"Satisfaction of Search" Never Stop Looking— Before and After Surgery

Daniel Y. Hong, MD¹; Stephanie N. Moore-Lotridge, PhD²; John J. Block, MD²; Hernan Correa, MD²; Jennifer L. Halpern, MD²; Ginger E. Holt, MD²; Christopher Stutz, MD³; Jeffrey E. Martus, MD²; Tim Schrader, MD⁴; Jonathan G. Schoenecker, MD PhD^{2,3}

¹Columbia University, New York, NY; ²Vanderbilt University Medical Center, Nashville, TN; ³University of Texas Southwestern Medical Center, Dallas, TX; ⁴Children's Healthcare of Atlanta, Atlanta, GA

Abstract: Diagnosing joint pain in the pediatric patient can be difficult considering the wide variety of possible pathology. Concurrent disease processes around the same joint confound assessment and can introduce cognitive bias where the surgeon most often focuses on the most common diagnoses, precluding further workup of other less common pathologies. Here, this concept is reiterated through two cases in which a synovial sarcoma, an extremely uncommon pediatric malignancy, was coincident with more common pathologies of the hip and knee. These cases highlight the importance of an unbiased evaluation of the patient and critical diagnostic workup as concurrent, unrelated pathologies do occur. Additionally, they highlight the importance of considering previously undiagnosed concurrent pathologies when patients deviate from normal recovery after surgery for their primary initially diagnosed pathology.

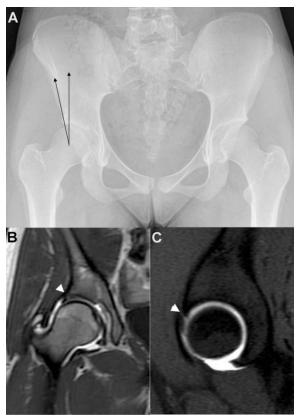
Key Concepts:

- "Satisfaction of search" must be considered when evaluating atypical presentations of common pathologies.
- Synovial sarcoma is an uncommon pediatric malignancy that commonly presents in the extremities as a slow growing, painful mass, with non-specific imaging findings.

Introduction

Joint pain in the pediatric patient at times is difficult to manage given the wide variety of possible pathology. Common etiologies include infection, trauma, and structural abnormalities, while the incidence of malignancy is much lower.^{1,2} Mesenchymal tumors, including soft tissue sarcomas and bone sarcomas, comprise the vast majority of malignancies in the pediatric hip and knee.³⁻⁵ Synovial sarcoma is rare and particularly difficult to diagnose due to a lack of

pathognomonic physical exam and imaging characteristics. Even more troublesome is when synovial sarcoma presents with more common concurrent disease processes, which introduces cognitive bias towards the more common diagnoses, potentially precluding further workup. Here, we present two cases of pediatric patients with joint pain and immobility that, following initial surgical procedures for more common pathology, were ultimately diagnosed with synovial sarcoma. Importantly, in both cases, deviation from normal



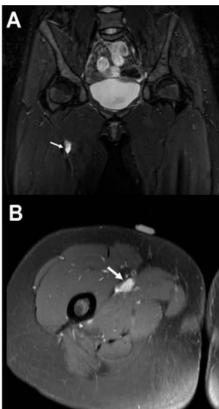


Figure 1 (left). A. X-ray demonstrates right hip acetabular dysplasia (black arrows show lateral center edge angle). B. Coronal T1 image, and C. Sagittal T1 fat-saturated images confirm diagnosis with insinuation of gadolinium contrast within the labrum (arrowheads).

Figure 2 (right). A. Coronal STIR sequence demonstrates an asymmetric nodular focus of increased signal intensity in the anteromedial proximal right thigh (arrow), not recognized during the initial image interpretation.

B. Post-gadolinium T1 fat saturated sequence shows an enhancing nodular focus in the deep fascia distal to the femoral artery bifurcation (arrow).

recovery prompted expansion of diagnosis leading to the second, potentially life-threatening diagnosis. These cases should serve as a reminder of the risks of "satisfaction of search," both during the initial workup and in convalescence, and the need to be hypervigilant for multiple, unrelated pathologies.

