Case Reports and Technical Notes

Factor VIII in Hemophilia

Case Report

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The general problem of surgery in the hemophiliac patient, particularly the management of intracranial bleeding, has long been difficult. Recent developments in the study and preparation of clotting factors have markedly changed the outlook. The purpose of this paper is to review the problem and to report the use of these newer preparations in a patient in whom an extensive posttraumatic subdural hematoma was removed from in front of the brain stem, without any problem in securing hemostasis.

There are really only two conditions to which the designation “hemophilia” can be properly applied, and these are Factor VIII deficiency and Factor IX deficiency. It is the former, or Factor VIII deficiency, which is involved in classical hemophilia. The substance appears to be an alpha 2 globulin, and the assay in severe cases may be as low as 1% or 2%. The disease itself is transmitted as a sex-linked recessive, becoming manifest in the male, but passed on through the female. Factor VIII is an essential precursor to clot formation, and in its absence, prothrombin is not converted to thrombin, so that clot formation will not take place or will occur very slowly.14

It has been stated1 that plasma levels of 20% to 30% of Factor VIII are necessary to provide hemostasis in major trauma or in surgery. The success of plasma transfusions used to obtain such levels was doubtful, and the repeated transfusions carried with them the very real danger of congestive heart failure.

In the last few years the preparation of Factor VIII concentrates has resulted in a distinctly brighter prospect for the hemophiliac patient, as it allows large quantities of Factor VIII to be administered in rather small fluid volumes, so that nearly any desired level of Factor VIII can be obtained without undue hazard to the circulatory dynamics.1,2,4,7,9,12,13

Early efforts to obtain high Factor VIII levels with animal concentrates were restricted by their antigenicity. At present, the two most promising concentrate preparations are the glycine-precipitated Factor VIII, first reported by Webster, et al.,13 in 1965 and clinically evaluated by Abilgaard, et al.,1 and cryo-precipitates of Factor VIII, reported by Pool and Shannon in 1965.5 The latter has received considerable attention, due to its relative ease of preparation. As the plasma can be used following extraction of Factor VIII, and the preparation can be carried out as part of a hospital blood transfusion service, it is also less wasteful.2,4,7,8,10,11

Case Report

This 21-year-old white man with recognized hemophilia had 32 previous admissions for bleeding episodes. Three days before admission he had been injured in an automobile accident, with superficial evidence of trauma to the head and left hand. He did not lose consciousness. He was taken to his local hospital and received transfusions of fresh plasma. Approximately 48 hours after injury he was noted to have developed a left 6th and 7th cranial nerve palsy, followed in the next 12 hours by a partial left 5th, 8th, and 9th nerve palsy.

Examination. The patient was transferred to our hospital where the findings above were confirmed. He was noted to have a variably slow pulse, between 50 and 60, a blood pressure with systolic readings ranging between 140 and 160, and a rapid respiratory rate of 28 to 32. In addition, he developed a miotic left pupil and absence of sweating on the left side of the face. Although lethargic, he was well oriented and

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responded appropriately to questions and commands. He was immediately started and maintained on cryoprecipitates of Factor VIII, so as to keep him at levels of 50% or better. On the day following admission, or 4 days after the accident, the left 5th nerve paresis became more marked and that of the 8th and 9th nerves became complete.

The next day the patient developed partial loss of pain sensation in his right side and had an equivocal right Babinski. A vertebral angiogram was performed, with Factor VIII levels maintained at nearly 75%. This showed displacement of the basilar artery backward and to the right. A brain scan was negative. The working diagnosis was extradural posterior fossa hematoma with either progressive bleeding or swelling of the mass. Although reassured by our colleagues in hematology that surgery was safe, we elected to wait and hoped for spontaneous resolution of his problem. On the sixth posttraumatic day, the patient began to develop a slight right 5th nerve palsy. Over the seventh day his condition appeared to stabilize, but on the eighth day he began to have intermittent Cheyne-Stokes respirations and showed right-sided weakness. Throughout this time lethargy increased but the patient remained oriented and fully responsive. The fundi at no time showed evidence of increased intracranial pressure. Later that day his conscious level decreased further and it was clear that he was deteriorating to the point where he would quickly die if his hematoma was not removed. First, a lumbar puncture was done. The pressure was 330 mm of H$_2$O, and it was decided to place a ventricular catheter with a puncturable reservoir, to lower and control the intracranial pressure during the posterior fossa craniectomy and in the postoperative period. During this time and in the surgery which followed, cryoprecipitates were administered to maintain levels of Factor VIII at 100%.

