Hemophilic Arthropathy

Jaime A. Carvajal Alba, MD, Jean Jose, DO, and Paul D. Clifford, MD

Hemophilia is a rare group of blood coagulation disorders that are usually caused by inherited x-linked recessive clotting factor deficiencies. Classically, females are asymptomatic carriers and males express the disease. The common form of hemophilia, type A (estimated incidence, 1 in 5000 live male births), is caused by an inherited deficiency in factor VIII and also is known as *classic hemophilia*. Hemophilia type B (1 in 30,000 live male births) is caused by a deficiency in factor IX and also is referred to as *Christmas disease*.[1] The rarest form of the disease is acquired, typically by the elderly, through an antibody-mediated autoimmune response against factor VIII.[2] Deficiencies of factors VIII and IX alter the intrinsic pathway of the coagulation cascade, resulting in a tendency to bleed.

Imaging studies can help determine presence and quantity of hemarthrosis and can provide guidance for arthrocentesis in the acute setting.

The hallmark of hemophilia is hemarthrosis, most commonly affecting the knee, ankle, elbow, and shoulder joints. Hemophilic arthropathy is a disabling immune-mediated arthritis caused by chronic and recurrent exposure of the synovium and articular cartilage to metabolized blood products. This process is not completely understood. Chronic deposition of hemosiderin and other blood products induces phagocytic synovial cells and chondrocytes to release cytokines and hydrolytic enzymes into joints, resulting in synovial hyperemia, synovitis, and chondrocyte apoptosis. Synovitis leads to further intra-articular bleeding and ultimately to diffuse high-grade chondral loss, subchondral bone destruction, and flexion joint contracture.[3]

Imaging is crucial in evaluation and treatment of hemophilia. Most bleeding episodes in patients with hemophilia occur within joints, and the most important initial management tool is prevention of hemarthrosis and subsequent arthropathy through intravenous (IV) clotting factor replacement therapy. Ideally, this therapy is started prophylactically, before or soon after the first joint bleed—before joint damage occurs. However, therapy is very expensive and not widely available in undeveloped areas.[4] Therefore, imaging studies not only help in the initial diagnosis but are critical in determining when these expensive IV therapies should be started. They also are used in patient follow-up to monitor how well treatment protocols are working. When prophylactic therapy is unsuccessful, intra-articular blood must be evacuated early to prevent future chondral loss. Imaging studies can help determine presence and quantity of hemarthrosis and can provide guidance for arthrocentesis in the acute setting. Secondary prophylaxis—prophylaxis initiated after onset of hemophilic arthropathy in an attempt to reduce or halt progres-

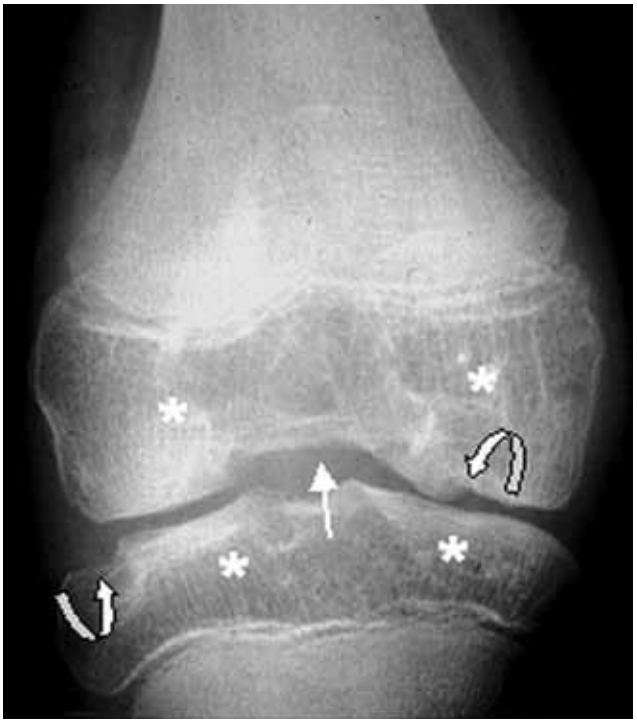

Figure 1. Frontal knee radiograph shows periarticular osteoporosis, epiphyseal overgrowth (asterisk), widening of intercondylar notch (straight arrow), joint surface irregularity, and incongruity (curved arrows).

