CHAPTER 9

HEMOPHILIC ARTHROPATHY: Consideration in the Differential Diagnosis for Ankle Pain and Joint Degeneration

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Ankle pain and joint degeneration has a multitude of etiologies. Identifying the cause of single or polyarticular joint pain can be difficult due to an extensive differential diagnosis. A thorough history and a complete physical examination is essential. Factors involved in narrowing the possible causes include disease chronology, distribution, inflamation, extra-articular manifestations, disease course, and patient demographics. This combined with laboratory tests and the use of diagnostic imaging modalities, will help confirm or preclude suspicions toward a final diagnosis and treatment plan. The differential diagnosis for ankle pain and joint degeneration may include the following: acute trauma, osteoarthritis, rheumatoid arthritis, sero-negative arthritis, pigmented villonodular synovitis, and hemophilic arthropathy to name a few.

BACKGROUND

Hemophilia is a sex-linked genetic coagulation disorder that occurs primarily in males whose clotting factors are nonfunctional or absent. Classic Hemophilia, or Hemophilia A, is a lowered clotting factor VIII and is the most common coagulation disorder. Christmas Disease, or Hemophilia B, involves clotting factor IX, and is the second most common disorder. The world-wide prevalence of hemophilia A is estimated to be 1 in 10,000 men, whereas hemophilia B, the occurrence is 1 in 25,000 men. The occurrence of the disease can be in varying grades or phenotypes; mild, moderate, or severe. These grades are based on the plasma concentration of the clotting factor. Mild disease is one in which the plasma concentration is greater than five percent of normal. Moderate disease affects those with plasma concentrations between one and five percent of normal. Finally the severe form of the disease is a plasma concentration of less than one percent. The higher the factor coagulant activity the fewer the clinical problems. Severe hemophilia affects approximately 45% of patients who have the disease, with serious bleeding occurring spontaneously or after trivial trauma.[1] Most of the bleeding events are located in large joints, especially the knee, ankle, and the elbow. Repeated episodes of intra-articular bleeding, causing damage to the joint, is known as hemophilic arthropathy.

PATHOPHYSIOLOGY

Bleeding presumably originates from the synovial vessels. Hemorrhage occurs into the joint cavity or into the diaphysis or epiphysis of the bone. In an acute bleeding episode, the synovial space is distended with blood. Muscle spasm may further increase the intrasynovial pressure. A common complicating feature that may occur is hemorrhage into the periarticular structures of joint.[2] Because of recurrent hemarthrosis, specific changes occur in the synovium and cartilage.

After the initial episode of hemarthrosis or a minor bleed, the joint may regain normal function. With multiple hemarthrosis or following a severe bleed, the absorption of intra-articular blood is incomplete, and the retained blood produces chronic inflammation of the synovial membrane. With each recurrence, the synovium becomes progressively more thickened and vascular.[1] Proliferating synovium often fills the and distends the joint, together with the weakening of the periarticular structures, this process predisposes the joint to recurrent episodes of bleeding. In this proliferating stage, the synovium becomes catabolically active due to the exposure of blood components and as a result induces cartilage destruction.[3] Proteolytic enzymes are freed within the joint space from blood leukocytes and the inflamed synovium, that degrade the cartilage and bone. The exact pathogenic mechanisms involved in this process are not precisely known. The hypertrophied synovium will continue to expand with repeated episodes of bleeding in a continued cycle of destruction. Synovial changes may have a leading role in the development of the joint damage and therefore precede the changes in cartilage.[1] Although intra-articular blood can produce a direct harmful effect on the cartilage and bone.[4] Several pathological processes are possibly involved, some occurring in parallel and others sequentially, although

they influence each other they probably do not depend on one another. Repeated episodes of hemarthrosis results in progressive loss of hyaline cartilage, particularly at the margins of the joint. Large punched-out areas of osseous destruction are sometimes produced by the subchondral hemorrhages, along with cavitation in the cancellous structure of the bone due to intra osseous hemorrhage.

In the terminal stages of hemarthrosis, it is manifested by fibrous or bony ankylosis of the larger joints. Complete destruction may take place in the smaller articulations because of a weaker joint structures and the thinner cortices. Other permanent sequella of hemarthrosis include atrophy and proliferation of bone, roughening of the articular surfaces with lipping and osteophyte formation, bone necrosis and cyst formation, stunted growth as the result of interference with the nutrition of the bone, and accelerated development and overgrowth of the epiphysis caused by excessive blood flow.[3]

GRADING

The frequency of intra articular bleeding and the presence of synovitis and other sequella allow hemophilic arthropathy to be classifies into four grades.[5] Grade I; transitory synovitis with no additional bleeding episodes. Grade II; permanent synovitis with joint enlargement, thickening of the synovial membrane, and limitation of joint movements. Grade III; grade II along with axial deformities and muscular atrophy. Grade IV; additional capsulosynovial fibrosis with severe limitation of movement that results in ankylosis.

CLINICAL PRESENTATION

In acute hemarthrosis, pain is the early and predominant symptom that may be excruciating. Swelling, tenderness, warmth and impaired mobility are commonly seen. Some hemophiliacs report a characteristic aura, consisting of a warm, tingling sensation before the onset of hemarthrosis. With subacute hemarthropathy, the patient has synovial hypertrophy and frequent bleeds in the affected joint. Destruction of the joint, atrophy of surrounding muscles, and joint contractures begin during this stage. Physical examination may reveal muscle spasm and limited motion of the affected joint. The joint may be warm, grossly distended and discolored, but external evidence of bleeding may be minimal or absent in chronically damaged joints because of thickening of the articular capsule. Chronic hemarthropathy is the progressing of hemarthropathy and leads to further degenerative changes. The chronic effects of joint bleeding is far more serious resulting in synovitis, articular cartilage damage, and joint deformity. As the articular cartilage erodes, patient develops more pain, restricted motion and deterioration of function. Generally, only one joint is affected at a time, although bleeding may develop simultaneously in two or more joints. The joints most commonly involve is the knee, ankle, and elbow.[6] Although the hips, wrists, shoulders, and small joints of the hands and feet may be affected.

