Comparison between juvenile idiopathic arthritis and proliferative synovitis in children: Utility of contrast-enhanced MRI

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Introduction

Knee complaints are common among children, which can result from acute traumatic injury or more insidious causes. The latter includes non-infectious synovial diseases from inflammatory (i.e.: juvenile idiopathic arthritis, JIA) and proliferative (i.e.: intra-articular tenosynovial giant cell tumor, TGCT; and primary synovial chondromatosis, PSC) causes, which are often under-recognized, leading to diagnostic delay and additional interventions.[1-3] Although the diagnosis of JIA is typically established without advanced imaging, in some ambiguous cases, magnetic resonance imaging (MRI) is the recommended tool to complement the clinical assessment, exclude alternative diagnoses, and if necessary, guide synovial biopsy.[4-5]

Currently, the existing published literature lacks a systematic approach to characterize the synovium in children, with most existing studies predominantly including adult patients with signs not pertinent to children.[1-3,6-7] Thus, the purpose of our study was to characterize and compare patterns of synovitis on contrast-enhanced knee MRI between children with JIA and proliferative synovitis.

Methods

Following institutional review board approval, a retrospective chart and imaging review of pediatric patients with JIA, TGCT, and PSC was conducted. For patients with multiple examinations, only one contrast-enhanced MRI examination was included, either the first study during clinically active disease (for JIA) or the study that preceded surgical intervention (for TGCT and PSC). MRI examinations that lacked both axial and sagittal fluid-sensitive images (short tau inversion recovery, STIR, T2-weighted, or intermediate-weighted fat-suppressed pulse sequences) or contained non-diagnostic and motion-degraded images were excluded. Demographics, symptomology, surgical and pathological notes were recorded. All MRI were retrospectively reviewed by two board-certified radiologists, blinded to the patients' history and diagnosis, and after randomization. Additionally, the same radiologists independently measured semi-quantitative features including thickness of the synovium at 11 predetermined intra-articular sub-regions, according to previously published methodology.[8-9] Descriptive statistics were used to summarize the study variables.

Results

Twenty-three children (13 girls, 10 boys, mean age, 12.5±2.9 years) included 13 with JIA and 10 with histopathology-confirmed proliferative synovitis. Those with JIA were more likely to be girls ($p=0.04$), report morning stiffness ($p=0.02$), and have longer follow-ups ($p<0.001$) when compared to children with proliferative synovitis. Cohort characteristics are further summarized in Table 1. MRI findings of synovial susceptibility ($p=0.01$) and more severe Hoffa-synovitis ($p=0.003$) were more prevalent with proliferative synovitis whereas concomitant findings of bony changes ($p=0.045$) and larger popliteal nodes ($p=0.01$) were more prevalent with JIA. Additional MRI features noted are presented in Table 2. Finally, JIA had thinner synovium when compared to proliferative synovitis overall ($p<0.001$) and within most subregions (p-range: <0.001-0.03), except for lateral parapatellar, anterior to ACL, and posterior to PCL subregions (Table 3).

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Table 1. Demographics of children with proliferative synovitis and JIA and contrast-enhanced knee MRI

Characteristics	TGCT (n=7)	PSC (n=3)	p^d	Combined proliferative synovitis (n=10)	All JIA-subtypes[b] (n=13)	p^d
Age (years)	13.1±3.0	12.3±1.2	0.55	12.9±2.5	12.2±3.2	0.58
Sex (girls: boys)	3: 4	0: 3	**0.04**	3: 7	10: 3	**0.04**
Laterality (R: L)	4: 3	3: 0	0.48	7: 3	4: 9	0.10
BMI class (n=21)[a]			0.46			1
Underweight & normal	5 (83)	1 (33)		6 (67)	7 (58)	
Overweight & obese	1 (17)	2 (67)		3 (33)	5 (42)	
Symptoms:						0.25
Incidental	1 (14.5)	-		1 (10)	-	
Swelling	2 (28.5)	-		2 (20)	-	
Swelling & pain (S&P)	2 (28.5)	-		2 (20)	5 (38.5)	
S&P + Stiffness	-	-		-	6 (46)	
S&P + Biomechanical[c]	2 (28.5)	3 (100)		5 (50)	2 (15.5)	
Duration of symptoms (days):	13 (10-13.5)	9 (5-33)	0.70	12 (6-14)	31 (8-67)	0.18
Duration of follow-up (months):	11 (7-19)	16 (12-22)	0.83	14 (8-19)	54 (35-73)	<**0.001**