**Operation.** In the sitting position, following reduction of the cerebrospinal pressure via the previously placed reservoir, a left suboccipital vertical incision was made just medial to the mastoid process. A small craniectomy was carried out similar to the approach to an acoustic neuroma. No hematoma was seen outside the dura, which was moderately tight despite aspiration of the ventricle. The lateral third of the left cerebellar hemisphere was excised, exposing a firm clot which lay in front of the brain stem. Access to the clot was established by working between the 5th and 7th, and the 8th and 9th nerves; subtotal removal was carried out. The upper portion of the mass was not pulled off the hypothalamus. The right border of the clot extended out of view in the region of the right fifth nerve. Inferiorly it reached the foramen magnum. There was absolutely no hemostatic problem; the field was completely dry at the end, and the patient did not require blood transfusion. The dura was closed, but a drain was left intradurally for 2 days.

**Postoperative Course.** Sweating returned almost immediately to the left side of the face, and respirations improved. The systolic blood pressure fell to more normal levels. The right-sided weakness increased, however, and the patient was unresponsive to speech for several days. By the fifth postoperative day he was again talking; the intracranial pressure had fallen to normal levels and the ventricular reservoir catheter was removed. His course has since then been one of steady improvement. The Factor VIII level was maintained at 50% for the first 6 to 7 postoperative days and then at 25% until suture removal on the 10th day. The patient was discharged from the hospital, walking, on the 35th day. The left cranial nerves remained paralyzed, but the right-sided weakness had disappeared and the sensory deficit was improving.

**Discussion**

It is of interest that intracranial hemorrhage, either spontaneous or traumatic, is reported to be the most common cause of death in the hemophiliac patient.3,8 Kerr followed 109 hemophiliacs for 5 years. In five of these patients there were 19 episodes of intracranial bleeding, either proven or probable, with five deaths, or a mortality of 33.1%. Only five of these episodes were associated with trauma, and only one of these patients died. In eight of the episodes there was no known cause of hemorrhage; two followed coughing, one was associated with an aneurysm, and one each with meningitis, nitroglycerine, and "bleeding phase." The majority of hemorrhages were subarachnoid
and intracerebral, often combined. There were only two subdural hematomas, and these followed trauma.

Davies, et al., have reported five patients with proven intracranial bleeding who were managed with the use of Factor VIII concentrates. One had a traumatic aneurysm treated by extracranial ligation and with intracranial exposure and packing; one had a subdural hematoma evacuated through a burr hole 3 days after injury. Both survived the operative procedures uneventfully. These authors feel that, with the aid of Factor VIII, intracranial hemorrhage can now be dealt with on its merits.

Fessey and Meynell reported five cases of intracranial hemorrhage in hemophilia, four classical and one with Factor IX deficiency. Two of these followed trauma. Four of the patients had no confirmation of hemorrhage other than presumptive symptoms. All patients were treated with fresh plasma and concentrates, and a much more rapid recovery was noted following the use of concentrates. No surgery, angiography, or lumbar punctures were performed. Four of the five recovered, and one succumbed to an extensive subdural hematoma for which the authors felt a craniotomy might have been beneficial.

Potter has reported seven patients including six children under 7 years with either Factor VIII or IX deficiency who sustained head injury. Five patients in this series had surgical treatment. Two patients had craniotomies, one for a solid subdural hematoma and one for intracerebral hematoma; one had a subgaleal evacuation of liquid and solid clot. Two had burr holes, one for a fluid extradural hematoma, and one for a liquid and solid subdural hematoma; the latter died, apparently from brain swelling. Two patients with neurological abnormality after trauma but without proven bleeding recovered on conservative therapy. All patients were given plasma concentrates of the deficient factor, before, during and after operation for 6 to 10 days.

Conclusions

There seems to be a general agreement that with the aid of Factor VIII concentrates the coagulation level of the hemophiliac patient may be restored to normal and held there for prolonged periods, and that many problems of intracranial hemorrhage may resolve under conservative management, whether the cause of hemorrhage be traumatic or spontaneous. At the same time, it is also clear that, given adequate hematological facilities and an opportunity for close collaboration between hematologists and neurosurgeons, there is no reason to deprive these patients of surgical help when it is indicated. Although we have found no reports of tumor surgery in the hemophiliac patient, there is no reason why this type of surgery need be withheld if Factor VIII concentrates are available.

References

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