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Nikhil Potpally, *Rutgers New Jersey Medical School*
Scott Rodeo, *Hospital for Special Surgery*
Paul So, *Rutgers New Jersey Medical School*
Kenneth Mautner, *Emory University*
Michael Baria, *Ohio State University*
Gerard A Malanga, *Rutgers New Jersey Medical School*

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A Review of Current Management of Knee Hemarthrosis in the Non-Hemophilic Population

Nikhil Potpally[1], Scott Rodeo[2], Paul So[1], Ken Mautner[3], Michael Baria[4], and Gerard A Malanga[1]

Abstract

The knee joint is one of the most frequently injured joints in the body, and the resulting injury may often lead to the presence of a bloody effusion, or hemarthrosis. The acute management of this condition can have long-lasting implications, and may ultimately result in the early onset of osteoarthritis in this population. Heme, a breakdown product of erythrocytes, and associated pro-inflammatory mediators, are known to have deleterious interactions with cartilage and synovium. The presence of blood in a joint following injury can precipitate these effects and accelerate the degenerative changes in the joint. Currently, there is no consensus on the optimal management of a traumatic knee joint injury with a hemarthrosis. Nontraumatic hemarthosis, seen most commonly in hemophilia patients, has a set of established guidelines that does not routinely recommend drainage of the joint. This article presents a rationale for joint aspiration to minimize the harmful effects of blood following traumatic hemarthrosis.

Keywords

knee hemarthrosis, youth, joint injury, posttraumatic osteoarthritis

Introduction

Knee trauma accounts for over half a million visits to the emergency department every year in the United States.[1,2] Among the pediatric age group, the most common cause of acute knee effusion with hemarthrosis occurs following acute trauma to the joint, which is commonly seen in sports injuries.[3] The management of hemarthrosis has both immediate and long-term effects in an individual. In the short-term, blood exerts an intracapsular pressure effect in the restricted joint space, leading to increased sensation of pain and limitation of normal range of motion of the joint and decreased muscle firing due to reflex inhibition of the quadriceps.[4] The long-term risk of osteoarthritis is increased following both traumatic and nontraumatic hemarthrosis.[5] Although degenerative changes may not be evident clinically or radiographically until decades later, the underlying pathogenesis of articular cartilage injury is believed to be initiated by the effects of blood and inflammatory mediators which are released within the joint following trauma. Through a series of biochemical reactions involving various metabolites, the articular cartilage eventually undergoes irreversible damage leading to degenerative changes of the joint over time[5,6] resulting in cartilage breakdown and arthritic changes at a young age.

The knee is the most commonly affected joint in both healthy, young patients and in those with hemophilia. Additionally, although the exact rates of hemarthrosis in patients with hemophilia are unknown, the majority of recurrent bleeds are known to occur within the knee joint and may lead to the necessity for joint replacement at a very young age.[7] In healthy youth who suffer a joint injury with a hemarthrosis, early degenerative changes may also occur. Therefore, the incidence of knee hemarthrosis is not insignificant, requiring evaluation and early treatment in the emergency department and/or outpatient setting.

Removal of blood from a joint via aspiration of hemarthrosis would appear to be standard practice, especially in a young athlete following a joint injury. However, there are no guidelines or consensus for managing joint injury in youth, despite the known negative effects of blood in the joint. This basic science knowledge has not translated to aggressive treatment of a hemarthrosis in youth with an obvious need for further study. In this article, we review the literature related to hemarthrosis, current treatment recommendations,

[1]Rutgers New Jersey Medical School, Newark, NJ, USA
[2]Hospital for Special Surgery, New York, NY, USA
[3]Emory University, Atlanta, GA, USA
[4]The Ohio State University, Columbus, OH, USA

Corresponding Author:
Gerard A Malanga, Rutgers New Jersey Medical School, 100 Bergen St, Newark, NJ 07103-2714, USA.
Email: gmalangamd@hotmail.com

and present a rationale for joint aspiration to minimize the harmful effects of blood, and potentially reduce the incidence of osteoarthritis following traumatic hemarthrosis.