Case Report 1

A 16-year-old female with a family history of DDH was seen in clinic for right medial thigh pain. The patient had undergone an extensive workup the year prior, during which her physical exam, response to a steroid injection, and imaging were consistent with a diagnosis of symptomatic DDH, warranting a peri-acetabular osteotomy (PAO) (Figure 1 A/B/C). The PAO mildly improved her symptoms. However, the reprieve in pain was temporary, returning once the patient discontinued use of her crutches. The patient returned to clinic and was evaluated for a potential obturator nerve complication. Repeat imaging (X-ray, MRI, and CT) was obtained and neurology was consulted. Culmination of this second workup revealed no neuropathology or

structural malformations beyond the anticipated dysplasia and healing of the PAO. The patient's proximal medial thigh pain continued; thus, an additional orthopaedic surgeon was consulted, and a third MRI was obtained. Close examination of the third and previous MRIs revealed a possible asymmetric nodular focus of increased water-weighted signal hyperintensity near the area of the patient's pain (Figure 2A, Figure 3 A/B). The contrasted MRI clearly defined a 1.2 x 0.8 x 2.1cm enhancing mass distal to the bifurcation of the common femoral artery (Figure 2B).

Differential diagnosis included peripheral nerve sheath tumor, vascular malformation, enhancing adenopathy, and soft tissue sarcoma. Recommendation was made for an incisional vs. excisional biopsy. Deep dissection of the area identified a poorly encapsulated mass within the femoral sheath, centered between the superficial and deep femoral artery (Figure 3A and 3B). The mass also infiltrated the anterior wall of the deep femoral vein and surrounding musculature (Figure 4A and 4B).

Volume 2, Number 2, August 2020

Intraoperative and final pathology revealed a hypercellular spindle cell pattern (Figure 5). FISH testing demonstrated a t(x;18) translocation, which was diagnostic for synovial sarcoma. CT and PET scans were significant for prominent right iliac chain lymph nodes. Given the diagnosis, the patient was referred for chemoradiation and wide surgical resection.

The patient underwent multiple rounds of neoadjuvant chemotherapy and radiation before surgical resection. Given the location of the tumor and contamination of the femoral sheath/artery, resection of the tumor mandated femoral artery and vein ligation and ultimately intercalary reconstruction of the vasculature. The patient remains disease-free 4 years from tumor removal (Figure 6 A/B); she is physically active and reports minimal restrictions. Postoperative complications included chronic venous thrombosis, pulmonary embolism, restenosis of the arterial graft requiring two stents, and chronic lymphedema.

Case Report 2

A 15-month-old female presented with an antalgic gait and a 25-degree knee flexion contracture. Given the lack of effusion or warmth around the knee, in addition to benign X-rays; an MRI was obtained, which revealed a lateral discoid meniscus covering 80-90% of the lateral compartment (Figure 7A). Mild intrasubstance degeneration affecting the posterior horn was noted. Additionally, a 1.1 x 0.6 x 1.1cm deep soft tissue lesion could be observed in the space between the popliteus muscle and the medial head of the gastrocnemius muscle (Figure 7B/C). The lesion extended interiorly from the joint line and minimally invaded the popliteus muscle belly. Eight days later, the lesion was further evaluated by ultrasound and at that time measured 0.7 x 0.7 x 0.8cm and was noted to be hypoechoic to isoechoic relative to the surrounding muscle, with no significant flow to the lesion.

