Traumatic intracranial hemorrhage in children with rare coagulation disorders

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Children with rare coagulation disorders are at high risk from intracranial bleeding with even minor head injury. Treatment by transfusion of fresh frozen plasma is limited because of the large volumes required for restoring the missing coagulation factor. Furthermore, even when concentrates of such a factor are available, their use may prove ineffective due to circulating specific antibodies. Three patients with rare coagulation disorders are presented who suffered head injury complicated by intracranial hemorrhage.

KEY WORDS □ hemophilia A □ Factor V deficiency □ thrombocytopenic purpura □ intracranial bleeding □ anti-Factor VIII antibodies □ coagulation disorder

CHILDREN with hematological disorders enjoy the significant progress made in recent years in terms of prevention and treatment of various complications related to their illness. However, prolongation of life in these children has also led to a higher incidence of complications, of which intracranial bleeding due to trauma is probably the most dreaded. Most reports of traumatic intracranial bleeding refer to children with classic hemophilia who were treated satisfactorily by antihemophilia globulin (AHG) infusion.

In this paper, we describe three children with rare hematological disorders. One patient had hemophilia A complicated by the existence of a circulating anti-Factor VIII antibody. A second patient had a Factor V deficiency, and a third had thrombocytopenic purpura. Traumatic intracranial bleeding brought all three patients to our attention, and we report the course and treatment of these difficult cases.

Case Reports

Case 1

This 10-year-old boy, a severe hemophiliac A with recurrent episodes of hemarthroses, was admitted to the emergency room 1 hour after falling at home and striking his head. He was known to have had anti-Factor VIII antibodies since the age of 4 years.

He did not lose consciousness or vomit. On examination, he was alert and cooperative. There was a small bruise over the left forehead, but no external bleeding. Physical and neurological examination was normal. Skull films did not show fractures. Blood tests revealed a partial prothrombin time (PTT) of 180 seconds and a blood anti-Factor VIII antibody titer of 1.2 Bethesda Units. A computerized tomography (CT) scan revealed a left frontal epidural hemorrhage.

As surgery was contemplated and the anti-Factor VIII antibody titer was found to be low, transfusion with antihemophilic factor (AHF) was initiated. The PTT was restored to 40 seconds after rapid infusion of AHF at a dose of 80 μ/kg. During that time, stupor and bradycardia were noted. The child was rapidly transferred to the operating theater, where a small trephination was made and a large blood clot removed.

Recovery was complete 36 hours later, during which time AHF concentrates were given in doses of 160 μ/kg/day. The PTT was checked daily. On the 5th postoperative day, the PTT reached 85 seconds, and on the 6th day it could not be brought below 130 seconds, due to high antibody titer which reached 48 Bethesda Units. Subsequently, AHF infusion was stopped; however, repeat CT scanning showed no residual epidural blood. The child was discharged on the 14th postoperative day without symptoms.

One month later, he was readmitted in stupor and with a high temperature. There was no history of head
trauma or convulsions. On examination, there was mild neck stiffness, dysphasia, and very mild right-sided hemiparesis. The fundi were normal. A CT scan showed subdural and subarachnoid blood collection over the entire left hemisphere, with a significant midline shift to the right.

A transfusion of AHF concentrate was immediately given; however, even with an intravenous push dose of 2400 units, the PTT was only shortened to 140 seconds, due to a very high activity of circulating anti-Factor VIII antibodies (48 Bethesda Units). With a fine needle (No. 25), 10 cc of blood mixed with cerebrospinal fluid (CSF) was aspirated through the existing trephination defect.

Any surgical procedure at that time was considered too hazardous. The child was kept under intensive care with high doses of steroids, and transfusion of anti-inhibitor coagulant complex (Autoplex)* in a dose of 100 units/kg every 8 to 12 hours. He recovered completely within 36 hours under the Autoplex treatment, which was discontinued on the 10th day, although the PTT was still 135 seconds. Two weeks later, he could walk and a CT scan showed significant improvement. He was discharged without neurological sequelae.

Case 2

This 4-year-old Arabic boy, known to suffer from Factor V deficiency, was admitted in August, 1981, following minor head injury. Trauma was followed by a few moments of unconsciousness, and he then vomited several times.

On examination, he was alert and cooperative. A subcutaneous hematoma was noticed adjacent to the right eyebrow. Otherwise, physical and neurological examination was normal. Skull films showed a frontal linear fracture. A CT scan revealed a bifrontal epidural hematoma.

Fresh frozen plasma transfusion was immediately started, and the child was placed under close observation. However, he underwent rapid neurological deterioration, and evacuation of the hemorrhage was obviously indicated. A No. 14 needle was drilled into the frontal epidural blood collection, and unclotted blood was obtained under high pressure. A small polyethylene catheter was introduced into the epidural space through the needle, and left in situ for continuous drainage of the blood collection. Improvement was rapid: 24 hours later the child was neurologically intact. The epidural catheter was removed after 36 hours, during which time 1400 cc of fresh frozen plasma was given. Transfusion was tapered off and subsequently stopped on the 8th day. The child was discharged with no residual neurological deficit.

