Case Report

Concurrence of Pigmented Villonodular Synovitis with Calcium Pyrophosphate Deposition in a Postacute Stroke Patient

CME Credits

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Abstract

Pigmented villonodular synovitis (PVNS) is a rare synovial proliferative disease featuring hemosiderin deposits. Calcium pyrophosphate deposition (CPPD) is a crystal-induced inflammatory arthritis common in the elderly. We reported the case of a 78-year-old male who was under stroke rehabilitation when acute inflammatory and hemorrhagic knee arthritis of his paretic lower limb occurred. CPPD was proven by synovial analysis. Ultrasonography showed widespread synovial nodular lesions in the affected knee and helped guiding difficult arthrocentesis. These led to a rapid diagnosis of PVNS with magnetic resonance imaging. In elderly stroke patients, knee pain, being a common complaint, warrants a careful diagnosis including adequate imaging. This case demonstrates that ultrasonography is an accessible and useful diagnostic tool.

Keywords: Calcium pyrophosphate deposition, knee, magnetic resonance imaging, pigmented villonodular synovitis, ultrasonography

Introduction

Pigmented villonodular synovitis (PVNS) is a benign rare disease involving the proliferation of joint synovium.[1] It typically presents as joint swelling, pain, and hemarthrosis. Calcium pyrophosphate deposition (CPPD) is a common inflammatory arthritis in the elderly due to calcium pyrophosphate (CPP) dihydrate crystal deposits.[2] Like PVNS, its most frequently involved joint is the knee.[3,4]

We present the case of a 78-year-old male, who was taking dual-antiplatelet treatment after stroke. He presented with acute severe knee pain at his paretic leg during inpatient rehabilitation. Through evidences from arthrocentesis, well-correlated musculoskeletal ultrasound (US), and magnetic resonance images, a rare diagnosis, coexistence of PVNS and CPPD, is made apart from other common causes of knee pain in this time frame.

Case Report

A 78-year-old male had acute pain, swelling, and heat at the knee of his paralyzed left lower limb after 1 month of inpatient rehabilitation for a new ischemic stroke at his right periventricular region. He also started dual-antiplatelet (aspirin and clopidogrel) treatment because of stroke recurrence. The patient had a history of hypertension, dyslipidemia, diabetes, gout, and chronic kidney disease but denied previous joint problems or recent trauma.

Acute severe pain, swelling, redness, and heat without ecchymosis of his left paretic knee led to the discontinuation of stroke rehabilitation. The passive and active ranges of the knee were limited. No particular point tenderness was identified. Neither valgus nor varus stress test was positive. Anterior and posterior drawer tests were not performed due to pain. No

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sign of new neurologic deficit was noticed. Laboratory tests showed mild leukocytosis (leukocyte = 11.90 × 10^3/μL) and high C-reactive protein (=12.91 mg/dL) level. A 0.2 ng/mL of procalcitonin level was within the 0.1–0.25 ng/mL cutoff level. The levels of antinuclear antibody, rheumatoid factor, and uric acid were within the normal range. Repeated US-guided knee arthrocentesis yielded massive bloody joint fluid. These two synovial fluid analyses had similar profiles. The second analysis showed that leukocyte was 17,600/mm^3 (neutrophil = 80% and lymphocyte = 4%). Synovial fluid cultures were negative. CPP crystal was found in one of the two samples.

Knee radiography [Figure 1] identified soft-tissue swelling, osteophytes, joint space narrowing, and chondrocalcinosis at medial joint space. Furthermore, bone erosions at lateral femur and lateral border of the medial femur condyle were worth noticing. US examinations [Figure 2] provided important diagnostic clues including interspersed fluid and proliferative synovium of multiple, villus-like, heterogeneous projections with hyperemia at the suprapatellar bursa and knee joint. A thin layer of hyperechoic signal within the intercondylar cartilage correlated with chondrocalcinosis on radiography. US allowed for evaluation of major knee structures, including unremarkable patella tendon, menisci, and collateral ligaments, aside from a synovial plica.

Magnetic resonance imaging (MRI) [Figure 2] confirmed PVNS as the most possible cause of proliferative synovium and hemarthrosis. Proton density fat-suppressed sequence outlined multifocal low-signal intensity nodules in the knee joint, suprapatellar bursa, and popliteal fossa with bone erosions. These structures showed further decreased signal intensity under T2-weighted fat-suppressed gradient echo sequence, compatible with a characteristic MRI "blooming artifact" of hemosiderin.