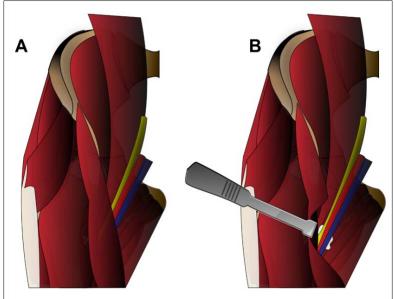


Figure 3. A & B. Artistic rendering of the anatomic region of the patient's tumor. In particular, the femoral nerve and contents of the femoral sheath are demonstrated. Drawing: Jonathan Schoenecker

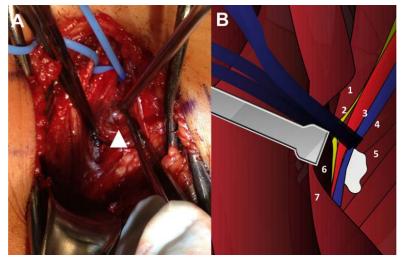


Figure 4. A. Open incisional biopsy of mass (arrow) immediately distal and medial to the common femoral artery (isolated by blue vessel loop). B. Artistic rendering of the tumor's anatomic location. Involvement of the following structure is illustrated: 1. Pectineus, 2. Femoral nerve, 3. Femoral sheath containing the superficial and deep (not pictured) femoral artery and deep femoral vein, 4. Pectineus continued, 5. Adductor longus, 6. Medial border of rectus femoris, and 7. Sartorius Drawing: Jonathan Schoenecker

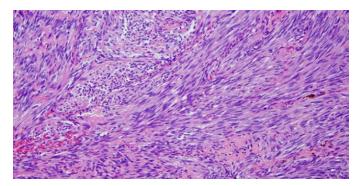


Figure 5. Monophasic synovial sarcoma. The spindle cells are arranged in long interlacing fascicles forming areas resembling a herringbone pattern. There are rare mitosis (1 per 10 high power fields). The vessels are thin and delicate. No epithelial elements are identified. (H&E, 200X)

The lack of extension was attributed to the discoid lateral meniscus, and arthroscopy with saucerization was performed. During the arthroscopy, it was observed that when the knee was in extension, the anterior portion of the meniscus was unstable and infolded; thereby blocking maximal extension of the right knee. The saucerization was successful, the instability was repaired arthroscopically, and the patient was placed in a cast in maximal extension. Four months following surgery, the patient continued to have a flexion contracture and intermittently favored the right leg. As her symptoms were failing to improve, ultrasound was repeated demonstrating no change in the size or appearance of the soft tissue mass. Through shared decision making, serial casting and observation was continued. At 7-months post-surgery, new onset pain in the popliteal fossa prompted repeat ultrasound and then MRI. The lesion was found to have markedly increased in size (2.5 x 1.8 x 2.5cm) and was macrolobulated in appearance, abutting the popliteus and medial gastrocnemius muscles (Figure 7D/E & Figure 8). Ultrasound revealed no definitive intralesional blood flow and no cortical disruption of bone was observed by MRI or radiographic analysis. An open biopsy was conducted which revealed a hypercellular spindle cell pattern with an SYT/SSX1 fusion transcript, consistent with the diagnosis of synovial sarcoma. Furthermore, akin to Case 1, FISH

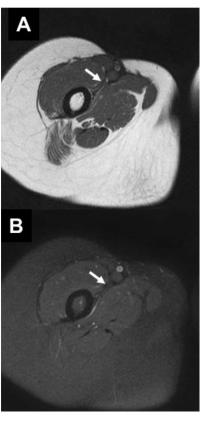


Figure 6. A. Axial T1 image, and B. Postgadolinium T1 fat saturated images 4 years after surgical resection demonstrate resection of nodular enhancing mass with minor postoperative scarring (arrows).

testing demonstrated a t(x;18) translocation. Given these results, the patient was referred for chemoradiation and wide surgical resection.

