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Hypertrophy of the synovial membrane with the background of juvenile idiopathic arthritis under the mask of tenosynovial giant cell tumour: a clinical case report

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Abstract: *juvenile idiopathic arthritis is the most common childhood rheumatologic disorder, characterized by chronic inflammation in the synovial joints. Its pathophysiology includes synoviocyte proliferation, pathological angiogenesis, and immune cell infiltration, leading to joint destruction and functional impairment. Tenosynovial giant cell tumor, a rare benign tumor affecting synovial tissues, often mimics juvenile idiopathic arthritis symptoms, complicating diagnosis. This case presents a 30-year-old male with a long history of juvenile idiopathic arthritis and recurrent uveitis, who was diagnosed with bilateral villonodular synovitis in the knee joints. Despite magnetic resonance imaging findings suggesting tenosynovial giant cell tumor, histopathological examination following knee arthroscopy revealed chronic moderate synovitis, confirming juvenile idiopathic arthritis pathology. The patient had not received disease-modifying antirheumatic drugs for several years, contributing to disease progression. The American College of Rheumatology highlights the importance of early disease-modifying antirheumatic drugs use, particularly methotrexate, to prevent joint damage in juvenile idiopathic arthritis. Delayed initiation of biologic disease-modifying antirheumatic drugs leads to poorer long-term outcomes, emphasizing the need for early intervention to control inflammation and prevent irreversible joint damage. This case underscores the diagnostic challenge of distinguishing juvenile idiopathic arthritis-related synovial hypertrophy from tenosynovial giant cell tumor and emphasizes the critical role of histopathological confirmation.*

Keywords: Arthritis; Tenosynovial Giant Cell Tumor; Disease-Modifying Antirheumatic Drug; DMARD; Tumor; juvenile idiopathic.

Introduction

Juvenile idiopathic arthritis (JIA) is the most common childhood rheumatological disorder, with a prevalence of 0.6–1.9 per 1000 children [1]. JIA is defined as arthritis of unknown aetiology with a duration of disease of more than 6 months, occurring in children under 16 years of age [2]. JIA is characterized by significant pathological changes in the synovial joint, including [3]:

ISSN 2786-6661
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- uncontrolled proliferation of synoviocytes, leading to thickening of the synovial membrane and an increase in the number of its layers;
- rapid pathological angiogenesis, promoting the formation of abnormal blood vessels;
- development of an aggressive pathological synovial membrane ("pannus"), which exhibits invasive properties and can destruct surrounding tissues;
- accumulation of immune cells, including granulocytes, macrophages, plasma cells, and lymphocytes;
- excessive production of inflammatory mediators, sustaining chronic inflammation and triggering additional synovitis.

Hyperplasia and hypertrophy of the synovial membrane contribute to intra-articular hypoxia, stimulating the production of pro-angiogenic factors such as vascular endothelial growth factor (VEGF), its soluble receptors (sVEGF-R1, sVEGF-R2), osteopontin (OPN), and angiopoietin-1 (Ang-1). Increased levels of these molecules correlate with synovial angiogenesis, as observed through Doppler ultrasound imaging. The formation of new pathological blood vessels enhances the supply of pro-inflammatory cells into the joint, facilitating the development of destructive synovial tissue (pannus). The infiltration of immune cells (granulocytes, macrophages, plasma cells, and lymphocytes) into the joint leads to the release of inflammatory cytokines such as TNF-α and IL-1β. These cytokines stimulate pannus synoviocytes to produce catabolic enzymes, including matrix metalloproteinases (MMP1, MMP3), aggrecanases, and cathepsins, which degrade the extracellular matrix of the articular cartilage. This degradation results in functional loss of the joint, decreased biomechanical strength, and impaired articulation. Moreover, cytokine activity triggers osteoclast activation through RANK expression, leading to bone erosion. In later stages, the destruction of cartilage and bone contributes to ankylosis and joint immobility. Since JIA affects the growing body, it can also disrupt skeletal development [4].

Tenosynovial giant cell tumor (TGCT) is a rare benign tumor that affects the synovial membrane of joints, synovial bursae, and tendon sheaths. It commonly presents with pain, swelling, stiffness, reduced mobility, and joint instability, though these symptoms are nonspecific, making diagnosis challenging [5].