Dr. Carvajal Alba is Orthopaedic Surgery Resident, Department of Orthopaedics, Dr. Jose is Clinical Assistant Professor, Department of Radiology, and Dr. Clifford is Chief, Musculoskeletal Section, Director, Musculoskeletal Fellowship, and Clinical Associate Professor, Department of Radiology, Miller School of Medicine, University of Miami, Miami, Florida.

Address correspondence to: Paul D. Clifford, MD, Department of Radiology (R-109), Miller School of Medicine, University of Miami, 1611 NW 12th Ave, West Wing 279, Miami, FL 33136 (tel, 305-585-6894; fax, 305-585-5743; e-mail, pclifford@med.miami.edu).

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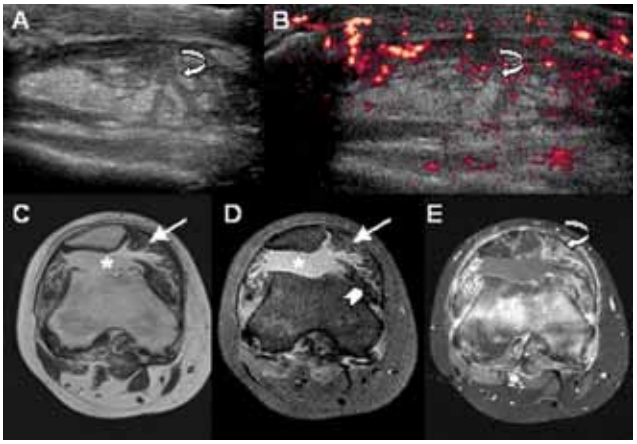

Figure 2. Transverse grayscale (A) and color (B) Doppler images of suprapatellar bursa show severe synovitis and synovial hyperemia (curved arrows). Axial proton density (C), T_1-weighted fat-saturated (D), and T_1-weighted fat-saturated postcontrast (E) images show severe synovial thickening (arrow), low-signal intensity from chronic hemosiderin deposition (chevron), complex joint effusion (asterisk), and pronounced synovial enhancement (curved arrow) in young adult with advanced hemophilic arthropathy.

sion—is controversial. It is unclear whether the benefits justify the costs of the therapy in this setting.[3]

Conventional plain radiographs of involved joints are commonly part of the initial assessment; however, their sensitivity in detecting the subtle cartilage and synovial changes characteristic of early hemophilic arthropathy is poor.[2] Early radiographic findings include dense joint effusion, soft-tissue edema, periarticular osteoporosis, and epiphyseal overgrowth. Common knee findings are squaring of the inferior pole of the patella and widening of the intercondylar notch (Figure 1). Epiphyseal overgrowth, widening of the intercondylar notch, and squaring of the inferior pole of the patella are dysplastic changes associated with chronic hyperemia in the developing child. The chronic hyperemia is secondary to the irritative and inflammatory effects of intra-articular blood. With disease progression may come joint surface irregularity with erosions, subchondral cysts, joint space narrowing, angular deformities, and ankylosis.

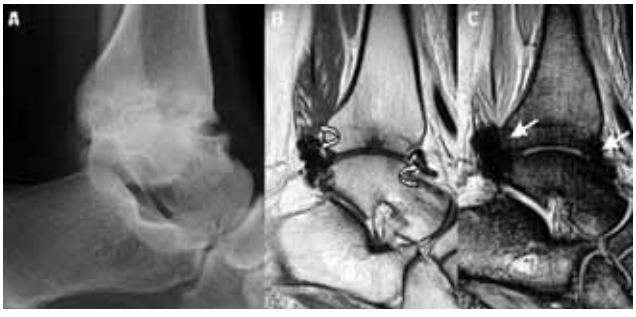

Figure 3. Lateral radiograph (A) and sagittal proton density image (B) show severe arthritic changes of tibiotalar joint in patient with severe hemophilic arthropathy. Prominent synovitis has low-signal intensity from hemosiderin deposition (curved arrows). Blooming artifact (arrows) is visible on (C) sagittal gradient echo sequence.