Note – With the exception of age (mean ± standard deviation), values are either number of patients (percentage) or median (IQR).
BMI = body mass index; IQR = interquartile range; JIA = juvenile idiopathic arthritis; MRI = magnetic resonance imaging; PSC = primary synovial chondromatosis; TGCT = tenosynovial giant cell tumor;
a BMI was not available for 2 children (1 JIA, 1 TGCT).
b JIA subtypes included 5 with oligoarticular, 3 children with enthesitis-related, 2 with polyarticular, rheumatoid-factor negative, 2 with undifferentiated, and 1 with psoriatic arthritis.
c Biomechanical symptoms include 2 children with limping (1 PSC, 1 JIA), 2 with buckling (1 TGCT, 1 PSC), 2 with locking (1 TGCT, 1 JIA), and 1 with mass (PSC).
d Student's t, Mann-Whitney U, or Fisher's exact tests were used.

Table 2. Qualitative assessment of MRI findings between children with proliferative synovitis and JIA

MRI findings	All synovitis (n=23)	Proliferative synovitis (n=10)	JIA (n=13)	p^c	Agreement (%)
Pre-contrast synovium					
GRE susceptibility (n=17)	7/17 (41)	6/7 (86)	1/10 (10)	**0.01**	83
Effusion-synovitis				0.18	91
Simple: Complex	6: 17	1: 9	5: 8		
Hoffa's synovitis				**0.006**	65
None-mild: Moderate-severe	11: 12	1: 9	10: 3		
Popliteus hiatus distention	17 (74)	9 (90)	8 (62)	0.18	100
Contrast-enhanced synovium					
Effusion size				0.41	74
Absent-small: Medium-large	12: 11	4: 6	8: 5		
Synovial enhancement				1	74
Linear-lamellar pattern	18 (78)	8 (80)	10(77)		
Nodular-frond-like pattern	5 (26)	2 (20)	3 (33)		
Distribution				0.11	74
Mostly effusion	7 (30.4)	5 (50)	2 (15)		
Mostly synovium	6 (26.1)	3 (30)	3 (23)		
Relatively equal	10 (43.5)	2 (20)	8 (35)		

Table 2. (Continued)

MRI findings	All synovitis (n=23)	Proliferative synovitis (n=10)	JIA (n=13)	p[c]	Agreement (%)
Other findings					
Extra-capsular edema	7 (30)	4 (40)	3 (23)	0.65	74
Juxta-capsular outpouching [a]	6 (26)	3 (30)	3 (23)	0.87	52
Osseous changes [b]	5 (22)	0	5 (38)	**0.045**	91
Popliteal lymph nodes	18 (78)	6 (60)		0.13	83
Number	-	1.0±0.6	12 (92) 2.0±0.9	0.43	
Short-axis dimension (mm)	-	2.8±1.3	5.1±2.5	**0.01**	
Chondromalacia	1 (4.3)	1 (10)	0	0.44	95

Note – Values are either mean± standard deviation or count (percentage).
GRE = gradient-recalled echo; JIA = juvenile idiopathic arthritis; MRI = magnetic resonance imaging; PSC = primary synovial chondromatosis; TGCT = tenosynovial giant cell tumor;
[a] Juxta-capsular outpouching included popliteal cyst (1 PSC and 2 JIA), tibiofibular joint (1 TGCT and 1 JIA), and around gastrocnemius (1 TGCT).
[b] All osseous changes involved bone marrow edema. No erosion, destruction or remodeling was observed.
[c] Fisher's exact or Mann-Whitney U tests were used.