TGCT is classified into two main subtypes:

- Localized TGCT (L-TGCT): Typically affects the fingers and toes.
- Diffuse TGCT (D-TGCT): More frequently involves large joints, especially the knees.

Magnetic resonance imaging (MRI) is the primary diagnostic tool, offering high sensitivity but low specificity [7]. As a result, misdiagnosis is common, often delaying appropriate treatment. MRI findings characteristic of TGCT include synovial membrane hyperplasia, hemosiderin deposition (appearing as a low signal on T1- and T2-weighted images), and involvement of soft tissues and bones [6]. Other imaging techniques have limited value and are primarily used to rule out alternative diagnoses.

Aim

To highlight the challenges in differentiating TGCT from JIA. To emphasize the importance of early, personalized baseline therapy for JIA using synthetic and biological disease-modifying antirheumatic drugs, tailored to disease monitoring, JIA progression, and recurrent uveitis management.

Description of the clinical case

Patient Presentation: In December 2024, the patient presented with complaints of swelling and discomfort in the left knee joint, though with positive clinical dynamics. The patient has considered himself ill since approximately 1998 and has undergone multiple hospitalizations, though details of previous treatments remain unclear. In 2013, he was hospitalized at KMKL No. 3 in the rheumatology department and diagnosed with juvenile rheumatoid arthritis, articular-visceral form (right-sided uveitis), seronegative variant, and right-sided gonarthrosis, with functional status (FS) 1. Since 2013, he has not received any DMARDs, only nonsteroidal anti-inflammatory drugs (NSAIDs). In 2021, he experienced a relapse of uveitis.

On October 23, 2024, a traumatologist diagnosed bilateral villonodular synovitis of the knee joints, more pronounced on the left, in the

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context of JIA and uveitis (in remission). Surgery was recommended, and after a comprehensive preoperative assessment, the patient was hospitalized to "Smart Medical Centre" on November 23, 2024. On November 23, 2024, under general anaesthesia, the patient underwent arthroscopy of the left knee joint with resection of the altered synovial membrane. The excised tissue was sent for histopathological examination. The postoperative period was uneventful, and the patient was discharged in satisfactory condition for follow-up with his treating physician. His treatment included pain management, anti-inflammatory therapy, and antibiotic prophylaxis.

The patient's medical history is structured in chronological order in Figure 1.

Histopathological findings from December 4, 2024, did not confirm TGCT but instead indicated chronic moderate synovitis of the left knee joint.

MRI Findings

Left Knee:

- MRI signs of pigmented villonodular synovitis;
- left-sided stage 1 deforming gonarthrosis;
- early degenerative post-traumatic medial meniscopathy;
- ligamentopathy of the anterior cruciate ligament;
- moderate synovitis.