Causes of Hemarthrosis

Broadly, knee hemarthrosis can be categorized based on traumatic or nontraumatic etiologies, with each group consisting of a wide range of pathologies. The mechanism of traumatic knee injury leading to hemarthrosis commonly involves forced twisting of the loaded joint.[8] Appreciating the anatomy and biomechanics of the knee joint, this abnormal rotation has the potential to impact bony, cartilaginous, and/or ligamentous structures. Whereas the pathologic effects of blood on articular cartilage on a molecular level is believed to be consistent among different age groups, the etiology of traumatic causes is varying. Posttraumatic hemarthrosis in adults is often caused by anterior cruciate ligament ruptures (70%), patellar dislocation injury (15%), meniscal tears (10%), osteochondral fragment fractures (2-5%), or other injury (5%).[8,9] Among both athletic and nonathletic adults, arthroscopic studies have consistently showed ACL injury as the most common cause of traumatic knee hemarthrosis,[10,11] often with associated meniscal injury.[12] However, in youth, studies have shown that the cause of knee hemarthrosis appears to be different.[13] One study using MRI for evaluation of traumatic knee effusion found that in younger adolescents, patellar dislocations were the most prevalent injury, whereas in older adolescents, ACL tears were identified as the most common injury.[13,14] In another study using arthroscopy for diagnosis, meniscal and ACL tears had equivalent rates in preadolescents aged 7 to 12, whereas ACL ruptures comprised the majority of injury in adolescents aged 13 to 18.[15] Regardless of etiology, traumatic knee injury requires urgent medical attention due to the associated intraarticular pathology.[16,17]

A subset of traumatic hemarthrosis also involves injury caused by minimal trauma. This type of injury, when present, should raise suspicion of an underlying bleeding diathesis in the majority of cases.[18] Postoperative hemarthrosis may also occur following arthroscopic surgery of the knee, but the incidence is normally low.[19] One study evaluated 8500 arthroscopic surgeries performed over 13 years, with only three cases of hemarthrosis noted.[19] The lateral retinacular release surgery was noted with the highest complication rate, with the potential for bleeding from injury to the superior lateral geniculate artery during this procedure.[20] In adults, hemarthrosis may also arise as a complication of total knee arthroplasty (TKA), but this form of bleeding is present in fewer than two percent of patients undergoing the surgery.[21] These patients can present months or years after their TKA, with a painful or swollen joint.[22]

Hemophilia is the leading cause of nontraumatic hemarthrosis and is the most common musculoskeletal manifestation of the disease.[9,23] As an inherited X-linked recessive condition, it is known to affect 1 in 5,000 males.[23] Deficiency of coagulation factor VIII or IX in hemophilia A or B, respectively, lead to recurrent spontaneous bleeds and subsequent contractures or degenerative disease in severely affected joints. The first instance of hemarthrosis usually occurs in children within the first few years of life, with the knee most commonly affected.[23] Recurrent bleeding episodes over time lead to the development of hemophilic arthropathy and associated pain, deformity, and disability.[24] As a result, management of hemophilia has been designed to prevent these recurrent bleeds and chronic synovitis.[7,24] Although clotting factor replacement is available, 20% of patients still experience chronic hemophilic arthropathy as a result of repeated intraarticular bleeding.[25]

Other sources of nontraumatic knee hemarthrosis in children and adolescents include synovial hemangiomas, a benign tumor of the vasculature.[26] Although rare, this condition can manifest as recurrent monoarticular swelling due to hemarthrosis with intermittent pain.[26] Diagnosis is often delayed, and this tumor may be congenital. Tenosynovial giant cell synovitis is another benign neoplasm that can present as monoarticular knee hemarthrosis and is believed to be due to the overexpression of colony stimulating factor-1.[27] Although uncommon, metastases of other malignancies to the knee or nearby *de novo* tumors may also present as hemarthrosis when the knee joint is involved. Patients receiving therapeutic anticoagulation may also present with hemarthrosis of the knee but this incidence is very rare.[9] Recurrent hemarthroses attributed to excessive anticoagulation or to anatomic causes, such as spontaneous articular pseudo-aneurysms occur most commonly in adults.[28]

