An Unusual Presentation of Hemophilia B: Pseudotumor of Proximal Tibia

Saurav Mittal, MS (Ortho), Sumit Arora, MS (Ortho), DNB (Ortho), Shilpa Khanna, MD (Peds), Lalit Maini, MS (Ortho), and V. K. Gautam, MS (Ortho), DNB (Ortho), MNAMS

Abstract

Hemophilia is one of the most common genetically inherited causes of bleeding disorders. The usual presentation is continuous bleeding from a wound. Very seldom, it presents as a pseudotumor of bone. When left untreated, it may induce compression and pressure necrosis of adjacent structures. Careful evaluation and a high index of suspicion are usually required to arrive at the correct diagnosis. In this article, we report the case of a 10-year-old boy with hemophilia B (Christmas disease) that presented as a pseudotumor producing a large defect in the proximal tibia.

Hemophilia is a coagulation defect caused by a functional or absolute deficiency of clotting factors. Deficiency of factor VIII (antihemophilic factor) leads to hemophilia A (classic hemophilia); deficiency of factor IX (plasma prothrombin component) causes hemophilia B (Christmas disease). Both disorders are X-linked–recessive, and therefore, primarily affect men, but are transmitted by women. The incidence of hemophilia B ranges from 1:50,000 to 1:100,000.[1] According to historical surveys, 1% to 2% of severe hemophiliacs (clotting factor level, <1% of normal) develop pseudotumors, which may originate in soft tissues or in subperiosteal or intraosseous areas.[2]

In this article, we report a rare case of a large pseudotumor of the proximal tibia in a patient with moderately severe hemophilia B. To our knowledge, such a presentation was not described in the English-language literature until now. The parents of the patient provided written informed consent for print and electronic publication of this case report.

Dr. Mittal and Dr. Arora are Senior Residents, Department of Orthopedic Surgery, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, India.
Dr. Khanna is Senior Resident, Department of Pediatrics, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, India.
Dr. Maini is Professor, Department of Orthopedic Surgery, Maulana Azad Medical College and Lok Nayak Hospital.
Dr. Gautam is Director Professor, Department of Orthopedic Surgery, Maulana Azad Medical College and Lok Nayak Hospital.

Address correspondence to: Sumit Arora, MS (Ortho), DNB (Ortho), c/o Mr. Sham Khanna, 2/2, Vijay Nagar, Delhi, 110009, India (tel, 91-986-832-9389; e-mail, mamc_309@yahoo.co.in).

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Case Report

A 10-year-old boy with a 6-month history of swelling and pain around the left knee joint and proximal leg was brought to the orthopedic outpatient department. The swelling was insidious in onset and gradually progressive. The pain was insidious in onset, dull-aching, localized to the proximal leg, and aggravated by exertion and relieved by rest. There was no history of significant trauma, fever, weight loss, anorexia, drug ingestion, or similar effects on other joints. There was no history of any surgical procedure.

On examination, a small (13×8 cm), firm mass was found at the upper end of the tibia over the anteromedial and anterolateral aspects (Figure 1). Its margins were well defined and its surface smooth. The overlying skin was normal, and the local temperature was not elevated. There was fixed flexion deformity of 10° with further flexion possible up to 100°.

Blood investigations (hemoglobin, platelet count, erythrocyte sedimentation rate) were within normal ranges. A radiograph of the left knee with the leg showed a geographic lytic lesion (6×4 cm) involving the epiphysis and the metaphysis of the anterior aspect of the proximal tibia with periosteal reaction (Figures 2, 3). The lytic lesion had crossed the physis. Another geographic lytic lesion (1.5×1.5 cm) was noted in the lateral aspect of the distal femoral epiphysis. Magnetic resonance imaging (MRI) of the region showed a large heterogenous lesion involving the anterior aspect of the proximal tibia with a soft-tissue component (Figure 4). The lesion contained 2 large areas of involvement separated by a bony septum. The lesion was hyperintense with areas of marked hypointensity on T_2-weighted MRI.