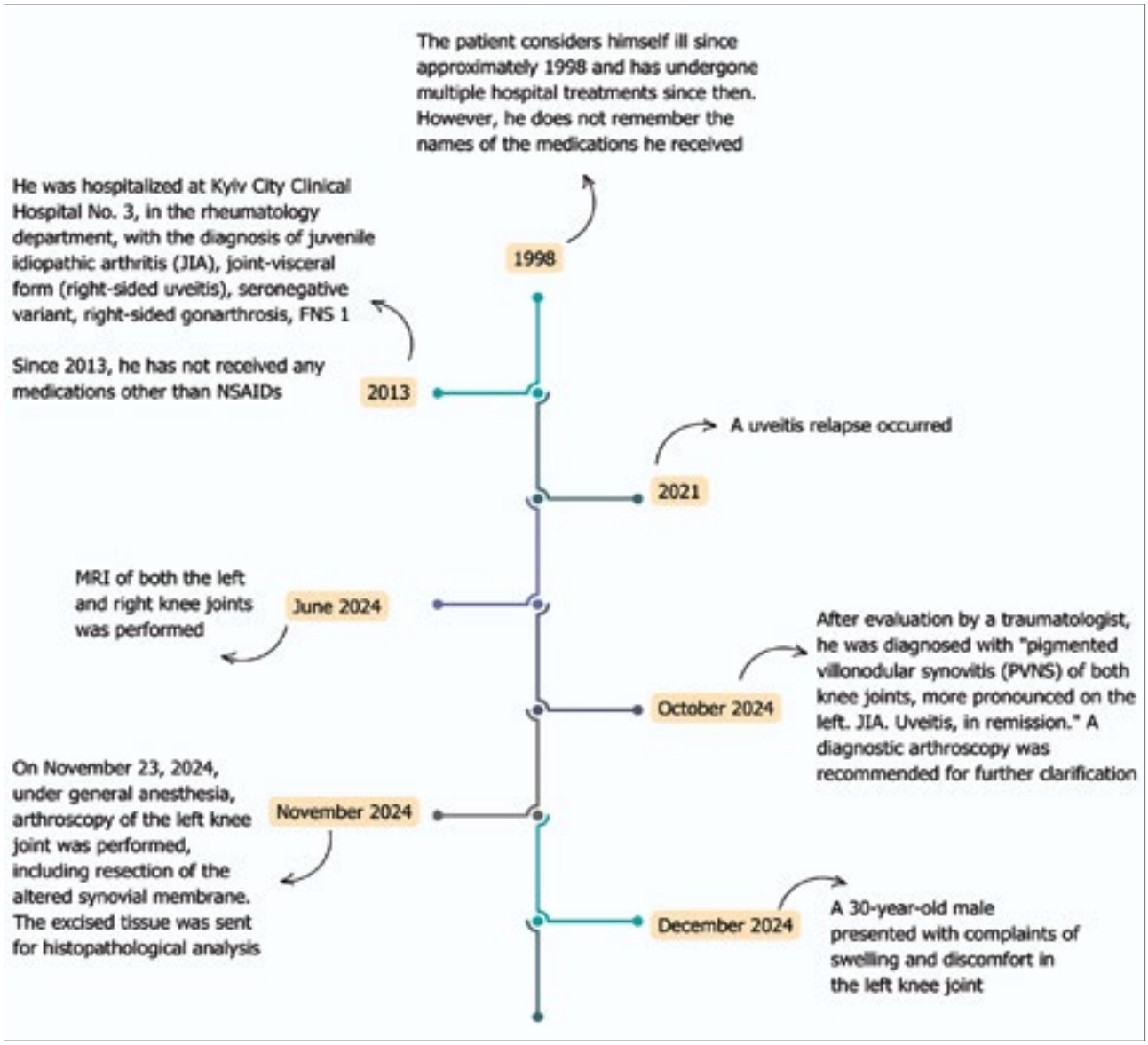

Figure 1. Chronology of the disease course in the patient.

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Right Knee:

- MRI signs of pigmented villonodular synovitis;
- right-sided stage 1 deforming gonarthrosis;
- degenerative post-traumatic medial meniscopathy (Stoller grade 2);
- ligamentopathy of the anterior cruciate ligament;
- synovitis.

Additional MRI findings (both knees):

- deformation of the anterior part of the medial femoral condyle and presence of a medial patellar plica;
- synovial proliferations appearing linear and spiral-like, filling the joint space;
- thinning of articular cartilage with early chondrodystrophy (Outerbridge grade 1);
- partial degeneration of the posterior horn of the medial meniscus, without surface rupture;
- hydration changes in the anterior horn, mild dehydration, and reduced height of the lateral meniscus;
- degenerative changes of the anterior cruciate ligament, with blurred contours;
- presence of up to 10 ml of pathological synovial fluid in the left knee and up to 15 ml in the right knee.

Histopathological Report (December 4, 2024): focal fibrosis and lipomatosis in the synovial tissue, moderate to severe plasma cell-dominant infiltration with lymphocytes, histiocytes, and macrophages. Formation of small papillary outgrowths with focal inflammatory infiltration. Chronic moderate synovitis of the left knee.

Clinical Examination (December 21, 2024): independent walking, with questionable limp. Normal skin colour over the joint. Surgical scars healed by primary intention, without swelling or hyperemia. Mild suprapatellar swelling, with a questionable patellar ballottement sign. No joint deformation. Range of motion: Flexion 120-130° (contralateral knee: 130°). Negative ligament integrity tests. Preserved muscle strength. Isometric loading tests painless. Localized discomfort on palpation over lateral postoperative scars. Peripheral sensation and pulses intact.