Pathophysiology of Joint Damage

Studies have shown that a single exposure of cartilage to blood can result in adverse effects on several components of the joint.[6] Following a joint hemarthrosis, the breakdown of erythrocytes results in the release of heme- an iron-containing complex. The interaction of heme-derived iron with monocyte and macrophage-generated oxygen metabolites, namely, hydrogen peroxide, generates the deleterious hydroxyl radical, which has been shown to play a key role in the pathogenesis of chondrocyte apoptosis.[6] Remodeling of the extracellular cartilage matrix of the joint is also consequently affected, even under low concentrations of blood exposure to articular cartilage, due to irreversible inhibition of proteoglycan synthesis.[4,6] Together, these processes lay the foundation for pro-inflammatory changes, overwhelming the homeostatic balance in the joint. In the absence of scavengers and compensatory mechanisms, plasma-free hemoglobin (PFH) split products can lead to toxic consequences including inflammation and pro-oxidant effects, endothelial cell dysfunction,

and vasoconstriction. Furthermore, red blood cell membrane disruption (eryptosis) releases macrophage migration inhibitory factor (MIF), which may further affect intraarticular tissues. Wei *et al*. noted plasma interleukin-33 (IL-33) levels are increased in patients during hemolysis.[29] IL-33 is a member of the IL-1 cytokine superfamily that potently drives production of a variety of cytokines and contributes to the pathogenesis of inflammatory diseases.

There are additional mechanisms of joint damage that occur in hemophilic joints, which contribute to the eventual presentation of hemophilic arthropathy. Recurrent bleeds lead to intraarticular changes highlighted by proliferation of synovium and destruction of articular cartilage.[7] This accumulation of blood and synovial proliferation leads to a relatively hypoxic environment in the joint and, in combination with pro-inflammatory factors, creates stimulus for angiogenesis to occur. The hypervascular and friable synovium is then more susceptible to recurrent bleeding,[9,30] establishing a vicious cycle leading to the ultimate development of hemophilic arthropathy. In chronic hemarthrosis, bleeding occurs on a mechanical basis with the hypervascular synovium trapped between opposing articular surfaces, where even the replacement of clotting factors does not stop the recurrent joint bleeds.[31]

Decreased range of motion, secondary to pain, synovial hypertrophy, and reactive blood vessels,[32] highlights the prominent clinically evident short-term effect of blood in the joint. In the absence of repeated bleeding, these changes are believed to be reversible.[24] Over the long term, the cartilage degeneration and resultant fibrotic changes lead to arthrofibrosis and mechanical limitations with the subsequent development of contractures as a result of long-term damage.[33] In combination with the early-onset arthritis arising from the degeneration of cartilage from chronic inflammation, these consequences of long-term damage lead to decreased quality of life. As studies illustrate that skeletally immature individuals, seen in children, are more susceptible to adverse effects of blood in the joint than those who are skeletally mature,[34] and require proper attention not only in hemophilia, but also following joint trauma.

Management of Traumatic Hemarthrosis

There is currently a paucity of literature detailing the management of hemarthrosis following traumatic knee injury in the non-hemophilic population. The fundamental goals of treatment are to stop the bleeding and address the underlying cause. Initial therapy primarily involves symptomatic management and limiting further joint damage. A rapidly developing joint effusion following an injury is generally associated with pain due to capsular distension. There may also be some degree of asymmetric warmth without erythema and a diminished range of motion. To arrive at the diagnosis, the history and physical examination are routinely followed by plain radiographs to rule out fractures. If radiographs or further magnetic resonance imaging do not offer a probable diagnosis, an orthopedic evaluation is usually recommended, with possible arthroscopy, to identify any ligamentous or meniscal damage in the joint. In youth, the initial goals of therapy consist of pain control and a thorough diagnostic evaluation.[3]

