Unmasking Hemophilia B After Hip Aspiration

A Case Report

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Abstract

Case: A 7-year-old boy presented with excruciating hip pain for 1 day, unable to bear weight. Magnetic resonance imaging (MRI) revealed small hip joint effusion and synovitis, which was treated by urgent operative aspiration to rule out infection. Subsequently, the postoperative site bled continuously, despite compression. The hip wound and blood cultures showed no growth. He was examined by a hematologist and had normal coagulopathy lab results. He was discharged and went home 4 days after aspiration and was scheduled for outpatient hematology work-up. He was readmitted 11 days after aspiration with continued pain and MRI was repeated, showing large hip hemarthrosis. Lab results at that time showed a prolonged partial thromboplastin time of 43.9 seconds. The patient was given fresh frozen plasma. The hip effusion was stable on ultrasound. He was found to have low factor IX <17% consistent with hemophilia B and was given recombinant factor IX (Benefix) of 2,000 units. The following day, his pain was markedly improved and he was discharged. At the 4-month follow-up, the patient was fully ambulatory.

Conclusions: This is a case of unexpected bleeding after hip aspiration which led to the life-changing diagnosis of Hemophilia B in a pediatric patient. Orthopedists should be wary of bleeding dyscrasias and involve consultants as needed.

Hemophilia is an X-linked recessive disease which impairs the body's ability to create clotting factor VIII in hemophilia A and clotting factor IX in hemophilia B. Hemophilia A (typical hemophilia) occurs once in 5,000 male births whereas hemophilia B (Christmas disease) occurs once in every 20,000[1].

A family history of hemophilia in about 2 out of 3 new cases permits early diagnosis and correct treatment[2]. The remaining third can go years without a diagnosis, endangering their well-being. Untreated hemophilia can lead to frequent bruising, hemarthrosis, uncontrollable bleeding episodes, and in severe cases, death. With such critical consequences, orthopedic surgeons should be wary of unusual postoperative bleeding events even in older, undiagnosed children with no reported history.

The patient's parents were informed that the case data would be submitted for publication, which they agreed to.

Case Report

A 7-year-old boy with no medical history presented with 1-day history of right hip pain after wrestling. The patient awoke that night with excruciating hip pain, unable to bear weight. He was sent to the emergency department (ED) by the pediatrician. ED vitals were as follows—blood pressure: 108/71, heart rate: 108, respiratory rate: 20, temperature: 37.4°C, and O_2 saturation: 100% room air. He had no constitutional signs. Hip magnetic resonance imaging (MRI) showed small right hip joint effusion/synovitis. Initial lab results are presented in Table I. Immediately after the MRI, the patient underwent operative aspiration and arthrogram, obtaining clear fluid without evidence of hemorrhage attributed to transient synovitis, a temporary inflammation of the hip joint synovium, most likely due to a virus. The operative site was bleeding upon return to the floor and compression was applied. That evening, the dressing was saturated with blood and was changed multiple times. He was noted to have 2+ femoral, tibialis posterior, and dorsalis pedis pulses, and the extremity was well-perfused with capillary refill <2 seconds. The initial bleeding evaluation included prothrombin time/activated partial thromboplastin time (PT/aPTT) and von Willebrand factor profile which were all normal. He had a mildly decreased fibrinogen with a normal thrombin time. Overnight, he continued to bleed from the hip joint puncture site despite consistent pressure dressing and strict bed rest. The patient was seen by vascular surgery and hematology/oncology. The hip wound and blood cultures showed no growth.

The patient was ambulatory with pain partially controlled with ibuprofen and was discharged home 4 days after joint

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TABLE I The Initial and Post-operative Laboratory Results

Lab Test and Reference Range	Results on the Day of Aspiration	1 Day After Aspiration	2 Days After Aspiration	11 Days After Aspiration (Levels Were Sent Prior to Receiving FFP)
CRP (0.0-9.0 mg/L)	<3.0	16.2		<3
ESR (0-23 mm/hr)	4	8		12
WBC (4.50-13.50/nL)	11.08	7.91		11.67
HGB (12.5-16.1 g/dL)	12.4	12.3		11.9
HCT (37.0%-45.0%)	36.8	36.5		34.7
Platelet (150-450/nL)	333	292		718
Fibrinogen (227-467 mg/dL)	165		379	
Thrombin time (13.6-19.4 s)			15.3	
Von willebrand Antigen (50%-160%)			90	67
Von willebrand activity (55%-200%)			96	52
Factor VIII activity (60%-150%)			154	94
Prothrombin time (12.0-15.0 s)	13.1			12.4
INR	0.99			0.92
Activated PTT (23.0-37.0 s)	25.3			43.9
Factor IX activity (60%-150%)				<17
Factor XI activity (55%-150%)				139
Factor XII activity assay (55%-180%)				139

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, FFP = fresh frozen plasma, HCT = hematocrit, Hgb = hemoglobin, INR = international normalized ratio, PTT = partial thromboplastin time, and WBC = white blood cell.