Antibiotics were temporarily used early in the course to cover possible septic arthritis. Colchicine and oral prednisolone were started for acute CPP arthritis later. Symptoms and laboratory findings improved dramatically thereafter. Repeated arthrocentesis also helped relieving knee swelling. The patient refused surgical excision or adjuvant intra-articular instillation of radioactive isotopes or adjuvant external beam radiotherapy for diffuse PVNS of the knee due to his high anesthetic risk and the possibility of recurrence. Watchful waiting with periodic follow-up was decided as a patient-centered treatment plan. His knee remained symptom free 9 months later while he remained wheelchair bound due to poor stroke recovery.

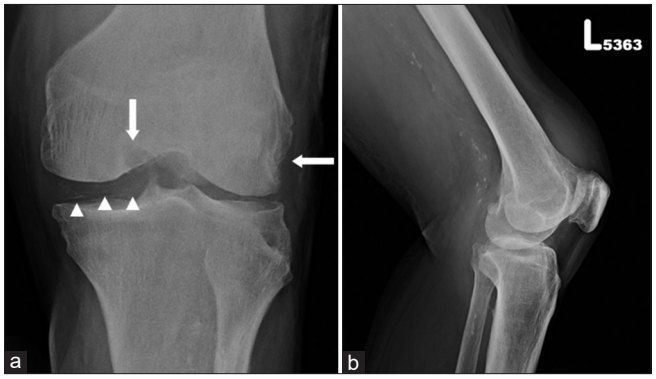

Figure 1: X-ray of the patient's affected left knee, (a) Coronal view. Joint space narrowing at the lateral aspect of the knee. Chondrocalcinosis at the medial joint space (arrowhead). Bone erosions were discovered at the lateral femur and the lateral border of medial femur condyle. (arrow), (b) Sagittal view. Increased suprapatellar bursal effusions and periarticular soft-tissue and subcutaneous swelling were seen. Calcification in popliteal artery identified

Discussion

We reported the coexistence of PVNS and CPPD causing acute knee arthritis with hemarthrosis in a postacute stroke patient. Poststroke knee pain is common and osteoarthritis is the most frequent diagnosis.[5] However, in this case, disproportionate inflammation and atraumatic hemarthrosis raised our suspicions for atypical causes. Blood and joint fluid analyses confirmed CPP existence and excluded septic arthritis, gouty arthritis,

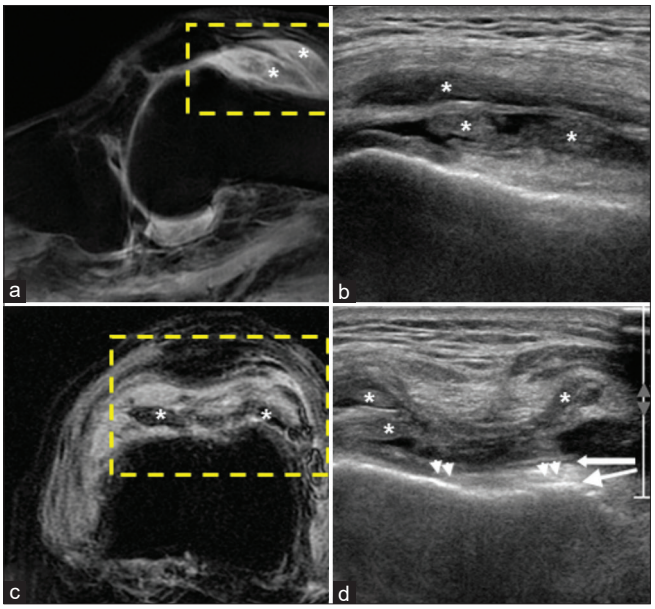

Figure 2: Ultrasound and magnetic resonance images of the patient's affected left knee at the similar level. (a) Magnetic resonance imaging proton density fat-suppressed sequence (sagittal) with high-signal intensity synovial proliferations with obscured internal contents (asterisk), (b) Ultrasound scan showing villus-like heterogeneous nodules. Septum-like structure separating the nodules (asterisk), possibly an embryologic remnant, a synovial plicae, (c) T2-weighted fat-suppressed gradient echo sequence (coronal) showing exaggerated low-signal intensity contents of the proliferated synovial nodules. The signal change from Figure 2a-c is characteristic of the hemosiderin components of pigmented villonodular synovitis in magnetic resonance imaging and is termed as "Blooming effect," (d) Ultrasound scan at suprapatellar region along the short axis (almost corresponding to the yellow dash box) in (c) also reveals proliferated synovial tissue (asterisk) with fluid collection. Chondrocalcinosis (arrowhead) of the calcium pyrophosphate deposition is noted at the femoral condyle and in the X-ray. The arrow indicates the "cartilage interface sign" or "the double-contour sign of gouty arthritis" as one of the patient's past history

rheumatoid arthritis, or seronegative arthritis. Radiography revealed characteristic CPPD and excluded late-stage rheumatoid arthritis and gouty arthritis. Musculoskeletal ultrasonography showed finding of hemarthrosis and synovial proliferation and led to the early confirmative diagnosis of PVNS by MRI which is the gold standard diagnostic tool. Differential diagnoses of acute atraumatic knee effusions are summarized in Table 1.

