Intracranial hemorrhage is the most dreaded complication of hemophilia and is now the leading cause of death in this disease. Silverstein, reviewing the world literature to 1960, reported a mortality of 71%. In his series, eight of 30 patients were treated with surgical intervention 11 times with only two survivals. With recent advances which allow the production of low volume, extremely potent concentrates of Factor VIII (anti-hemophilic globulin, or AHG), the outlook for survival and successful surgical intervention in classical hemophilia is greatly improved. The following case report describes the surgical management of a subdural hematoma in a hemophiliac patient using the most widely available Factor VIII concentrate, cryoprecipitate, to correct the clotting defect. The successful outcome of this case testifies that intracranial surgery may be safely performed in the hemophiliac patient.

Case Report

This 22-year-old university student, with recognized classical hemophilia, was admitted to Victoria Hospital on May 19, 1967, because of a seizure that had followed 2 days of severe bifrontal headache. There was no history of recent injury. The diagnosis of classical hemophilia had been made in infancy following 21 days of bleeding from a minor gum injury. Since then, the patient had experienced intermittent prolonged external bleeding from minor injury, soft tissue hemorrhages, mild hemarthroses, and an episode of gastrointestinal bleeding. All of these bleeding episodes had been controlled with small amounts of fresh frozen plasma.

Examination. Examination revealed only neck stiffness and early papilledema. Skull x-rays were normal. Echoencephalography showed a midline shift of 4 mm to the right. The partial thromboplastin time (PTT) was 83 sec (normal, 33–45 sec) with a Factor VIII level of 6% (normal, 50–200%). Four units of cryoprecipitate were given with no improvement in his symptoms. That evening a left frontal adhesive seizure occurred, and the patient was placed on Dilantin and Decadron. A RISA brain scan revealed an area of increased uptake overlying the left cerebral convexity, consistent with that of a subdural hematoma. Surgical treatment had to be delayed until sufficient cryoprecipitate for operation and the first 7 postoperative days could be accumulated. During this forced delay, the patient’s neurological status steadily deteriorated. By May 21, he was dysphasic and had a mild right facial palsy. There were periods of marked confusion, restlessness, and intermittent focal seizures involving the right face and shoulder girdle musculature. The headache remained severe and uncontrollable.

On May 23, left carotid angiography was performed 2 hours after the intravenous administration of 4 units of cryoprecipitate, which had elevated the Factor VIII level to 30%. The angiogram confirmed the presence of a moderate-sized subdural hematoma on the left. There was no abnormal bleeding from this procedure, but in the evening an episode of status epilepticus required 300 mg of Sodium Luminal and 4 mg of Valium intravenously for control. The following day the patient received an additional 6 units of cryoprecipitate.

Operation. On May 25, 6 days after admission, the patient was prepared for operation with 10 units of cryoprecipitate, which elevated the Factor VIII level to 51%, and reduced the PTT to 40 sec. The partially liquefied hematoma was evacuated through two burr holes placed in the frontal and parietal regions. There was no unusual bleeding, and
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the technique differed in no way from that in a nonhemophiliac individual.

Postoperative Course. Recovery was uneventful. The PTT was maintained at a normal level with large amounts of cryoprecipitate. In total, 126 units were used, of which 102 units were administered in the postoperative period. This is equivalent to 31.5 litres of fresh frozen plasma. Initially, 6 units of cryoprecipitate were used every 6 hours, and on the second postoperative day a graduated reduction of the dosage was begun. No cryoprecipitate was given after the 6th postoperative day, and by the 10th day the PTT was once again 80 sec. The wounds healed well, and the sutures were removed on the 8th postoperative day without incident.

A postoperative angiogram performed on June 8 after the administration of Connought Factor VIII concentrate showed that there was no longer any evidence of the subdural hematoma. At the time of discharge 2 days later, the patient showed great improvement from his preoperative state. He was free of headache and had had no seizures. The profound dysphasia had regressed to the point of minimal expressive difficulties. He is attending his university again and remains well.

Discussion

Classical hemophilia is a sex-linked recessive disorder of blood coagulation due to a primary Factor VIII deficiency that occurs in Caucasians with a frequency of 2 to 3 per 100,000. Minot and Taylor\(^1\) demonstrated in 1947 the presence of Factor VIII in normal blood and its absence or deficiency in classical hemophilia. Biggs,\(^3\) in 1955, developed a technique for the assay of Factor VIII and demonstrated that there was a close correlation between the clinical severity of hemophilia and the level of Factor VIII in the blood. The clinical and laboratory assessment of the severity of the disease\(^4\) is as follows: patients with severe hemophilia bleed spontaneously with Factor VIII levels less than 1%; moderate hemophiliacs, as in the case presented here, bleed from minor trauma with Factor VIII levels of 1–10%; mild hemophiliacs bleed only after more severe trauma with Factor VIII levels greater than 10%. Biggs also demonstrated that a total correction of the hemostatic defect in hemophilia was possible if Factor VIII was supplied in amounts adequate to produce normal or near normal levels (50–200%). The modern management of bleeding episodes in a hemophiliac patient is dependent on this fundamental work.

Spontaneous bleeding in hemophilia is controlled with a Factor VIII level of 10–15%. Traumatic bleeding requires a level of at least 30%. With whole plasma it is not possible to achieve Factor VIII levels above 25% or maintain them above 10% for more than 2 to 3 days.\(^5\) To achieve the necessary high levels, efforts in the past decade have been directed toward the development of increasingly potent preparations of Factor VIII, ranging from fresh frozen plasma to concentrated preparations of human and animal Factor VIII. This work has culminated in the production of various highly potent, human concentrates of Factor VIII. The most widely used and available of these is cryoprecipitate, produced by the isolation of Factor VIII in the cold insoluble precipitate of fresh frozen plasma. This technique, which represents a great advance in the care of the hemophiliac, was described by Pool and Shannon in 1965.\(^2,10\)

Cryoprecipitate overcomes many of the disadvantages of earlier preparations.\(^2,10\) From a pint of fresh whole blood, the yield of Factor VIII is only 3 ml. This is reconstituted with normal saline to a total volume of 13 ml, which represents 1 unit of cryoprecipitate. The low volume avoids the problem of circulatory overload when enormous quantities of Factor VIII are required, as in this case, where Factor VIII equivalent of 7 litres of fresh frozen plasma was used in the first 24 hours following surgery. Cryoprecipitate is a human blood product, thus avoiding the problem of antigenicity encountered with animal concentrates. Cryoprecipitate is also relatively simple and inexpensive to prepare. It can be produced in a hospital blood bank equipped with storage facilities at \(-60^\circ\)C refrigeration, a refrigerated centrifuge, plastic dual pack collection systems, and a ready supply of fresh whole blood. As it can be stored in the frozen state in low volume, cryoprecipitate can be prepared in anticipation of need, and reconstituted as required. Pool and Shannon\(^10\) have shown that it can be frozen and stored for 6 months without significant loss of potency.

Recent reports\(^9,19\) state that intracranial hemorrhage has become the most common