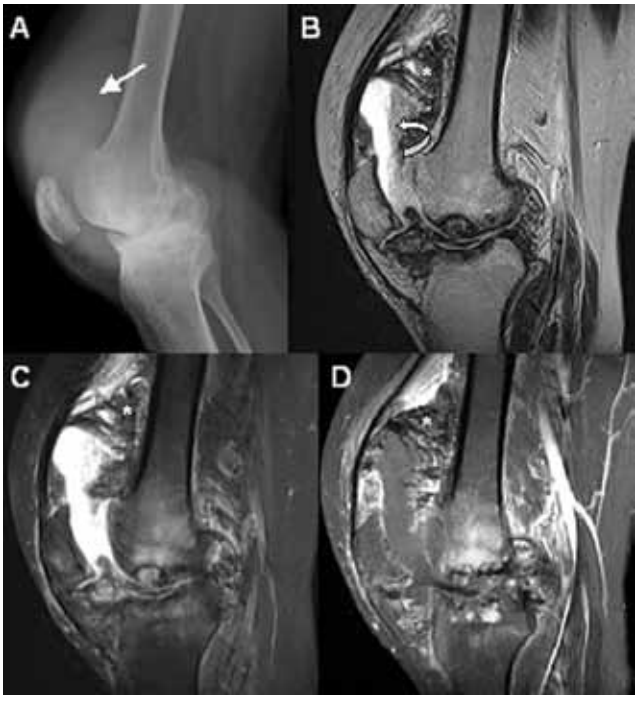

Figure 4. Lateral radiograph (A) and sagittal T_2-weighted (B), fat-saturated proton density (C), and T_1-weighted fat-saturated postcontrast (D) images show severe hemophilic arthropathy. Large, dense, complex joint effusion (arrow) is consistent with hemarthrosis. Note severe enhancing synovitis, synovial hypertrophy, and fibrosis with low-signal intensity caused by hemosiderin deposition from chronic hemarthrosis, most prominently in suprapatellar pouch (asterisk). Also note fluid-fluid level from hemarthrosis degradation (curved arrow).

Present in advanced stages in the elbow are growth disturbances, erosions of the radial notch of the ulna, and widening of the trochlear notch.[5] Classification systems (eg, Arnold-Hilgartner scale, Pettersson score) have been developed to assess the severity of the arthropathy and the outcomes of different therapeutic interventions radiographically.[6] Use of newer modalities, however, has led to the development of more sensitive scoring systems, such as the Denver MRI scale and the European score, which provide a more accurate assessment of response to treatment protocols.[3]

Ultrasound is an inexpensive, radiation-free modality that can be used to detect hemarthrosis and synovial inflammation in the early stages of the disease, especially in the knee.[7] Given improvements in technology and the cost concerns of some of the other imaging modalities, ultrasound is positioned to become more important in imaging not only for hemophilic arthropathy but also for musculoskeletal disease in general. Hemarthrosis is identified as an anechoic or hypoechoic collection in the intra-articular space. Synovitis manifests as synovial thickening and nodularity on grayscale images.[3] Color and power Doppler images show flow increased by synovial hyperemia (Figure 2). In addition, ultrasound is sensitive in detecting intramuscular hematomas, such as those of the iliopsoas, quadriceps, and gastrocnemius

muscles, which are common in this patient population.[3] Hematomas initially may increase the thickness of the involved muscle and show increased echogenicity in the acute phase of hemorrhage. Approximately 4 to 10 days after onset, they progressively become anechoic and more organized. Although computed tomography is better than conventional radiography in detecting subchondral cysts and erosions, magnetic resonance imaging is the optimal imaging technique for evaluating hemophilic arthropathy because of its superior depiction of synovial and chondral changes during all stages of the disease.[2] Synovitis usually is the first characteristic finding in early stages of the disease, and hemarthrosis is classically identified as a complex joint effusion with fluid-fluid levels. Fluid levels are caused by degrading and layering of complex fluids, such as blood. Classically, there is a radiographically visible separation between the supernatant (fluid floating superiorly) and the underlying sediment containing hemosiderin breakdown and other higher density proteinaceous products (precipitant or dependent fluid).

Synovial hypertrophy appears as a low to intermediate signal on T_1-weighted and proton density sequences and as an intermediate to high signal on T_2-weighted and fluid-sensitive sequences. The hemosiderin deposition characteristic of the disease is seen as low-signal intensity on all imaging sequences. This low-signal is accentuated with gradient echo sequences, in which, local magnetic field heterogeneity caused by blood degradation products (iron) results in low-signal voids that distort surrounding structures (susceptibility blooming artifact) (Figure 3).[5] In advanced stages of the disease, subchondral cysts are hyperintense on fluid-sensitive sequences. The magnitude of cartilage damage can best be quantified with proton density fast spin-echo sequences with or without frequency-selective fat suppression. Intravenous gadolinium may help differentiate hypertrophied synovium from cartilage and joint effusion (Figure 4).[3]

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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This paper will be judged for the Resident Writer's Award.