IOP - Images

Case resolution

Diagnosis

Hemophilic arthropathy

Discussion

Hemophilia consists in the congenital deficit of the factor VIII (hemophilia A or classic hemophilia) or factor IX (hemophilia B or Christmas' disease) clotting activity in plasma. Even though it is a congenital disorder linked to the X chromosome, up to one third of the cases results from spontaneous mutations in the genes that code for clotting factor VIII and clotting factor IX.

Worldwide prevalence of hemophilia A is 1 per 5000 males, and that of hemophilia B is 1 per 30,000 males; it does not show prevalence in any particular race.

Bleeding severity is usually correlated with the levels of the clotting factor. Bleeding areas that threat the patient's life and require immediate treatment are head, neck and the gastrointestinal system. However, these ones are also the areas that show the lowest bleeding rates (<10%). On the contrary, the areas that most frequently bleed are joints (70-80%) and muscles (10-20%). The joints usually involved are knees, elbows, ankles, shoulders and hips.

The physiopathology of the hemophilic arthropathy seems to be multifactorial. Recurrent bleeding in the joint leads to the storage of hemosiderin, which has a direct degenerative toxic effect on the cartilage. The increase in intra-articular hemosiderin also stimulates synovial hyperthrophy and inflammation, and repeated synovitis also leads to the progressive destruction of the cartilage and the sub-chondral bone. Consequently, a combination of degenerative joint damage and inflammatory processes, which occur in parallel since the early stages of the condition, cause joint destruction and resulting severe functional deterioration. Hemophilia shows three stages (Köning):

- *Acute stage or recurrent bleeding stage:* the condition is characterized by pain, inflammation and movement limitations. The patient usually reports that he knows he is bleeding before any of the aforementioned evidence ("aura"). Bleeding could be associated with mild rigidity and tension or tickling feeling. When bleeding is frank, the joint becomes hot and tense. Afterwards there are movement limitation and secondary muscular spasms.

- *Sub-acute stage or panarthritis stage:* after blood absorption, there is an inflammatory reaction in the synovial tissue, what leads to tissue inflammation plenty of blood vessels. Then there is recurrent bleeding and the synovial tissue starts producing enzymes which cause more inflammation within the joint. Recurrent bleeding hurts less and the degree of mobility impairment is lower.

- *Chronic stage or fibrosis and contracture stage:* bleeding leads to synovial destruction and this is replaced by scar tissue (fibrosis). Nonetheless, after bleeding, the iron remains stored in the joint ant the enzymes produced by the synovial tissue start causing changes in the cartilage that covers the epiphysis. The cartilage breaks and becomes rough. These changes eventually generate an arthritic and destroyed joint. At this stage, the patient usually experiences pain, functional impairment and deformity.

The most accurate diagnosis is made by medical history and lab tests, which show normal or increased bleeding time, increased activated partial thromboplastin test and a normal platelet count, with quantitative study of factors VIII and IX.

Images play a key role in the follow-up of this condition at all stages, to check development and monitor treatment.

Conventional X-rays are useful, although they do not show anomalies at the early stages of this condition. Ultrasound is useful as quick and affordable test to screen joint bleeding and assess the advance or resolution of pseudo-tumors. It is also quite useful to assess extra-articular bleeding.

MRI is a very accurate diagnostic method which evaluates both intra-articular and extra-articular repercussions and the degree of damage (there are different consensus scales, such as Denver's and the European Score). MRI can assess injuries potentially reversible (joint effusion/joint bleeding, synovial hypertrophy and hemosiderin) and irreversible (bone erosions, sub-chondral cysts and joint cartilage loss).

With MRI it is possible to pinpoint exactly the location of joint effusion, and assess magnitude, blood quality, the presence of blood clots and the possibility of re-bleeding. On the other hand, MRI evaluates extra-articular hemophilic repercussions and other muscle-skeletal conditions unrelated to hemophilia.

Synovial hypertrophy is the first sign of joint involvement after bleeding: at early stages (exudative stage), the synovial membrane is smooth and even, whereas, at the proliferative stage, it becomes rough and uneven.

The detection of hemosiderin makes it possible to differentiate hemophilic joint bleeding from other disorders. Regarding so, differential diagnosis includes juvenile idiopathic arthritis, tuberculous arthritis, and pigmented villonodular synovitis.

The treatment of hemophilia consists in replacing the missing blood clotting factor, which is administered intravenously. When bleeding occurs within the joint, it is essential to give the patient treatment as soon as possible so as to avoid long-term injury. Clotting factors concentrates are manufactured out of human blood (hemoderivatives) or using cells genetically designed which carry a human factor gen (recombinant products). Persons with mild hemophilia A sometimes use desmopressin (also called DDAVP), a synthetic hormone which stimulates factor VIII release.

When indicated, invasive treatment consists in chemical synoviorthesis, radio-synoviorthesis (synovectomy with radioisotopes), and surgical synovectomy.

Conclusion

Early detection and treatment of synovial involvement in hemophilic patients are the only proved strategies to avoid the advance of joint disorders and the development of irreversible joint changes.

MRI has proved to be a very sensitive study to detect the early stages of the hemophilic arthropathy, which this way can be visualized earlier than they can by conventional X-ray and even by medical history. At advanced stages of the condition, there is high correlation between bone injuries in X-rays, and synovial and cartilage changes visualized in MRI. Moreover, MRI shows anomalies which are characteristic in chronic synovitis in 50% of patients with normal X-ray.

MRI should be the imaging diagnostic technique of choice for the initial assessment of the hemophilic arthropathy, the determination of stage and the patients' follow-up so as to monitor the different kinds of treatments available.