IMAGING

Radiographically, the diagnosis is often suggested by recurrent changes from hemarthrosis. The initial episode of intra-articular bleeding is usually associated with joint effusion without osseous or articular involvement. With recurrent bleeds peri-articular osteoporosis and regional soft tissue swelling are common.[7] In adolescents, the hyperemic joint may lead to localized accelerated growth and limb length discrepancies.[8] Osseous irregularity, erosion, and subchondral cysts may eventually develop. Synovial effusions may appear radiodense due to the hemosiderin deposition. Joint space preservation is an important diagnostic clue in this early stage of arthropathy. As osseous erosions continue to occur, joint space narrowing is seen and associated with cartilaginous destruction. With continued destruction, complete obliteration of the joint space will occur along with osteophyte formation and eburnation.[8]

Magnetic Resonance Imaging can detect early erosions not visualized on conventional radiography and is probably the best modality for assessing intra-articular abnormalities associated with hemophilic arthropathy.[9] Hemarthrosis can be visualized as a low to intermediate signal on T1-weighted MR images and increased signal on T2-weighted MR images. Chronic peri-articular changes are often visualized as decreased signal intensity on both T1 and T2-weighted MR images. Synovial hypertrophy results from fibrosis and appears as nodular areas of low to intermediate signal intensity on T1 and T2-weighted MR images. Subchondral cysts containing inflammatory fluid show an increased signal on T2-weighted MR images while fibrotic cysts are hypointense. Because articular cartilage is well visualized on MR imaging, focal areas of thinning or absent cartilage can be easily detected.[10]

TREATMENT

Conservative and prophylactic treatments should always be attempted prior to surgical intervention. Conservative treatment may include oral anti-inflammatory medication, compressive dressings, immobilization and the protection of the joint with braces and splints. Prophylactic therapy has been used in patients with severe hemophilia in order to convert their phenotype into the phenotype of moderate hemophilia.[11] In raising the serum clotting factor, 1 unit/kg of clotting factor will increase the serum clotting factor by 2%.[6] The half-life of factor VIII is 12 hours so infusions are administered every 8 to 12 hours to maintain steady levels. The half-life of factor IX is longer and its infusions can be given over a longer period of time.[12] Clotting factor VIII replacement therapy has been available since 1958, and factor IX since 1972. The goal of prophylactic replacement therapy is to prevent the concentration level of the factor from falling below 1% of normal and to reduce episodes of spontaneous intra-articular bleeds.[13] Acute hemorrhages should be treated immediately with factor replacement to resolve the bleeding episode and limit the amount of blood in the joint. For recurrent chronic episodes, factor replacement is given at frequent prophylactic intervals over a period of three to six months. The goal is to break the vicious cycle of bleeding and allow the synovium to return to a normal state.

It is much easier to prevent joint damage than to repair it after it has happened. Once a joint is damaged it cannot be restored to its original state, but treatment may slow down the process or stop additional damage. Treatment of symptomatic damaged joints may be accomplished through synovectomy. Non-operative synovectomy is the use of chemicals injected directly into the joint to control hypertrophic synovial tissue. Radiation from radioactive isotopes have been reported to cause fibrosis in the subsynovial connective tissues of the joint capsule and the synovial villi.[14] It also affects the vascular system of the synovial membrane causing closure of some vessels.[15] Steroids have been used sparingly due to the deleterious effects they can produce on intra articular cartilage. In chronic advanced severe synovitis there is already such destruction of the intra articular cartilage with diminished joint space. Intra articular dexamethasone may have a fibrosing activity on the damaged cartilage offering an alternative as a palliative treatment, specially focused on pain and functional impairment, before a more aggressive procedure is required.[5]

Operative synovectomy can be classified as open or closed based on the technique employed. If the joint damage is not too severe, a closed or arthroscopic synovectomy can be performed. The synovium is removed through the arthroscope without having to cut open the joint. The advantages is early joint mobilization and a shorter recovery period.[16] Open synovectomy is considered with advanced disease, joint narrowing, cartilage, and/or osseous involvement. This procedure allows visualization and access for the removal of hypertrophied synovium and osteophytes, with the ability for osseous remodeling.

Arthroplasty and arthrodesis are performed in end-stage joint disease. The total replacement or fusion of the effected joint may completely eliminates hemarthrosis and symptoms of disabling arthropathy. Post-arthroplasty may have limited joint range of motion due to the extensive involvement of the disease on periarticular soft tissues.[2]

CONCLUSION

Ankle pain and deformity has many presentations and causes. The treatment of hemophilic arthropathy with or without synovitis/destructive joint changes, consists of the application of a carefully structured and monitored rehabilitation program. The use of factor replacement therapy as prophylaxes, or for the stoppage of acute bleeds, when implemented at and early age may delay the progress of joint destruction. Synovectomy may be indicated in patients classified as having grade I or II synovitis with failure of conservative methods. By ablating the synovial membrane, episodes of additional bleeding are reduced or abolished, with suppression in the deterioration of the joint surface. As with any treatment plan, the progressive process of destruction of the joint may not be halted completely, and the need for arthrodesis or total joint replacement may be inevitable.

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