The patient underwent multiple rounds of neoadjuvant chemotherapy and radiation that were complicated by several central line infections throughout the treatment course. Unfortunately, the patient's tumor did not completely respond to chemotherapy, and radical excision was conducted. Positive margins prompted a further excision was performed 3 months later, along with the placement of an interstitial brachytherapy implant to boost radiation in subsequent external beam radiation treatments. Upon completion of radiation treatment, no residual masses were observed. Postoperative/treatment complications included transverse fracture of the proximal tibial metaphysis and distal femoral metaphysis secondary to a minor fall, a persistent right knee flexion contracture, and notable right limb length discrepancy (Figure 9). She subsequently was treated with contralateral proximal tibia epiphysiodesis.

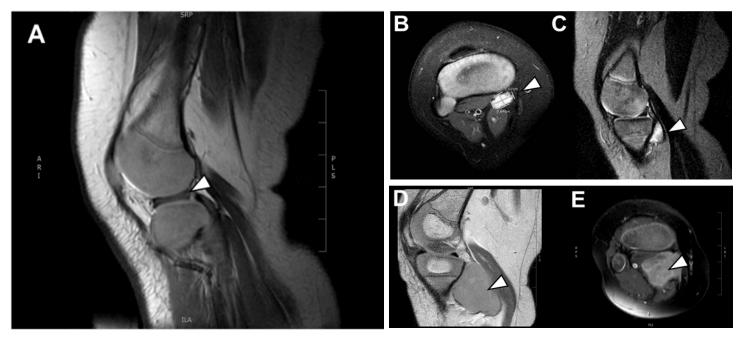


Figure 7. A. T1 weighted sagittal MRI demonstrating the discoid lateral meniscus (white arrow) upon initial presentation; B. Axial T2 imaging; C. Sagittal T1 imaging with contrast illustrating hyper intensity of deep soft tissue lesion between the popliteus muscle and the medial head of the gastrocnemius muscle upon presentation. Following arthroscopic treatment and serial casting, when pain and joint contracture did not resolve, repeat MRI was obtained (7 months later); D. Sagittal T1 PD; and E. Axial T1 FS revealed a markedly larger, macrolobulated, soft tissue lesion.

Discussion

Joint pain in the pediatric patient is difficult to manage given the wide variety of possible pathology. Concurrent disease processes confound an already difficult assessment, as they can introduce cognitive bias towards the most common diagnoses, precluding further workup of other, less common, pathologies. Of all the potential less common secondary diagnoses to consider, it is essential to always consider malignancy. Malignancy is rare in the pediatric population, but accurate diagnosis translates into "best care" practices. Although delay in diagnosis does not change the ultimate survival outcome for a patient, it can impact surgical morbidity. The most common malignancies in children are leukemia (20%), CNS tumors (15%), and lymphoma (10%), while soft tissue and bony tumors are less frequent, as described by Conrad et al.⁸ The hip and knee are common anatomical locations for soft tissue and bony tumors. A study done by Ruggieri et al. found that 20% of all pediatric bone tumors involve the pelvis or proximal femur.⁵ In that study, 11% out of 752 pediatric patients with bone

lesions of the hip were malignant. Likewise, bony lesions indicative of osteosarcoma, the second most common primary bone cancer, are frequently detected in the metadiaphysis of long bones around the knee.⁹ With regards to soft tissue tumors, Kacar et al. found that soft tissue sarcomas compromised of 23.8% of all soft tissue tumors and 14.8% of all malignant tumors in a pediatric population.¹⁰ The most common pediatric soft tissue sarcomas are rhabdomyosarcoma (50.9%) and fibrosarcoma (23.9%).¹¹

Synovial sarcoma is predominantly found in younger patients and accounts for 5% of all pediatric sarcomas.⁴ In a large study done by Ladanyi et al., the mean age of initial diagnosis was 35 years with 44% of patients under the age of 30 at diagnosis.¹¹ There was no gender predilection found and synovial sarcoma were typically found in the deep soft tissue of the extremities. There is an equal distribution between the proximal and distal extremity, and the tumor is commonly found in a juxta-