On needle biopsy of the lesion, only blood came out. A provisional diagnosis of aneurysmal bone cyst was made, and the patient was sent home on an above-knee slab. He was then brought back to orthopedic emergency

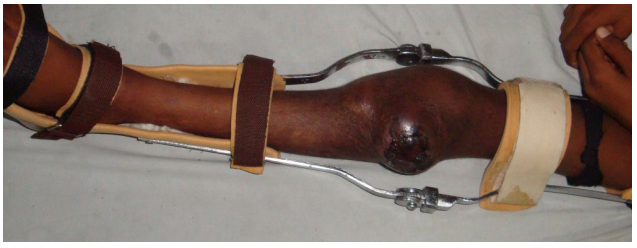

Figure 1. Clinical photograph shows huge swelling around left knee. Area of skin necrosis is also seen over anterolateral aspect of knee.

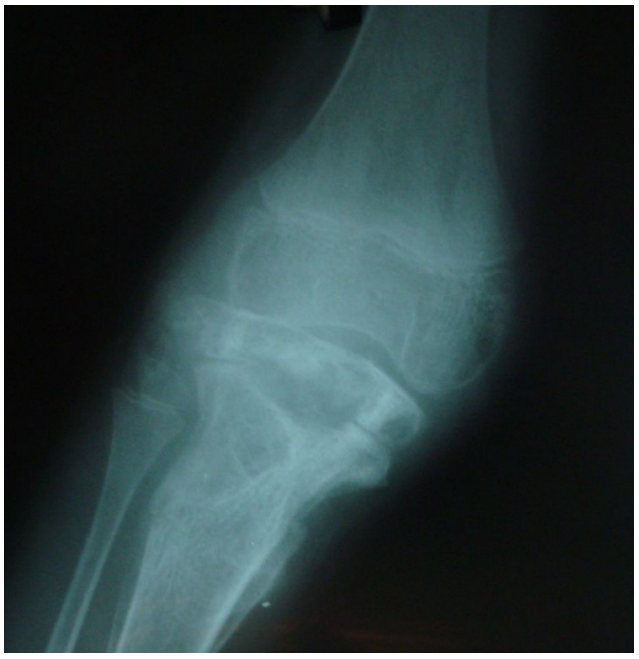

Figure 2. Anteroposterior radiograph of left knee shows osteolytic area in proximal tibia involving metaphysis and epiphysis with periosteal reaction. Small osteolytic lesion is also seen involving lateral aspect of distal femur epiphysis.

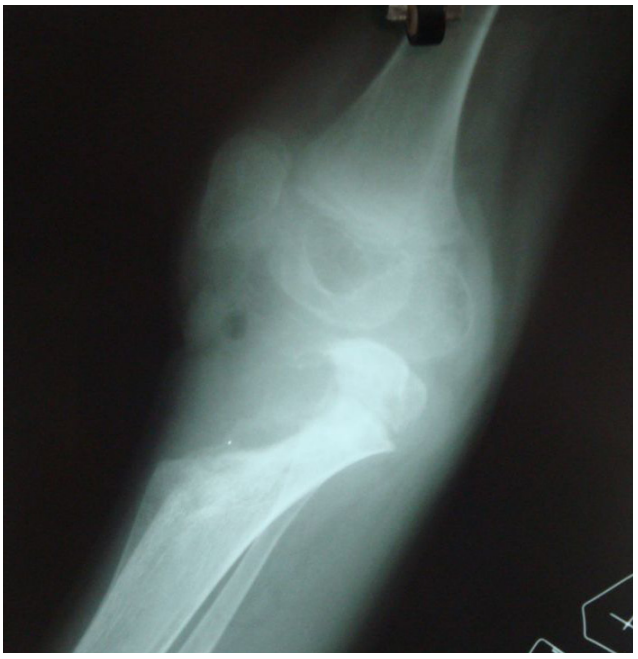

Figure 3. Lateral radiograph of left knee shows large osteolytic area involving anterior aspect of proximal tibial metaphysis and epiphysis. Osteolytic area is also seen involving distal femoral epiphysis.

with severe left knee pain and a soaked slab. On examination, he was severely anemic. When the slab was removed, blood was found oozing from the biopsy needle entry site, and the knee region was grossly swollen. Hemoglobin level was 50 g/L, and platelets were normal.