aspiration with plans for outpatient hematology work-up. Seven days from initial presentation, he presented to ED with continued limp and pain. A hip ultrasound was taken which showed a moderate, stable effusion, and the patient was sent home with outpatient pediatric and orthopedic follow-up. Eleven days after initial presentation, he again presented to the ED with severe pain and was readmitted. MRI was repeated, which showed large hip hemarthrosis. He was given morphine for pain control, valium for muscle spasms, and tranexamic acid for postoperative bleeding. The hip effusion was stable by ultrasound. The coagulopathy panel test was repeated showing prolonged PTT of 43.9 seconds which had been normal during his previous hospital admission. Patient samples were sent for factor IX, XI, XII, and XIII level testing, and then he was given fresh frozen plasma. The results of coagulation testing showed a low factor IX level (<17%) consistent with mild hemophilia B; all other factor levels were normal. He was given a recombinant factor IX (Benefix) of 2,000 units. A PTT mixing study showed correction of the PTT, providing additional evidence of a factor deficiency rather than an inhibitor. A repeat factor IX level test was performed 3 weeks after the initial level and was confirmed to be low at <16%.

The following day, his pain was markedly improved and he was discharged home. He had a very slight limp and no longer required pain medications. After further discussion with their family, the parents revealed a cousin with hemophilia B. They also recalled their child had slightly prolonged bleeding after circumcision and had received a blood transfusion after biting his tongue in the past. At 4-month follow-up, the patient was fully ambulatory and complained of some joint aches.

Discussion

In the United States, the median age of mild hemophilia diagnosis is 36 months, moderate hemophilia is 8 months, and severe hemophilia is 1 month[2]. For severe hemophiliacs undiagnosed at birth, diagnosis often occurs early in life because the patient experiences spontaneous bleeds or persistent cuts and bruising. However, in mild hemophilia, the disorder can often be overlooked for years. Children with untreated hemophilia can experience frequent bleeding and bruising, hemarthrosis, lifelong disabilities, or in extreme cases, intracranial hemorrhaging and death[3-6]. The life expectancy for severe hemophilia is 63 years whereas moderate and mild hemophiliacs life expectancy is 75, 10 years less than healthy men[7,8]. Without the correct treatment, patients have the potential to die before adulthood[8].

Current treatments for hemophilia include factor replacement therapy in which the missing factor is resupplied intravenously to encourage blood clotting[9,10]. Factor replacement does carry the risk of the patient developing an antibody against the extrinsic factor called an inhibitor which can make the factor infusion much less effective. This has been reported to occur in 15% to 25% of patients with hemophilia A. It has

been reported to occur in hemophilia B patients but is thought to be much less common[11]. Synovectomies can reduce recurrent hemarthrosis, improve joint pain and function, as well as slow the reduction in range of movement and development of flexion contractures[12]. Synovectomies improve short-term symptoms; although do not stop progression of arthropathy[12]. Radiosynovectomy also effectively decreases the frequency and the intensity of recurrent intra-articular bleeds[13,14]. Radiosynovectomy, although not widely used at this point, is considered safe in children since the radiation dosage is miniscule[12]. Recent trials have shown early successful results using gene therapy to produce the lacking factor to establish adequate clotting[9,15].

There are few recent orthopedic studies about hemophilia because the current prophylactic treatments lessen the necessity for surgery, although a review article concerning management of hemophilic knees was published in 2017[12]. Hemophilia is relevant to orthopedists because 60% of spontaneous bleeding events occur in joints, commonly the knee, leading to bone erosion, synovial impingement, chronic synovitis, articular cartilage damage, and osseous destruction[12,16,17]. These can cause pain, reduce range of motion, and cause muscle atrophy[16].

Because hemophilia is often diagnosed during the first few years of life, it may be overlooked as a possibility in older pediatric patients. When a patient shows unusually heavy or unexpected bleeding after a surgical procedure, the orthopedist should not hesitate for a hematology consult. In this case, it is unusual that the aPTT was normal during the initial admission and prolonged on follow-up. The differential diagnosis of a prolonged PTT with a normal PT with bleeding symptoms includes a deficiency of factor VIII, IX, or XI. The differential diagnosis of a prolonged PTT with a normal PT in the absence of bleeding symptoms includes factor XII deficiency, a lupus anticoagulant, or the presence of heparin in the specimen. A low factor IX was documented during the second admission which led to the diagnosis of hemophilia B and was confirmed on a subsequent test of the sample. While acquired factor IX deficiency due to an inhibitor or autoantibody has rarely been reported in pediatric patients, in the presence of an inhibitor, the PTT mixing study should not show correction[18]. The patient ultimately responded to treatment with recombinant factor IX. The resulting diagnosis is life changing. Our patient was a young, active boy and had the potential for a life-threatening intracranial bleed with any significant head trauma. His family had been planning to drive all-terrain vehicles, but safely changed their minds, after the diagnosis. ■

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