For a first-time traumatic patellar dislocation, conservative nonoperative management is generally the suggested treatment.[3] This includes ice, compression, immobilization, and often limited weight-bearing with crutches. Based on the pathology noted on imaging and relevant physical exam findings, surgical treatment may be recommended. If the diagnostic workup reveals no structural damage, follow-up with an orthopedic surgeon is recommended. Generally, regardless of the traumatic cause of injury, the hemarthrosis is not aspirated unless there is significant swelling and pain or suspicion of infection.[3] Physicians tend to let the hemarthrosis self-resolve and rely on the body's natural mechanisms of blood evacuation. However, based on animal studies it has been found that the resorption of blood from a joint space takes at least four days.[30] Aspiration of blood within two days following the inciting bleed has been suggested as a means of minimizing long term cartilage deterioration, which can potentially prevent symptomatic OA later in life.[4]

In the treatment of postoperative hemarthrosis, there is currently no consensus on how to best provide treatment. The decision to manage the knee hemarthrosis conservatively versus surgically is controversial, more so in the postoperative patient than in the acute trauma patient.[35] Conservative treatment strategies are often temporary and may lead to recurrence of bleeding. Imaging, including magnetic resonance angiography or standard angiography, may be considered for further evaluation. Recurrent bleeding can also be managed through immobilization of the joint, temporary cessation of any concurrent anticoagulant medications, synovectomy, or embolization.[22] Studies report well-documented success of needle aspiration of acute hemarthrosis that was present for less than five days.[35] However, this relatively simple method of aspiration loses effectiveness once the hemarthrosis is present for more than 1 week, due to the intraarticular fibrin organization[35] and clotting pathophysiology already underway.

In either instance of traumatic hemarthrosis, the current literature does not clearly delineate what should be done in regard to the accumulated blood in the joint, namely, whether to aggressively evacuate it or let the body naturally resorb it. In postoperative hemarthrosis, the affected population is overwhelmingly middle-to-older aged adults, where the short-term toxic effects of blood in the joint are more relevant than the long-term consequences. In contrast, management of a hemarthrosis following a traumatic injury

in a child has both short- and long-term implications. The prevention of early onset osteoarthritis as a result of blood inducing damage on cartilage should be one of the goals in management of traumatic hemarthrosis, and we believe that current treatment protocols do not adequately emphasize the importance of this issue and the long-term sequelae of hemarthrosis, especially within the pediatric population.

Management of Nontraumatic Hemarthrosis

Hemarthrosis of the knee can also arise from nontraumatic causes in this population and is overwhelmingly attributed to underlying clotting or collagen disorders.[18] Guidelines for hemophilia management emphasize stopping the bleeding as quickly as possible to avoid potential permanent joint damage.[36] A hemophilic knee bleed is classically managed with early infusion of the appropriate factor concentrate (VIII or IX), followed by adjunctive pain control.[37,38] Arthrocentesis of the intraarticular blood is not routine, and has largely been limited to instances of severe bleeding.[37] Some studies cite the risks of precipitating further bleeding or developing joint infection as the primary concerns against universal aspiration. However, more recent studies report accelerated recovery time in early aspiration of hemarthrosis in hemophilia when combined with the appropriate factor replacement.[39] Although prognostic benefits have been suggested from drainage of hemophilic hemarthroses,[23,40] this practice has not become widely accepted within this population. Instead, the blood is usually left in the joint for the body to spontaneously absorb over time unless a significant quantity is present.