Volume 2, Number 2, August 2020

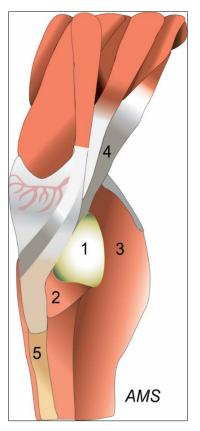
Figure 8 (left). Artistic rendering of the anatomic region of the mass. Anatomical landmarks include 1. the tumor, 2. popliteus, 3. medial gastrocnemius, 4. semitendinosus, and 5. the tibia. The lesion was abutting the popliteus muscle and the medial head of the gastrocnemius muscle. Drawing: Abigail May Schoenecker

Figure 9 (right). Bone length film approximately 9 years after initial presentation that demonstrates tibial shortening resulting in a 3cm limb lengthening discrepancy.

articular location, although rarely in the joint itself (about 6-10% of cases). 12 Patients typically present with a slow growing mass and persistent, worsening, or unexplained pain. As Laffan et al. described, imaging findings are nonspecific and unhelpful in diagnosis.³ Studies have attempted to identify prognostic factors for synovial sarcoma, but there remains great controversy. Diagnosis is primarily made upon histologic and chromosomal analysis. There are two main subtypes of synovial sarcoma: biphasic and monophasic. Biphasic refers to the presence of both epithelial and spindle cell components, while monophasic is spindle cell alone. The t(X; 18)(p11; q11) translocation is highly specific for synovial sarcoma, with multiple studies reporting occurrence of the chromosomal abnormality in over 90% of cases. 13,14 Synovial sarcoma is treated with chemoradiation and wide surgical resection.

While cases of synovial sarcoma about the knee have been misattributed to meniscal pathologies, ¹⁵⁻¹⁷ review of current literature shows no cases in which synovial sarcoma was diagnosed in a patient with hip dysplasia. Symptomatic DDH in the adolescent population typically presents with abnormal gait or hip pain, although these symptoms are nonspecific. As radiographic classifications and nomenclature better define the developmental conditions that might generate hip pain, it is increasingly important to combine the clinical assessment of the patient with the radiographic evaluation to generate a meaningful diagnosis.

The diagnoses of hip dysplasia or a lateral discoid meniscus in these cases act as diagnostic confounders as





well as red herrings to the actual symptomatic and potentially life-threatening issue of synovial sarcoma. "Satisfaction of search" describes a form of bias in which one observed radiographic or MRI finding interferes with the discovery of others as the clinical inquiry is deemed "satisfied," as described elsewhere. 18,19 Similar as to the adage in trauma, "The second injury is the most common injury missed," pediatric orthopaedic surgeons must always be hypervigilant to avoid diagnostic "satisfaction of search" and look for multiple pathologies. Proper imaging interpretation requires thorough evaluation of potential multiple, unrelated, abnormalities within the imaged field of view, thus reducing satisfaction of search errors. Further, as highlighted in these two cases, it is essential to expand the diagnostic inquiry beyond the initial concluded pathology when patients fail to recover through a typical predictable pattern. With the proper awareness of this known pitfall, consideration of clinical context, and attentiveness, only then can the diagnosis of uncommon pathologies be made.

Volume 2, Number 2, August 2020

Additional Links

- Synovial sarcoma overview: https://www5.aaos.org/OKOJ/vol8/issue7/ONC019/
- Common radiology fallacies including satisfaction of search:
 https://www.healthimaging.com/topics/diagnostic-imaging/5-cognitive-biases-common-radiology-and-how-beat-them-back
- Basics of hip dysplasia osteotomies:
 http://www.posnacademy.org/media/Pelvic+Osteotomies+for+Developmental+Dysplasia+of+the+Hip+/1_gtz6qqjc/19140162

