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Differentiating giant cell tumor of bone from patellofemoral syndrome: a case study

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Balancing the assessment of musculoskeletal dysfunctions with a high level of suspicion for non-mechanical origins can be a challenge for the clinician examining a sports injury. Without timely diagnosis, non-mechanical complaints could result in surgery or loss of limb. This case describes the discovery of a Giant Cell Tumor of Bone (GCTB) following the re-evaluation of an athlete who had undergone five years of conservative management for patellofemoral pain syndrome (PFPS). Knee injuries account for 32.6% of sports injuries with PFPS being the most common and most likely diagnosis for anterior knee pain. GCTB is a benign aggressive bone tumor with a predilection for the juxta-articular region of the knee, comprising up to 23% of all benign bone tumors, and commonly occurs in the second to fourth decades. This case report illustrates the difficulty in accurately diagnosing healthy athletes, reviews common differentials for knee complaints and explores helpful diagnostic procedures.

Trouver le bon équilibre entre l'évaluation des dysfonctionnements musculo-squelettiques et un niveau élevé de suspicion d'origines non mécaniques peut présenter un défi pour un clinicien qui examine une blessure sportive. Sans un diagnostic rapide, les plaintes non mécaniques pourraient nécessiter la chirurgie ou aboutir à la perte d'un membre. Ce cas décrit la découverte d'une tumeur à cellules géantes (TCG) de l'os à la suite de la réévaluation d'un athlète qui avait subi cinq ans de traitement conservateur du syndrome fémoro-rotulien douloureux (SFP). Les blessures au genou représentent 32,6 % des blessures sportives, et le SFP est le diagnostic le plus fréquent et le plus probable pour la douleur de la partie antérieure du genou. La TCG est une tumeur osseuse bénigne agressive avec une prédilection pour la région juxta-articulaire du genou, comprenant jusqu'à 23 % de toutes les tumeurs osseuses bénignes et généralement se produisant au cours de la deuxième, troisième et quatrième décennie. Cette étude

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de cas montre la difficulté du diagnostic précis des athlètes en bonne santé, examine les écarts communs pour les plaintes liées au genou et explore les procédures utiles de diagnostic.

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Introduction

Differentiating between mechanical and non-mechanical pain is one of the most important steps in the assessment of a patient; although this can be challenging with athletes. Mechanism of injury, associated symptoms, red flags and risk factors picked up in the medical history can lead clinicians toward potential non-mechanical origins of a complaint. However, aspects of the history can also distract clinicians initially. Once management begins, poor compliance and re-aggravation can also skew prognosis for the working diagnosis. We present the case of a recreational soccer player who was originally diagnosed and treated for mechanical knee pain. Re-evaluation of the case resulted in a potentially limb sparing discovery of a locally aggressive benign bone tumor. This case stresses the importance of maintaining a high level of suspicion, even when faced with seemingly healthy athletes. The following report will highlight how athletic injuries may mask pathology, while discussing common sources of anterior knee pain and detailing tumors of the knee.

Case Presentation

An otherwise healthy 30-year-old female presented to a chiropractor with a complaint of right knee pain. She reported that this condition began approximately five years ago and attributes it to playing soccer. Past impressions have included an irritated meniscus and patellofemoral pain syndrome. The symptoms have recently become progressive, although she did get relief from icing.

Examination of the patellofemoral joint and muscles of the knee were unremarkable. There was positive medial joint line tenderness on palpation. Orthopedic tests for ligamentous stability were negative for excessive motion; however, Slocum test, anterior-posterior glide with external rotation of the shin reproduced the knee pain. Functional examination found single leg standing and squat aggravated the chief complaint and McMurray's test produced pain, without click. Duck walk was found to be non-painful at the hip, but reproduced medial joint line tenderness of the right knee. The patient was referred to her family doctor for a second opinion and imaging. A plain film series and MRI scan of the knee were then requisitioned to rule out meniscal injury and the patient was referred to physiotherapy for assessment and treatment.

When assessed by the physiotherapist, the patient reiterated her history of chronic, intermittent right medial knee pain with recent increase in intensity and frequency. A recreational soccer and ultimate Frisbee participant, she had discontinued playing due to an abdominal muscle pull. Aggravating activities for her knee pain included ascending and descending stairs, running, playing sports, sit to stand movements and prolonged sitting or jumping. Her knee pain was eased by ice only. Her pain intensity, as rated by a Numeric Pain Rating Scale, varied between 0-5/10. She did not report symptoms of inflammation. She denied any locking or giving way of the knee. Her history included a red flag of previous melanoma, which was removed surgically several years prior. No medications were prescribed or being taken for her knee pain.

On physical examination, dynamic valgus of the right knee was noted with single and double leg squatting while reproducing medial joint line pain. This pain could be modified with correction of the dynamic valgus pattern.