The clinical diagnosis of a bleeding disorder with a pseudotumor was made, and the patient received a transfusion of whole blood and underwent testing for bleeding disorders. Prothrombin time, platelet count, and factor VIII assay were within normal limits, but factor IX assay showed only 1.1% activity. Activated partial thromboplastin time was 52 seconds, approximately double the normal upper limit. The definitive diagnosis of hemophilia B with a bony pseudotumor of the proximal tibia and distal femur was made. The patient was splinted in an orthosis (Figure 1) and started on prophylactic intravenous antibiotics. In addition, he was started on a transfusion of factor IX concentrates, 80 IU/kg on day 1, followed by 40 IU/kg every alternate day for 10 days as standard replacement protocol.[3]

The patient's swelling and pain subsided over the next 3 to 4 weeks. At 6-month follow-up, the pseudotumor of the proximal tibia was smaller, and the pseudotumor of the distal femur was completely resolved (Figures 5, 6). At 12-month follow-up, the patient was completely asymptomatic. Follow-up continued.

Discussion

Hemophilia is the most common congenital coagulation factor deficiency.[3] It includes a group of disorders that manifest as abnormalities of the coagulation mechanism. The usual presentation, continuous bleeding from a minor wound, is caused by functional deficiency of specific clotting factors. Patients with hemophilia B (Christmas disease) have functional deficiency of factor IX—an X-linked–recessive disorder. Patients with the mild form of this disorder have more than 5% of functional plasma levels of factor IX, which can cause excessive bleeding only during surgery or trauma; patients with the moderate form (1%-5% of functional plasma levels) or severe form (<1% of functional plasma levels) are at risk for bleeding from unrecognized trivial trauma and even for spontaneous bleeding.[3]

Only 1% to 2% of patients with severe hemophilia present with a pseudotumor mass. When left untreated, such a mass may induce compression and pressure necrosis of adjacent structures. Pseudotumors usually appear in the iliac wing, thigh, or calf, and consist of a slowly expanding encapsulated coagulum of chronic and acute hemorrhage.[2,4] Pseudotumor pathology has at least 3 factors: pressure necrosis of bone, new bone formation, and a soft-tissue component that consists of constantly forming, usually plum-sized multiple hematomas of jellylike consistency.[5]

The most important radiographic signs of pseudotumors are periosteal reaction, new bone formation, bone destruction caused by pressure necrosis, and a soft-tissue mass with or without calcium deposits.[5] Hemophilic pseudotumors of bone can be easily confused with bony neoplasms. As these lesions often resemble Ewing tumors or osteogenic sarcomas in various stages of maturity, they should be considered in the radiologic differentials. At times, it may be difficult to differentiate them from aneu-

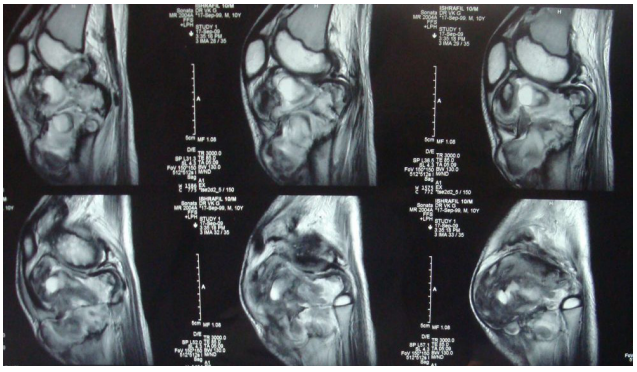

Figure 4. T_2-weighted magnetic resonance imaging of left knee shows heterogenous lesion involving anterior aspect of proximal tibia with soft-tissue component.

