His scalp veins were prominent, the anterior fontanelle full and bulging, his neck moderately stiff, and he had a positive Kernig's sign. His head circumference was 44 cm. He was admitted as suffering from meningitis. Blood stained cerebrospinal fluid was obtained by non-traumatic ventricular tap (lumbar puncture failed), the xanthochromic supernatant of which contained numerous white blood cells (with predominance of polymorphs), and a protein content of more than 1,000 mg%. *Staphylococcus pyogenes* grown on culture of the fluid was penicillin resistant but sensitive to erythromycin, which was exhibited. Hydrocephalus was first noted on 10 October.

The child became more and more irritable, with a tense bulging anterior fontanelle, increased nuchal stiffness, and a PCV which remained around 20%. On 17 October, bilateral subdural taps yielded no fluid up to a depth of 1.0 cm. A lumbar puncture produced uniformly blood stained CSF and two days later a ventricular tap yielded xanthochromic fluid under pressure. The hydrocephalus progressed; on 20 October 1968 there was sunset appearance of the eyes, on 14 November his head circumference was 50 cm and, despite blood transfusions, his PCV never went above 20%. A neurosurgical opinion was sought at this stage.

An air ventriculography was performed on 15 November. The right ventricle was entered through the lateral angle of the anterior fontanelle. Dark brown CSF under pressure was obtained, removing 50 ml. and injecting 30 ml. of air. At the conclusion of the radiographic

procedure, 30 ml. of CSF, also dark brown due to stale blood, were removed from the left ventricle. The ventriculograms showed hydrocephalus (Fig. 1).

FIG. 1. Air ventriculograph (brow up position) showing hydrocephalus.

The child's head circumference increased to 52 cm on 18 November. Because of the disturbing progression of his hydrocephalus, a neurosurgical intervention was advised.

His pre-operative PCV rose to 27% with blood transfusions and on 27 November, with a blood transfusion continuing during the operation, a left ventriculo-peritoneal shunt was performed, using a Till-Wade valve. The ventricle was entered at a depth of about 1.5 cm obtaining xanthochromic fluid under pressure. The wounds in the scalp and neck oozed more than usual, but haemostasis did not give undue trouble.

Two days after the operation, the child became pale again, bled from the neck and scalp wounds, and also from an injection site, requiring firm strapping to control the oozing of blood. On 7 December, he became floppy with very tense, full anterior fontanelle and gross abdominal distension and, in spite of post-operative blood transfusion, his PCV was 9%. Diagnostic paracentesis abdominis yielded fresh unclotted blood with a PCV of 15%. The abdominal distension subsided within a week. A haematological investigation for haemorrhagic diathesis was asked for.

On 16 December, the relevant haematological data obtained were as follows: bleeding time, 1 min 30 sec; clotting time, more than 21 min; platelets, 250,000/c.mm; white cell count, 6,400/c.mm with normal differentials, but the markedly abnormal prothrombin consumption index (80%) suggested a defect in intrinsic prothrombin activation, possibly haemophilia. The thromboplastin generation test performed two days later showed defect in the patient's plasma, suggesting Factor VIII deficiency. His Factor VIII level was subsequently established at 0.9%.

He was transfused with lyophilized plasma on 18 December, since when his bleeding has been under control and the enlargement of the head arrested. His PCV came up to 30%, the anterior fontanelle became flat, and on 12 January 1969 the sun-setting of his eyes was corrected. However, on 2 February 1969, he developed a tense left parietal subcutaneous haematoma probably due to minor trauma and he was given two units of cryoprecipitate intravenously. The haematoma gradually resolved over a period of a fortnight. He was discharged home in a satisfactory clinical state on 22 February 1969, and has remained well since then.

Further interrogation of the parents revealed that the child was in perfect health until he came to U.C.H. and there was no antecedent head trauma. The child was circumcised at home when he was 2 weeks old without any incident and there was no family history of a bleeding tendency.

DISCUSSION

The usual story of how surgery may precipitate symptoms in a haemophiliac is of a child who, after an apparently straightforward circumcision, develops persistent bleeding from the penis, or of an older child who, after the loss or extraction of a tooth, bleeds incessantly from the tooth socket. In this instance, this 3-month-old patient who had been circumcised at home without event and had not yet cut his first tooth, let alone lost it, needed to have a ventriculo-peritoneal shunt for rapidly progressing hydrocephalus after ventricular haemorrhage before his haemophilic state was unearthed. The rarity of intracranial haemorrhage as an initial presentation of haemophilia was highlighted by Hartmann and Diamond (1957) who found that, of 29 haemophiliacs who bled initially in infancy, 26 followed circumcision, one bled from the umbilicus, and only two had intracranial haemorrhage. At U.C.H., Ibadan, only six haemophiliacs have been on record in 12 years. When a rare disease presents in one of its unusual forms, the difficulty of diagnosis is increased.