Thessely's test was negative, while McMurray's test was painful without click. Manual muscle testing was rated using the Oxford scale with left gluteus medius rated 4, 4- on the right, hamstrings 4+ bilaterally, and gluteus maximus 4 bilaterally. She was diagnosed with patellofemoral pain syndrome (PFPS) with a differential diagnosis of right medial meniscal injury.

Plain radiographs were taken and demonstrated a multiseptated "soap bubbly" lytic lesion in the medial femoral condyle (Figure 1). Differentials suggested by the radiologist included giant cell tumor (GCTB), aneurysmal bone cyst (ABC), osteoblastoma, or chronic osteomyelitis and advanced imaging was recommended. The MRI scan provided a more detailed description of the nature and size of the lesion and helped rule out malignancy (Figures 2 and 3). A well-circumscribed multi-septated lesion with a sclerotic border measuring 4.5 x 2.9 cm with several fluid-fluid levels was visualized. There was no cortical disruption, periosteal reaction or expansion of the medial femoral condyle; also no soft tissue mass was visualized and there was no bone marrow edema.

The patient was referred to an orthopedic oncologist for assessment. Due to patient symptomatology and the locally aggressive but benign behavior of the lesion on imaging, surgical management was the best option for this patient. During the surgical procedure, first a biopsy was perform which revealed benign multinucleated giant

Figure 1.
Right knee, anterior-posterior view plain film radiograph. This pre-surgical image demonstrates a multiseptated "soap bubbly" lytic lesion in the medial femoral condyle. Differentials suggested by the radiologist included giant cell tumor (GCTB), aneurysmal bone cyst (ABC), osteoblastoma, or chronic osteomyelitis.

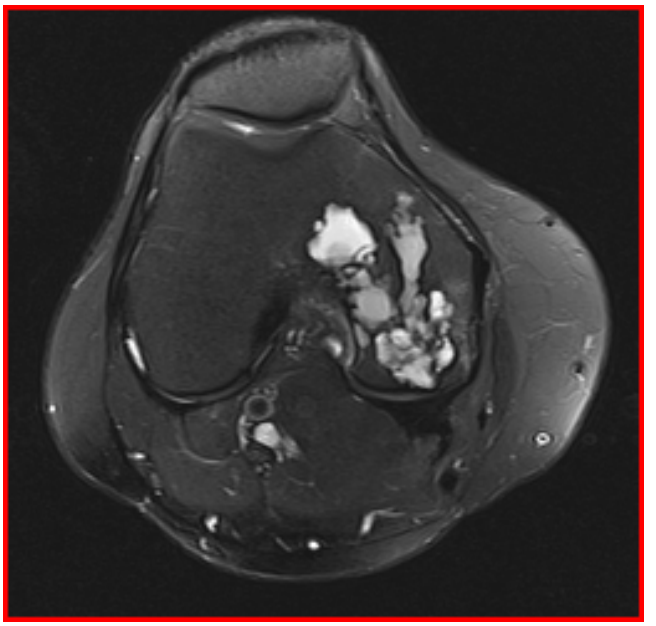

Figure 2.
Right knee magnetic resonance imaging (T2 weighted fat-saturated) axial view. This pre-surgical image demonstrates a lesion in the medial femoral condyle projecting anterior-posterior 4.5 x 2.9 cm with the visualization of several fluid-fluid levels.

cells in a mononuclear stroma, while the mononuclear cells showed moderate atypia and extensive hemosiderin deposition, suggestive of GCTB. Based on this benign diagnoisis, aggressive curettage and high speed burring were performed to remove the tumor. During surgery both solid tumor and blood filled cystic areas were identified. The final pathology revealed a GCTB with a secondary ABC. A portion of the distal femoral medial condyle was removed until only normal appearing bone remained. A periarticular plate and screws were used to support the morcellized cancellous allograft bone (Figure 4 and 5).

Discussion

This case highlights an example where an underlying pathological condition went clinically unnoticed for a number of years. Considering the good health of the patient and the fact that the only symptom was knee pain, this should not be a surprise. In fact, we are trained knowing that serious pathology comprises a very small percentage of complaints presenting to a musculoskeletal practitioner. Therefore, the point of this case presentation is to emphasize the importance of the re-evaluation, a thorough work up and a second opinion in cases with persistent symptoms. Further, it is an excellent starting point for a review of the differential diagnosis of persistent knee pain (Table 1).

In retrospect, the patient could have been asked more pointed questions regarding red flags (in this case the re-evaluation history only included general questions about health status and whether or not there were any changes in the health history). Red flag symptoms including night sweats, weight loss, malaise etc. could be present in tumours of metastatic origin, but none were present in this case aside from history of melanoma and unremitting pain. The reproduction of pain during the orthopaedic tests could have been due to compressive forces on the

Figure 3.
Right knee magnetic resonance imaging (T2 weighted fat-saturated) coronal view. This pre-surgical image demonstrates a well-circumscribed multi-septated lesion with no signs of malignant characteristics.