Table 3. Semi-quantitative assessment of synovial disease using contrast-enhanced knee MRI

Synovial thickness	All synovitis (n=23)	Proliferative synovitis (n=10)	JIA (n=13)	pb
Overall thickness (mm)	2.2±0.9	2.6±0.6	1.9±1.0	**<0.001**
Anterior subregions:				
Suprapatellar	2.3±1.3	2.8±1.5	2.0±1.0	**0.002**
Infrapatellar	2.0±1.0	2.3±1.0	1.8±1.0	**0.02**
Medial parapatellar	1.9±0.9	2.3±0.8	1.7±0.9	**0.02**
Lateral parapatellar	1.8±1.0	2.1±0.9	1.6±1.1	0.12
Intercondylar subregions:				
Intercondylar	2.0±1.1	2.2±0.8	1.8±1.2	**0.03**
Anterior to ACL	1.7±1.6	1.8±1.7	1.6±1.6	0.74
Posterior to PCL	1.9±1.1	2.4±1.2	1.5±0.7	0.06
Posterior subregions:				
Medial perimeniscal	2.8±1.9	3.4±1.9	2.2±1.8	**0.003**
Lateral perimeniscal	3.4±2.2	3.6±1.6	3.3±2.6	**<0.001**
Others, if present [a]				
Popliteal cyst (n=3)	1.5±0.4	1.5±0	1.5±0.5	0.80
Around intra-articular body (n=4)	1.7±1.0	1.7±1.0	-	-
Synovial hypertrophy score				0.17
No synovitis (0-4)	9 (39)	2 (20)	7 (54)	
Mild synovitis (5-8)	8 (35)	4 (40)	4 (30)	
Moderate synovitis (9-12)	5 (22)	4 (40)	1 (8)	
Severe synovitis (>12)	1 (4)	0 (-)	1 (8)	

Note – Values are either mean± standard deviation or count (percentage).
ACL = anterior cruciate ligament; JIA = juvenile idiopathic arthritis; MRI = magnetic resonance imaging; PCL = posterior cruciate ligament; PSC = primary synovial chondromatosis; TGCT = tenosynovial giant cell tumor;
[a] Popliteal cysts were present in 2 children with JIA and 1 with PSC; intra-articular body was present in 2 children with PSC and 2 with TCGT.
[b] Student's t or Mann-Whitney U tests were used.

Discussion:

We investigated the synovial patterns on contrast-enhanced knee MRI examinations and found that the synovium is thinner with JIA than proliferative synovitis. Additionally, bony changes and larger popliteal lymph nodes are more common among children with JIA whereas synovial susceptibility and more severe Hoffa-synovitis are common with proliferative synovitis.

The synovium lines the deep layer of the articular capsule and is responsible for the production of joint fluid, which lubricates and facilitates low-friction loading and wear-resistant movement.[6,10] Synovial dysfunction, characterized by synovial thickening and effusion, is recognized as a precursor to premature and accelerated osteoarthritis, leading to progressive joint destruction.[10-11] Normal synovium is barely perceivable on MRI unless it is thickened;[12] synovial hypertrophy and certain MRI findings can reflect differences in the underlying pathophysiology. On histopathology, the diseased synovium in patients with TGCT contains giant cells and histiocytes that are laden with hemosiderin, which is most conspicuous on GRE images as susceptibility artifact.[7,13] However, this finding is neither sensitive or specific for TGCT and can be observed in inflammatory synovitis that contain blood products, post-traumatic hemarthrosis, and hemophilic arthropathy.[14-16] The latter may explain the single case of JIA with synovial susceptibility observed within our study.

In our study, children with JIA had thinner synovium when compared to those with proliferative synovitis. These findings emphasize the importance of properly distinguishing between joint effusion and synovium, which is only possible on contrast-enhanced images because fluid-sensitive images can over-estimate the total amount of intraarticular fluid.[4,8,17] Currently, the existing literature on the use of quantitative methods to assess synovial hypertrophy has predominantly focused on adults with osteoarthritis8-9 and children with JIA.[18-21] Our study utilized the former 11 subregion method,[9] which has not been previously applied to pediatric patients[18-21] or compared values between patients with JIA and proliferative synovitis, which is critically important as clinical distinction can be occasionally challenging. In our cohort, 53% of JIA patients had a normal synovial hypertrophy score, which is in concordance with Hemke and colleagues, who found that minimal and moderately active JIA patients had synovial hypertrophy in less than 50% of cases.19 In contrast, only 14% of children with proliferative synovitis had a normal score.