Laboratory Findings

- ANA-positive, RF-negative, anti-CCP-negative
- ESR: 4 mm/h
- CRP: 6 mg/L

Diagnosis: [M08.00] Juvenile rheumatoid arthritis, multiple localizations. Juvenile idiopathic arthritis, articular-visceral form (oligoarthritis, recurrent uveitis). Bilateral gonarthritis, activity

ILAR Classification of JIA (International League of Associations for Rheumatology)

Subtype	Typical Age of Onset	Gender Ratio	Laboratory Data	Typical Signs	Risk of Uveitis
Oligoarthritis	2–4 years ✓	F/M = 3:1	ANA + 70% (60%) ✓	1–4 joints, often monoarticular; frequent involvement of knees, ankles, and wrists; prolonged remission and favorable prognosis ✓	Sometimes (10-30%) ✓
RF-negative polyarthritis	Bimodal, 2–4 years and 10–14 years	F/M = 3:1 і 10:1	ANA + 40–50% (40%)	Different patterns of joint involvement and variable prognosis, >5 joints	Sometimes (10%)
RF-positive polyarthritis	Teenager	F/M = 9:1	AHA-	Early-onset RA in adults, symmetrical involvement of small joints, persistent inflammation, and progressing bone erosion, mild systemic symptoms	Rarely

Figure 2. ILAR Classification of JIA

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grade 2, FS 2. Status post left knee arthroscopy and synovial resection (November 23, 2024). Pain syndrome and postoperative synovitis of the left knee joint.

Histopathological findings suggest chronic moderate synovitis rather than TGCT, confirming the underlying JIA pathology.

Treatment plan:

- arcoxia 90 mg once daily after breakfast for 1 month;
- methotrexate 15 mg intramuscularly once a week (long-term treatment);
- folic acid 7.5 mg orally once a week, 24 hours after methotrexate injection;
- blood tests (CBC, urinalysis, ALT, AST, bilirubin, creatinine) in 1 month, then every 3 months;
- follow-up consultation in 1 month.

Results

This clinical case illustrates the progression of JIA, joint-visceral form, in a 30-year-old male with a history of right-sided uveitis and bilateral gonarthritis. The patient reports symptoms since approximately 1998, with multiple hospitalizations. Notably, since 2013, he has not received any disease-modifying therapy, apart from NSAIDs.

The patient presented with swelling and discomfort in the left knee joint. MRI findings suggested TGCT, along with deforming gonarthrosis (Grade 1), degenerative post-traumatic meniscopathy, anterior cruciate ligamentopathy, and synovitis. Based on these findings, diagnostic arthroscopy was recommended to clarify the diagnosis.

On November 23, 2024, under general anesthesia, the patient underwent arthroscopy of the left knee joint with resection of the altered synovial membrane. However, histopathological analysis ruled out TGCT, contradicting the initial MRI-based suspicion. Instead, findings confirmed chronic moderately severe synovitis in the context of JIA. This case highlights a prolonged disease course without DMARD therapy and a misdiagnosis of TGCT, emphasizing the importance of histopathological confirmation in cases of suspected TGCT in patients with underlying inflammatory arthropathies.

Discussion

The American College of Rheumatology (ACR) emphasizes the importance of early use of DMARDs such as methotrexate, leflunomide, and sulfasalazine in the treatment JIA. Methotrexate is the first-line treatment for oligoarthritis, polyarthritis, and persistent uveitis when NSAIDs and intra-articular steroids are insufficient. Recently, some studies analyzed how the timing of starting biological DMARDs (bDMARDs) influences the long-term outcomes of JIA in adulthood, showing that patients who start bDMARDs later are less likely to achieve remission without treatment [8]. This has significant implications for clinical practice, as it supports the concept of a "window of opportunity," which is also promoted for JIA, guiding the strategy of "treat-to-target" now widely used in JIA treatment.

Poor prognostic factors in JIA include polyarticular involvement, type of joint involvement, presence of rheumatoid factor and anti-citrullinated protein antibodies, delayed diagnosis, and late initiation of biological treatment. Studies have shown that early treatment with DMARDs and bDMARDs can help mitigate joint damage in patients with JIA and improve long-term outcomes. A meta-analysis of 12 published studies confirmed that patients receiving delayed DMARD therapy had a higher risk of radiological joint space narrowing and bone erosion [9]. The combination of DMARDs, corticosteroids, and biologic agents effectively reduces synovitis, progression of tissue damage, and systemic complications. Early use of biological agents contributes to better disease activity control, reduces steroid dependence, or shortens their duration of use [3]. DMARDs also significantly reduce the risk of uveitis in patients with JIA [10]. Early use of methotrexate within the first year of disease and combination therapy with a TNF inhibitor had the highest protective effect [11]. In latest studies, groups treated with adalimumab and other biologic agents had no cases of uveitis [12].