Figure 4.
Right knee, anterior-posterior view plain film radiograph. This post-surgical image demonstrates the hardware (A periarticular plate and screws) utilized post-curettage to cover and support the site of morcellized cancellous allograft bone used for reconstruction.

Figure 5.
Right knee, lateral view plain film radiograph. This post-surgical image demonstrates the side view of the periarticular plate and screws used to cover and support the allograft reconstruction post-curettage.

bone itself. Regardless of the exact mechanism of pain, the decision to refer the patient for a second opinion and imaging was largely based on a lack of specific findings from the physical examination and the history of unresolved symptoms with no past imaging.

Differential Diagnosis of Knee Pain

Roughly 33% of all sports injuries involve the knee (Table 1).[1] PFPS is the most commonly diagnosed clinical condition in athletes with non-traumatic anterior knee pain.[1-2] In a military population, with comparable incidence rates, females were found to suffer from PFPS 2.23 times more frequently than males.[3-4] At a specialty center dealing with musculoskeletal trauma, meniscal injury was the most common knee injury with an incidence of 23.8/100,000 per year.[5] Recent investigations found strong evidence that participation in soccer, rugby, downhill skiing and squash were strong risk factors for acute meniscal tears.[6] It is difficult to truly estimate the incidence of meniscal injuries. Incidental findings of meniscal tears on MRI and during arthroscopic procedures have been widely documented, with some reports observing meniscal tears on MRI in 61% of asymptomatic subjects.[7] However, it can still be considered a highly probable differential diagnosis for traumatic mechanical knee pain in active individuals.

The earlier popular, but controversial, rationales for the mechanism of PFPS is that of mal-alignment of patellar tracking. It is with more recent kinematic research that

Table 1.
Common sources of knee pain.

Common Pathologies Leading to Anterior Knee Pain (AKP)	
Articular Cartilage Injury	Patellar Tendinopathy
Bone Tumors	Patellofemoral Arthritis
Chondromalacia Patellae	Patellofemoral Pain Syndrome
Hoffa's Disease	Pes Anserine Bursitis
Iliotibial Band Syndrome	Plica Synovialis
Loose Bodies	Prepatellar Bursitis Previous Surgery
Neuromas	Quadriceps Tendinopathy
Osgood-Schlatter Disease	Referred from L/S or Hip Joint Pathology
Osteochondritis Dissecans	Saphenous Neuritis
Patellar Instability/Subluxation	Sinding-Larsen-Johansson Syndrome
Patellar Stress Fracture	Symptomatic Bipartite Patella

Table 2.
Common bone tumors and conditions by age of incidence. Asterisks (*) indicate tumors commonly affecting the femur or tibia around the knee.

Age		
0-20 years	20-50 years	>50 year
Osteoblastoma	Non-Hodgkin's Lymphoma*	Paget's Disease
Osteoid Osteoma*	Osteosarcoma	Lymphoma
Fibrous dysplasia	Giant Cell Tumor*	metastatic carcinoma
Hodgkins Lymphoma	Aneurysmal Bone Cyst	Multiple Myeloma
Osteochondroma*	Chondroblastoma	Chondrosarcoma
Ewing sarcoma	Spindle cell sarcoma (eg Fibrosarcoma)*	
Osteosarcoma		
Osteomyelitis		
Aneurysmal Bone Cyst		
Chondroblastoma		

the proximal links in the lower extremity are more significantly associated with the dysfunction noted in PFPS.[8] Positive risk factors for the development of PFPS identified in the literature include: muscular weakness around the knee and/or hip; single leg stance strength deficits; decreased trunk proprioception; tight illiotibial band; general ligament laxity; large Q-angle; patellar compression or tilting.[9-10] Abnormal vastus medialis oblique/vastus lateralis reflex timing has also been considered; however this is proving to be less significant than first theorized according to recent systematic reviews.[11] The female athlete is in a high risk category due to relatively larger Q-angles, potential ligamentous laxity, differences in muscular girth, and even effects of hormone fluctuations throughout the menstrual cycle.[3,12-13] One weakness to the patellar tracking theory is the poor correlation with expected lateral tilt or displacement of the patella on radiographs and symptomatology.[14] More recent observational trials have demonstrated significantly lower cross-sectional girth and diameter of the quadriceps musculature as measured

on MRI; however a significant difference in the ratio of vastus lateralis and vastus medialis was not demonstrated.[14] Further research using MRI paired with kinematic analysis revealed that what is more important is abnormal femur motion and not that of the patella.[15] This abnormal femur motion in PFPS is suggested to be the result of reduced hip torque into abduction and external rotation noted on a step down task.[16] Similarly, decreased hip abduction force and associated increased hip adduction angle at the end of a run of variable distances was measured in PFPS subjects.[17]

