Hemophilia

Objectives
1. List the two clotting factors in which deficits result in hemophilia
2. Describe laboratory workup for clotting deficiencies
3. Discuss the importance of inhibitors
4. Describe the natural history of hemophiliac arthropathy
5. Discuss methods currently available for altering the natural history of hemophiliac arthropathy
6. Describe management of an acute muscle hemorrhage in a hemophiliac child

Discussion points
1. What levels of factors VIII or IX result in severe, moderate, or mild hemophilia?
2. What is the role of home therapy for children with hemophilia?
3. Correlate radiographic findings of hemophiliac arthropathy with the intraarticular arthropathy
4. What is a common cause of femoral nerve palsy in children with hemophilia?
5. What is a pseudotumor?

Discussion

Classic hemophilia or Hemophilia A results from a deficiency of factor VIII; Christmas disease or Hemophilia B from a deficiency of factor IX. Hemophilia A and B are both transmitted in an X linked recessive pattern. These are the only inherited coagulopathies of major orthopaedic interest. 1 unit equals the amount of activity of the clotting factor in 1ml of pooled, normal plasma. Concentration of factors VIII and IX are usually given in percentage of normal activity; severe hemophilia denotes a level of < 1% if normal activity moderate, 1-5%; and mild, > 5%. Spontaneous hemorrhage generally occurs only in patients with severe hemophilia.

The history of hemophilia management is of some interest. Transfusion of clotting factors only became possible in the late 1960's with cryoprecipitate, made from pooled plasma. Although the benefits were immediately evident, the pooling process collected plasma from many donors, dramatically increasing risk of disease transmission, and large numbers of young men with hemophilia growing up during those years contracted hepatitis or AIDS. Factors VIII and IX are now prepared with recombinant DNA techniques, eliminating the risk of disease transmission. Routine surgery now can regularly be performed. Protein replacement therapy still, however, carries the limitation
of antibody formation, commonly called inhibitors. About 15% of patients with severe hemophilia presently develop inhibitors. There are methods available to counteract the effect of inhibitors, but these are quite expensive at present. There is a great deal of interest in gene therapy for hemophilia, clinical trials were started in 1999.

The average age of diagnosis for a child with severe hemophilia is 1.2 years. The first joint bleed follows the first bleed by an average of 6 months. Consideration of child abuse is not unusual at the time of diagnosis. Screening lab work for coagulation disorder includes CBC with platelet count, prothrombin time, partial thromboplastin time, and bleeding time. Most children with severe hemophilia are now managed with home replacement therapy administered by a family member. Prophylactic regimens have reduced the number of joint hemorrhages. The ankles are the joints most often affected in early childhood, the knee and elbow later. Blood in the joint is irritating to the synovium, when the amount of iron absorbed by the synovial cells becomes excessive, lysozome release ensues. Lysozomes are harmful to articular cartilage and incite a further synovial reaction. Eventually, the synovium becomes fibrotic. As synovial function diminishes, lysozial destruction of the articular surface proceeds with ankylosis the end result of an untreated joint. Early treatment with factor replacement and aspiration of the joint for large bleeds have arrested progression of hemophiliac arthropathy in a great number of children. By the time radiographic changes of joint space narrowing and erosion are established, the joint is severely destroyed. For cases of chronic synovitis unresponsive to factor replacement, synovectomy is useful. This is presently often performed arthroscopically, which definitely reduces postoperative stiffness and pain. Radioactive synovectomy is used in some centers and eliminates the need for extensive factor replacement. The rate of recurrent synovitis may be higher.

Muscle hemorrhages are common, and may represent an emergency situation for the orthopaedist not regularly caring for children with hemophilia. The forearm, iliopsoas, quadriceps, and calf are most often involved. Prompt administration of factor replacement is needed. The clinical status of the limb is assessed regularly, and if compartment release is necessary, it can then be promptly performed. Bleeding into the iliopsoas can produce femoral nerve palsy. Early administration of factor replacement therapy is usually effective. A pseudotumor begins as a hemorrhage that becomes encapsulated. Fortunately, such lesions have become less common with better therapy.

References