Regarding TGCT pathogenesis, genetic alterations, particularly mutations in the CSF1 gene, lead to the proliferation of stromal cells in the synovium. Tumor tissue contains

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histiocyte-like cells, multinucleated giant cells, inflammatory cells, and hemosiderin deposits [13]. Diagnostic criteria for TGCT according to the WHO classification of soft tissue and bone tumors (5th edition):

Mandatory: Intra- or extra-articular location; varying proportions of small histiocytic cells, large amphiphilic cells, foamy cells, multinucleated giant cells.

Desirable: CSF1 gene rearrangement (translocation).

Conclusions

The diagnosis of TGCT is challenging due to the lack of specific clinical and radiological signs, making synovial membrane biopsy essential for confirmation. While MRI is a valuable tool for detecting synovial pathology, it is insufficient for a definitive diagnosis without histopathological data. This case highlights the risk of misdiagnosing JIA-related synovial hypertrophy as TGCT, leading to a delay in appropriate treatment. JIA is a chronic rheumatologic disease that, if left untreated, can cause progressive synovial overgrowth and joint destruction. Early initiation of DMARD therapy is crucial to suppress immune hyperactivity, reduce inflammation, and prevent pannus formation, ultimately helping to maintain low disease activity and preserve joint function.

Financing

We did not have any financial support.

Conflict of interests

The authors declare that they have no conflict of interest.

Consent to publication

Written informed consent was obtained from the patient prior to submission of this article for consideration as a case-based review.

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of article.

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Гіпертрофія синовіальної оболонки на тлі ювенільного ідіопатичного артриту під маскою теносиновіальної гігантоклітинної пухлини: клінічний випадок

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Анотація: *ювенільний ідіопатичний артрит є найпоширенішим дитячим ревматологічним розладом, що характеризується хронічним запаленням у синовіальних суглобах. Його патофізіологія включає проліферацію синовіоцитів, патологічний ангіогенез та інфільтрацію імунних клітин, що призводить до руйнування суглоба та функціонального порушення. Теносиновіальна гігантоклітинна пухлина, рідкісна доброякісна пухлина, що вражає синовіальні тканини, часто імітує симптоми ювенільного ідіопатичного артриту, що ускладнює діагностику. Цей випадок представляє 30-річного чоловіка з тривалою історією ювенільного ідіопатичного артриту та рецидивуючого увеїту, у якого діагностовано двосторонній виллонодулярний синовіт у колінних суглобах. Незважаючи на результати магнітно-резонансної томографії, які свідчать про теносиновіальну гігантоклітинну пухлину, гістопатологічне дослідження після артроскопії колінного суглоба виявило хронічний помірний синовіт, що підтверджує патологію ювенільного ідіопатичного артриту. Пацієнт не отримував протиревматичні препарати, що модифікують хворобу, протягом кількох років, що сприяло прогресуванню захворювання. Американський коледж ревматології підкреслює важливість раннього використання протиревматичних препаратів, що модифікують*

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захворювання, зокрема метотрексату, для запобігання пошкодженню суглобів при ювенільному ідіопатичному артриті. Запізнілий початок прийому біологічних протиревматичних препаратів, що модифікують хворобу, призводить до погіршення віддалених результатів, що підкреслює необхідність раннього втручання для контролю запалення та запобігання необоротному пошкодженню суглобів. Цей випадок підкреслює діагностичну проблему розрізнення синовіальної гіпертрофії, пов'язаної з ювенільним ідіопатичним артритом, від теносиновіальної гігантоклітинної пухлини та підкреслює критичну роль гістопатологічного підтвердження.

Ключові слова: артрит, ювенільний ідіопатичний, теносиновіальна гігантоклітинна пухлина, протиревматичний препарат, що модифікує захворювання, DMARD

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