Recent studies have suggested improved efficacy and safety with the selective cyclo-oxygenase 2 inhibitors,[41] but this has not been accepted into standardized treatment regimens. In cases of recurrent hemarthrosis, the presence of synovial hypertrophy from chronic synovitis increases the likelihood of recurrent bleeds. Therefore, synovectomy in these patients is often performed to reduce the frequency of subsequent bleeds, although this may not prevent the development of secondary arthritis.[23] In other sources of acute nontraumatic intraarticular bleeds, management of patients with benign neoplasms causing knee hemarthrosis usually involves synovectomy, which addresses the issue of recurrent bleeds to prevent additional episodes of hemarthrosis.[42] This is most commonly due to pigmented villonodular synovitis (tenosynovial giant cell tumor). In patients presenting with hemarthrosis as a complication of anticoagulation, arthrocentesis followed by reversal of anticoagulation with the appropriate drug is therapeutic.[9] Cases of ruptured intraarticular aneurysms are managed with arterial embolization. In contrast to traumatic hemarthrosis, nontraumatic hemarthrosis has management strategies for bloody knee effusions that have been relatively consistent over a long period of time. Hemophilia treatment includes prophylactic replacement of the deficient factor in order to reduce the incidence of recurrent bleeds and delay the development of hemophilic arthropathy. In essence, nontraumatic hemarthrosis is managed by addressing the underlying pathologic factor(s).

Complications of Aspiration

Aspiration of a hemarthrotic joint has not been routinely recommended or performed in the current treatment in both hemophilic and non-hemophilic populations despite research detailing the toxic effects of blood to various joint structures occurring within days. Arguments against universal aspiration of hemarthrosis include the potential need for anesthesia (in children) and risk of infection.[36,43] Especially within a pediatric population, sedation had been suggested to be necessary prior to evacuation of blood from a joint.[43] However, this has never been validated in any study, and with appropriate technique, the procedure can be done without using more than local anesthetic agents. The greatest concern related to the aspiration of a joint is the development of a septic joint by introducing outside bacteria. The estimated incidence of this complication appears to be close to 1 in 3,000 procedures,[44] although with sterile technique and when performed by experienced physicians, the incidence is likely much lower. In one study, the aspiration of a hemarthrosis in the emergency department following traumatic injury was shown to result in improved pain scores and greater sensitivity of physical examination maneuvers in diagnosing ligamentous injury.[14] An improved physical exam could allow for more accurate evaluation and diagnosis, potentially reducing the need for further diagnostics such as MRI, or even arthroscopy in certain cases.[14] Ultrasound guidance during the aspiration can ensure a more directed needle entry into the hemarthrosis and visualization of complete removal of the blood. Consideration could also be made for lavage with a small amount of sterile normal saline until blood-free. Finally, given the release of various inflammatory cells and cytokines following a hemarthrosis, injection of anti-inflammatory substances such as low-dose corticosteroids or other modulators of cytokines including IL-4 and IL-10 may provide synergistic activity in preventing cartilage breakdown and early osteoarthritis.[45] This could be done using the same needle used during the aspiration to avoid a second injection. Incorporation of joint aspiration into treatment guidelines has a valid place in both traumatic and nontraumatic causes of hemarthrosis, as its complications are outweighed by the short- and long-term benefits.

Conclusion

Considering the negative effect of blood and the release of inflammatory mediators following an acute joint injury

with hemarthrosis, there appears to be a scientific and clinical rationale for recommending aspiration of a hemarthrosis after injury in young patients. Unfortunately, at this time there are no established guidelines in the treatment of an acute hemarthrosis, and essentially no specific recommendation for aspiration in spite of the known toxic effects of blood on chondrocytes with the potential for development of early arthritis in this population. A prospective, controlled clinical trial should be conducted in order to assess the long-term risks and benefits of early intervention with aspiration of knee hemarthrosis in youth after an acute injury to prevent early arthritis in this group.

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ORCID iDs

Nikhil Potpally https://orcid.org/0000-0003-4229-6690
Michael Baria https://orcid.org/0000-0003-4351-9585
Gerard A Malanga https://orcid.org/0000-0001-8384-7036

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