Spontaneous intracranial haemorrhage in haemophiliacs is rare, and almost always there is a history of trauma (Singer and Schneider, 1962). When this is absent, as in our patient, minor trauma might have been missed or the history not forthcoming. Thus Imhof (1951), in his review of haemophiliacs between 1913 and 1950, recorded a history of trauma in 31% of those with intracranial bleeding, Silverstein (1960) in 45% in his series, Kerr (1964) in 26%, and Fessey and Meynell (1966) in 20%. Bouts of coughing such as was experienced by this patient may through sudden alteration in intracranial dynamics precipitate intracranial bleeding, as in case 6 of Kerr (1964).

Lumbar puncture and ventricular tap were employed in our patient to confirm the clinical sus-

picion of meningitis. The tendency of the haemophiliac to bleed intracranially is increased in the presence of meningitis (Hartmann and Diamond, 1957) and death is not unknown, as exemplified by case 10 of Kerr (1964) in whom meningococcal meningitis preceded a fatal intracranial haemorrhage. Not all agree about the use of diagnostic procedures in these patients. Fessey and Meynell (1966) avoided them for fear of producing fatal results. But others have shown that the usual investigations can be undertaken when intracranial haemorrhage is suspected (Silverstein, 1960; Kerr, 1964; Davies *et al.*, 1966; Travis, Mitchell, Youmans, and Kindt, 1968; Ferguson, Barton, and Drake, 1968).

Haemorrhage may occur into any of the intracranial compartments. In some series, the commonest site was the subdural compartment (Jones and Knighton, 1956; Silverstein, 1960), in others intracerebral haemorrhage, or a combination of subarachnoid and intracerebral haemorrhages, predominated (Imhof, 1951; Kerr, 1964). In all series, the rarity of intraventricular haemorrhage has been emphasized. The first report of such an occurrence in a probable haemophiliac was a necropsy record by Traneus (1870) in a 2-year-old child. There was no laboratory report and his diagnosis of haemophilia was later rejected. The first authentic documentation of ventricular haemorrhage in proven haemophiliacs was by Silverstein (1950) who, in an exhaustive review of world literature, reported ventricular involvement in four of his 12 cases of intracerebral haematoma, two each at surgery and at necropsy. There was no conclusive evidence of intraventricular haemorrhage in case 1 of Davies *et al.* (1966), who had blood stained CSF and moderate hydrocephalus on contrast studies. Our patient represents the fifth example of intraventricular haemorrhage in a haemophiliac in the literature.

There have been reports of successful surgical management of intracranial bleeding in haemophiliacs (Travis *et al.*, 1968; Ferguson *et al.*, 1968). Yet, to date, there is no record of a successful ventriculo-peritoneal shunt for hydrocephalus after intraventricular haemorrhage. Operation was performed in our patient because of the rapid progression of neurological signs and proof of the site of haemorrhage. Had we known that he was a haemophiliac before operation, surgical intervention of this nature would still have been contemplated in view of the rapid progression of the hydrocephalus, but with energetic replacement of the deficient clotting factor. What sustained our patient post-operatively and led to the successful surgical outcome was the use of lyophilized plasma at first, and later of cryoprecipitate, a potent Factor VIII con-

centrate introduced by Pool and Shannon (1965) which has the merit of securing adequate haemostasis without overloading the circulation. It is the recent development of such preparations containing a high concentration of Factor VIII which has made the surgery of intracranial haemorrhage in haemophiliacs less hazardous and more beneficial (Potter, 1965; Davies *et al.*, 1966; Brown, Hardisty, Kosoy, and Bracken, 1967; Prentice, Breckenridge, Forman and Ratnoff, 1967; Travis *et al.*, 1968; Moody and Mullan, 1968; Ferguson *et al.*, 1968) and has led to a marked fall in the mortality of this dangerous complication from about 70% reported by Imhof (1951) and Silverstein (1960), through the 33% of Kerr (1964), to the 20% of Davies *et al.* (1966).

SUMMARY

A case is described of a 3-month-old Nigerian boy with ventricular haemorrhage as the initial manifestation of his haemophilic state. A ventriculo-peritoneal shunt was successfully performed because of the rapid progress of his hydrocephalus. Haemostasis was achieved using lyophilized plasma, and later cryoprecipitate. Routine investigations and the necessary surgical treatment of intracranial haemorrhage are feasible in haemophilia if normal haemostasis can be obtained.

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