Bony changes and larger popliteal nodes were significantly more common among children with JIA than proliferative synovitis. While osteitis and pressure erosions can occur in patients with proliferative synovitis, these preferentially involve smaller (i.e.: ankle) and low capacity joints (i.e.: hip and shoulder),[1,22-26] which do not apply to the relatively capacious knee joint. In contrast, bony changes in JIA associate with disease status and reflect local inflammation. In skeletally-immature younger children with an abundance of cartilage, marginal erosions are uncommon and regional hyperemia and epiphyseal osteitis increase the risk for future growth disturbance and deformity.[27] Popliteal lymphadenopathy, preferential disease involvement among girls, and increase incidence of morning stiffness observed in our study group are well-established features of JIA.[12,19-20] Hoffa-synovitis were more severe with proliferative synovitis than JIA, which has not been previously reported in children, but the precise

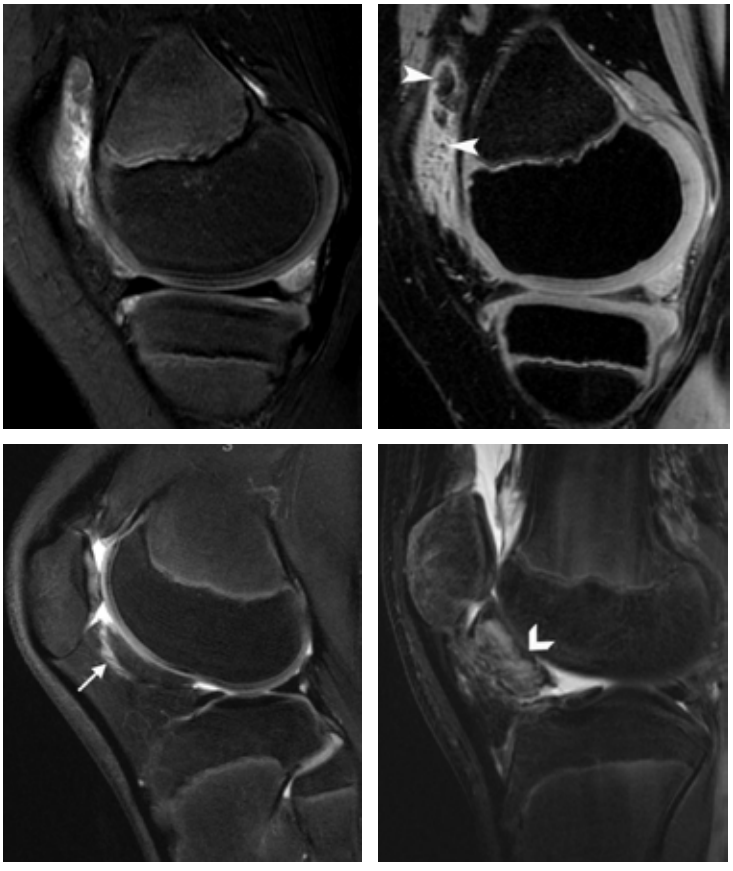

Figure 1. Synovial susceptibility and Hoffa synovitis. **(A)** Sagittal T2-weighted fat-suppressed and **(B)** gradient recalled echo (GRE) images from a 10-year-old girl show synovial susceptibility (arrowheads), an uncommon finding in JIA; **(C)** Sagittal T2-weighted fat-suppressed images from an 11-year-old girl with JIA and mild Hoffa synovitis, localized at the synovial cleft (arrow) and **(D)** from a 17-year-old boy with tenosynovial giant cell tumor (TGCT) and severe Hoffa synovitis with surface hemosiderin staining (chevron).

pathophysiology is unclear (Figure 1). Among adults with osteoarthritis, Hoffa-synovitis has been postulated to contribute to immune regulation and regional inflammation, directly impacting disease progression within the knee joint.[28-30]

Due to its retrospective nature, this study had inherent limitations. Diagnosis of JIA clinically often not requiring contrast-enhanced knee MRI examinations or tissue biopsy, thus, reducing our sample size. Second, inherent heterogeneity of the patient population may attenuate the comparison between groups but better reflects routine clinical practice and makes our results more generalizable. Finally, although the readers were blinded the clinical diagnosis, they were not blind to the findings on imaging findings, which may have biased their assessment.

Conclusion

In our study group of children with non-infectious synovitis, MRI findings of synovial susceptibility, more severe Hoffa-synovitis, and thicker synovium were significantly more prevalent with proliferative synovitis than JIA.

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