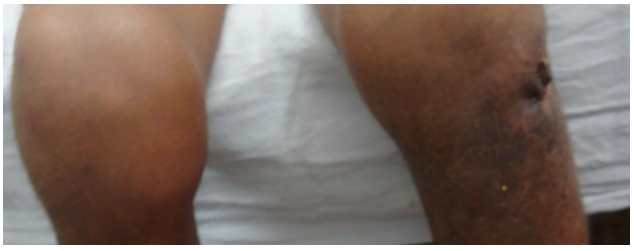

Figure 5. Clinical photograph shows resolution of knee swelling and healing of skin necrosis area after 6 months of adequate conservative treatment.

rysmal bone cysts with considerable bone destruction. Other lesions that can be considered in the differential diagnosis are fibrosarcoma, plasmacytoma, malignant fibrous histiocytoma, brown tumor, tubercular lesion, gumma, chondroma, giant cell tumor, and hydatid cyst.[5,6]

As in our patient, hemophilia may directly present as pseudotumor without any previous history of bleeding disorder. The pseudotumor can remain asymptomatic and not show any signs of growth for a long time. As the tumor expands, the risk for complications increases. Fine needle aspiration cytology is contraindicated in such cases, as it may have life-threatening consequences.[2,7,8] There is no standardized therapy for hemophilic pseudotumors.[7,8] Many authors have advocated conservative management for such patients; few have indicated that primary surgical treatment is more beneficial than prolonged substitution therapy.[2,5,7,8] Brant and Jordan[5] reported good results with radiation therapy. Operative management is warranted when all conservative measures have failed or when a pseudotumor grows despite adequate therapy.[7,9] Thus, therapy must be based on each patient's current problem reports and constitution and must be undertaken in collaboration with orthopedists and pediatric hematologists.

Learning Points

• Careful evaluation and a high index of suspicion are required to arrive at the diagnosis of hemophilic pseudotumor.

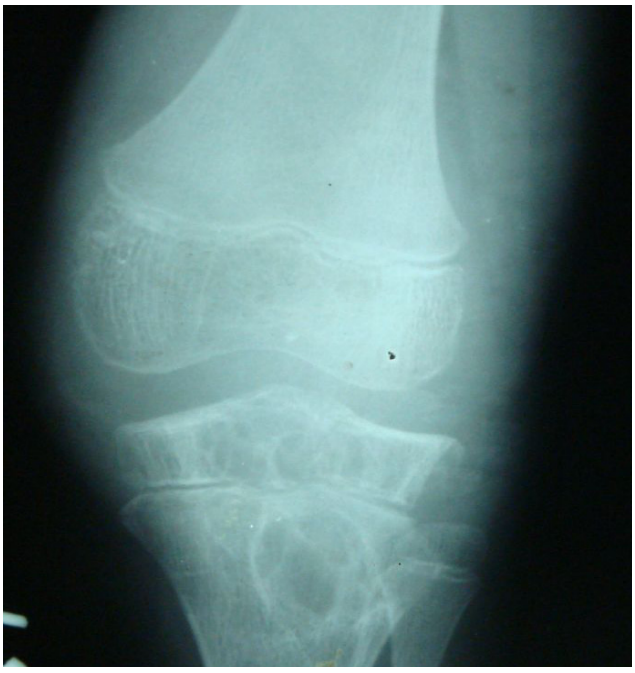

Figure 6. Anteroposterior radiograph of left knee shows smaller pseudotumor of tibia and complete resolution of pseudotumor of femur after 6 months of adequate conservative treatment.

• A coagulation profile must be obtained, especially in pediatric age group, before proceeding with any invasive procedure.

• These patients may respond adequately to replacement therapy and use of splints.

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.