Investigations on the natural history of PFPS have been poor, making it difficult to know when to consider alternative differential diagnoses. Two studies have attempted long-term follow-up of patients with PFPS. The group found that 27% of athletes recovered within an average of 8 months, while the remaining patients continued to have pain at 5 years.[4] Of the unrecovered population, half reported being able to cope with the pain, and only 20% of athletes were forced to completely cease sport participation, and 6% reporting time off work.[4] Variables strongly associated with poorer prognosis include: female gender, pain severity on visual analog scale, Anterior Knee Pain score, patellar hypermobility, and a sedentary lifestyle.[4, 18]

Misdiagnosis in Athletes

Misdiagnosis, specifically tumors about the knee in athletes is an important issue looked at in the literature.[19] One report from a large orthopedic hospital helped illustrate the incidence of misdiagnosed knee pathology in athletic populations.[20] The investigators reviewed 667 cases and found 25 tumor patients which were originally misdiagnosed as an athletic injury, and resulted in inappropriate invasive procedures.[20] The authors concluded that 15 patients had suffered significant detrimental effects to their final clinical outcomes due to misdiagnosis, 3 of which resulted in limb amputation.[20] While the incidence of these cases was found to be relatively low, the results are potentially devastating to the patient. The most common cause for misdiagnosis reported by the authors was poor quality radiographs and refusal to consider alternative diagnoses in the absence of clinical improvement.[20]

Tumors Around the Knee

Although GCTB is an uncommon cause of knee pain, it has been reported to accounts for 13.7% (8–23%) of all benign primary bone tumors.[21] GCTB is considered to be "quasi-malignant" or a "borderline" malignancy making up a 5-8% of all primary malignant bone tumors.[21-22] It is associated with a very low risk of lung metastasis, even in the absence of histologic malignancy, although it is treated locally as a benign tumor.[21] The vast majority of patients with GCTB are between 20–50 years of age.[22-23] GCTB has a predilection for juxta-articular locations (i.e. metaphysis and epiphysis) and is located most commonly around the knee.[23]

ABC is also an uncommon cause of knee pain, 6% of benign bone tumors, which occurs typically in the first two decades of life.[22] ABC frequently causes bone destruction and cortical expansion prior to their discovery.[23] In adults ABC can also form secondary to an underlying GCTB or other benign bone tumor. [21, 25-25] In the case presented above, pathological analysis of the excised tissue found evidence of both GCTB and secondary ABC. There are other bone tumors that fit this case presentation based on location and demographic information (Table 2).

Patients with benign aggressive bone tumors usually present with rapid onset of symptoms and functional disability, unlike the patient in this case report who had persistent, but slowly worsening symptoms over a course of 5 years. The typical management of benign aggressive lesions including GCTB and ABC is tumor resection by aggressive curettage and high speed burring followed by reconstruction with either bone graft or cement, or less commonly by en bloc resection.[26-27] A retrospective review of 621 patients at a Chinese hospital specializing in musculoskeletal oncology reported a local recurrence rate of 8.6% after extensive curettage and burring.[20]

Imaging

Most guidelines prefer a conservative approach to imaging; however, when considering athletes imaging utilization tends to increase. Indications for knee imaging includes traumatic injury with inability to fully extend the knee, severe ecchymosis with anterior cruciate ligament tear suspected, and persistent unexplained knee pain, to rule out surgical pathology and neoplasms.[28] To evaluate these structures, MRI is preferable, however, it is up to the clinician to know if the structures are just as easily demonstrated on US. Plain radiographs or MRI can identify previously undiagnosed bone tumors prior to any surgical intervention including arthroscopy, thus avoid-

ing inadvertent tumor rupture, spread of lesion and sometimes amputation.[20]

Summary

We have presented a case of underlying knee pathology that had remained undiagnosed for a number of years. The important feature to note during the evolution of this case was the re-evaluating clinician's willingness to engage in collaborative care when faced with progressive or unresolving symptoms. On a subsequent evaluation, the patient's presentation still appeared mechanical on physical exam; however, symptoms were increasing in severity making the clinical progression appear more urgent, warranting imaging. While MRI remains a sensitive imaging modality for early diagnosis, radiographs may be a logical first step.

One challenge with this case is the self-limiting nature of PFPS in the absence of ligamentous instability or intra-articular injury. This allows patient to continue to access pain management over a period of time, often seeking out various health care providers due to frustration, while allowing serious pathology to go unsuspected. This case illustrates the importance of a thorough re-evaluation, consideration of differentials and follow-up for persistent self-limiting complaints. Maintaining a high level of suspicion in athletic or active populations should be exercised early so as to avoid delayed diagnosis and hasten recovery.

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