Case 3

This 6-year-old Arabic girl was in good health until November, 1981, when she developed acute follicular tonsilitis for which ampicillin was given orally. Three days later, she suffered a sudden left-sided focal seizure, followed by generalized convulsions. She was hospitalized elsewhere, and was treated with Dilantin (phenytoin sodium), ampicillin, and hydrocortisone. A dense left hemiplegia developed, and she was referred to the Hadassah Medical Center. Questioning revealed a history of mild head trauma.

On examination, the patient was stuporous, febrile, and mildly dehydrated. There were no meningeal signs. The fundi were normal. Left spastic hemiplegia and central facial paresis were present, with bilateral pyramidal signs. The skin all over her body was covered with purpural rash. Skull and chest films were normal. A CT scan showed a large right temporal intracerebral hematoma, with a midline shift to the left.

Direct blood smear revealed a platelet count of 15,000/cu mm, and a white blood count of 23,000/cu mm, of which 90% were mature granulocytes. Hemoglobin was 13.6 gm%, PTT was 31 seconds, and prothrombin time (PT) was 65%. Bone marrow smear was rich with young megakaryocytes and reactive myeloid cells, indicative of reactive (immune) thrombocytopenic purpura.

The patient received steroid therapy and thromboocyte transfusion, and there was gradual improvement in her neurological condition. A CT scan 2 weeks later showed a resolving hematoma. Although she was treated by repeated infusions of thrombocytes within the next weeks, the blood platelet count never exceeded 96,000/cu mm. However, when she was discharged 1 month after admission, there was marked improvement in her neurological condition. She is ambulatory and is being followed as an outpatient; she is still receiving a maintenance dose of steroids. A recent CT scan showed brain atrophy, with complete resolution of the hemorrhage.

Discussion

About 10% of hemophilic patients have circulating anti-Factor VIII antibodies.1 Head injury in these children may end fatally due to failure of the clotting mechanism to respond to transfusion of AHF concentrates. This is in sharp contrast to the recent significant progress in treatment of hemophiliacs without circulating inhibitors.10-13-15

The first report of traumatic intracranial bleeding in a hemophiliac patient treated with inhibitors seems to be that of Edson, et al.,3 in 1973. These authors reported surgical evacuation of a subdural hemorrhage in a patient with progressive neurological deterioration. However, they used quite complicated methods to control bleeding, including repeated exchange blood transfusions, immunosuppression with

* Autoplex obtained from Hyland Laboratories, Glendale, California.
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cyclophosphamidne and corticosteroids, and infusion of epsilon-aminocaproic acid combined with very large doses of AHF concentrates. Subsequently, complications included hemolysis, platelet dysfunction due to hyperfibrinogenemia, leukopenia, and Gram-negative sepsis. These complications, combined with the massive amounts of Factor VIII concentrates required in such patients to restore the missing factor, present a most difficult challenge in their management.

A breakthrough in the treatment of the hemophilic patient with circulating inhibitors was first achieved by Fekete, et al., who, in 1972, used an activated prothrombin complex. Their complex contained Factors II, V, VII, VIII, IX, X, XI thrombin, and Factors IXa and Xa. These authors were followed by others who successfully used this form of treatment.

In 1974, an activated form of prothrombin concentrate, Autoplex, was first used in patients with circulating inhibitors. It has since been used by others and found very effective in controlling hemorrhage in these patients. The active ingredients of Autoplex remain unknown, and there does not appear to be a reliable laboratory test for monitoring therapy, as PTT remains prolonged in most instances.

There have been only four reported cases of traumatic intracranial bleeding in hemophilic children with inhibitors; these children were treated by Autoplex infusion with favorable results. Of these, one was a 6-year-old boy who sustained a large parieto-occipital epidural hemorrhage and who completely recovered without surgery. He received treatment with Autoplex, 100 μ/kg/day every 8 to 12 hours for 14 days, followed by 3 days of single-dose infusions of 50 to 100 μ/kg. His lethargy cleared within 24 hours, and serial CT scans revealed progressive resolution of the hematoma. The remaining three patients were treated surgically.

The only complication with Autoplex has been hypofibrinogenemia in children receiving repeated doses. This was not encountered in our Case 1. Although of promising future, we do not think that Autoplex can replace surgery in cases where intracranial hemorrhage endangers life. It is, however, an irreplaceable adjuvant in the management of patients with Factor VIII inhibitors who sustain intracranial bleeding, and who would have otherwise been in a hopeless situation.

In contrast with hemophilia, reported cases concerning traumatic intracranial bleeding in patients with Factor V deficiency (parahemophilia) are rare. Interestingly, anti-Factor V antibodies have also been described. Because the activity of Factor V decreases rapidly with storage, conserved blood and dried plasma are unsuitable for adequate replacement therapy, and fresh frozen plasma is the treatment of choice. Factor V blood level should reach at least 10% to provide normal hemostasis in major surgical inter-

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