References

- 1. Swischuk LE. Pediatric hip pain. Emergency Radiology. 2002;9(4):219-24. doi: 10.1007/s10140-002-0223-x.
- 2. Houghton KM. Review for the generalist: evaluation of pediatric hip pain. Pediatric Rheumatology. 2009;7(1):10. doi: 10.1186/1546-0096-7-10.
- 3. Laffan EE, Ngan B-Y, Navarro OM. Pediatric soft-tissue tumors and pseudotumors: MR imaging features with pathologic correlation: part 2. Tumors of fibroblastic/myofibroblastic, so-called fibrohistiocytic, muscular, lymphomatous, neurogenic, hair matrix, and uncertain origin. Radiographics. 2009;29(4):e36.
- 4. Miller RW, L Young Jr J, Novakovic B. Childhood cancer. Cancer. 1995;75(S1):395-405.
- 5. Ruggieri P, Angelini A, Montalti M, et al. Tumours and tumour-like lesions of the hip in the paediatric age: a review of the Rizzoli experience. Hip International. 2009;19(6_suppl):35-45.
- 6. F. C, A. U, R. CC, et al. Variability in the presentation of synovial sarcoma in children. The Journal of Bone and Joint Surgery British volume. 2008;90-B(8):1090-6. doi: 10.1302/0301-620x.90b8.19815.
- 7. Rougraff BT, Davis K, Lawrence J. Does length of symptoms before diagnosis of sarcoma affect patient survival? Clinical Orthopaedics and Related Research®. 2007;462:181-9.
- 8. Conrad EU. Pitfalls in diagnosis: pediatric musculoskeletal tumors. Pediatric Annals. 1989;18(1):45-52.

- 9. Khanna G, Bennett DL, editors. Pediatric bone lesions: beyond the plain radiographic evaluation. Seminars in roentgenology; 2012.
- 10. Kacar A, Paker I, Akcoren Z, et al. Solid tumors in Turkish children: a multicenter study. World journal of pediatrics. 2013;9(1):25-31.
- 11. Ladanyi M, Antonescu CR, Leung DH, et al. Impact of SYT-SSX fusion type on the clinical behavior of synovial sarcoma: a multi-institutional retrospective study of 243 patients. Cancer research. 2002;62(1):135-40.
- 12. Jones BC, Sundaram M, Kransdorf M. Synovial sarcoma: MR imaging findings in 34 patients. AJR American journal of roentgenology. 1993;161(4):827-30.
- 13. Sreekantaiah C, Ladanyi M, Rodriguez E, et al. Chromosomal aberrations in soft tissue tumors. Relevance to diagnosis, classification, and molecular mechanisms. The American journal of pathology. 1994;144(6):1121.
- 14. Nagao K, Ito H, Yoshida H. Chromosomal translocation t (X; 18) in human synovial sarcomasanalyzed by fluorescence in situ hybridization using paraffin-embedded tissue. The American journal of pathology. 1996;148(2):601.
- 15. Papadakis SA, Bisbinas I, Mitsitsikas T, et al. Synovial sarcoma arising in the knee. Pitfalls in the diagnosis and management. European Journal of Orthopaedic Surgery & Traumatology. 2001;11(4):255-7. doi: 10.1007/BF01686905.
- 16. Bergovec M, Smerdelj M, Bacan F, et al. Intraarticular synovial sarcoma of the knee rising from a lateral meniscus a case report. Orthopaedics & traumatology, surgery & research: OTSR. 2018;104(2):227-30. Epub 2018/01/23. doi: 10.1016/j.otsr.2018.01.002. PubMed PMID: 29355742.
- 17. Jamshidi K, Yahyazadeh H, Bagherifard A. Unusual Presentation of Synovial Sarcoma as Meniscal Cyst: A Case Report. Arch Bone Jt Surg. 2015;3(4):296-9. Epub 2015/11/10. PubMed PMID: 26550597; PMCID: PMC4628639.
- 18. Berbaum K, Franken Jr E, Rooholamini S, et al. Satisfaction Of Search In Diagnostic Radiology. Investigative Radiology. 1989;24(12):S113.
- 19. Ashman CJ, Yu JS, Wolfman D. Satisfaction of search in osteoradiology. American Journal of Roentgenology. 2000;175(2):541-4.