PVNS is a rare benign proliferative disease of the synovium with hemosiderin deposition. Knee joint is most frequently affected, followed by hip, ankle, shoulder, and elbow.[3,4] Diagnosis may be difficult and late as clinical manifestations are nonspecific, including joint pain, warmth, swelling, and limitation of mobility. PVNS is classified into localized type and diffuse type.[1] Hemarthrosis is a feature of PVNS, especially in its diffuse type. The multinodular thickening of synovium is infiltrated with synovial cells, macrophages, histiocytes, giant cells, and plasma cells with characteristic granular hemosiderin deposits in phagocytic cells microscopically.[6] Bone erosion is possible in the advanced stage.

The US and MRI findings of PVNS in this case correlate well. In PVNS, US can be used to (1) provide clues to support advanced imaging such as MRI, (2) exclude other conditions, (3) monitor disease activity through change of synovium and effusion, (4) detect early osteochondral change, and (5) guide knee arthrocentesis and focus on invasive treatment in complicated cases with indications. US could demonstrate joint effusion and proliferative synovium of PVNS, but MRI remains the

Table 1: Diagnostic features of acute atraumatic knee effusions

Conditions	History	Laboratory study	Synovial analysis	Image
Pigmented villonodular synovitis	Most frequently in the fourth decade Most often at the knee followed by hip, ankle, shoulder, and elbow	Nonspecific	Hemorrhagic in appearance Noninflammatory: <2000 leukocyte/mm^3	Synovial thickening with heterogeneous projections/mass MRI gradient echo sequence: "Blooming artifact" Bone erosions or cysts
Calcium pyrophosphate deposition	Most common among the elderly Often involves the knee, wrist, shoulder, and hip Previous attack with spontaneous resolution Fever if severe	Elevated CRP and ESR	Maybe cloudy in appearance Calcium pyrophosphate dihydrate crystal (positive birefringence) Inflammatory: >2,000 leukocyte/mm^3	Possible chondrocalcinosis Sometimes associated osteoarthritis
Gouty arthritis	More often at the first metatarsophalangeal joint, followed by the midfoot, ankle, and knee Previous attack with spontaneous resolution Fever if severe Presence of tophi Use of diuretics	Elevated uric acid Elevated CRP and ESR	Maybe cloudy in appearance Monosodium urate crystal (negative birefringence) Inflammatory: >2000 leukocyte/mm^3	Tophi Tophaceous erosion if severe, with characteristic "overhanging edge"
Septic arthritis	History of joint surgery Previous or concurrent urinary infection Skin infection or lesion (e.g., vesiculopustular lesion) Fever Sequential monoarthritis in several joints	Leukocytosis Elevated CRP and ESR Possible elevation of procalcitonin Blood culture may be positive	Maybe cloudy in appearance Inflammatory: >10,000 leukocyte/mm^3 Positive finding in Gram stain Synovial culture may be positive	
Osteoarthritis	More common in the elderly Crepitus during ROM		Transparent in appearance Noninflammatory: <2000 leukocyte/mm^3	Joint space narrowing Sclerosis Osteophytosis Subchondral cyst
Rheumatic arthritis	Sequential monoarthritis in several joints	Positive rheumatoid factor and/or anti-CCP elevated CRP and ESR	Inflammatory: >2000 WBC/mm^3	Synovitis Tenosynovitis Bone erosion Bursitis Tendon rupture and resulted in deformity as swan-neck or boutonniere deformities
Seronegative arthritis	"Sausage toe" appearance Eye lesion Skin lesion (as in psoriatic arthritis) History of gastrointestinal or urinary infection (as in reactive arthritis)	Negative rheumatoid factor Possible HLA-B27 positive Elevated CRP and ESR	Inflammatory: >2000 leukocyte/mm^3	Syndesmophyte Possible bamboo spine (as in ankylosing spondylitis) Possible sacroiliitis (as in ankylosing spondylitis)

MRI: Magnetic resonance imaging, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ROM: Range of motion, HLA: Human leukocyte antigen

Table 2: Ultrasonography and magnetic resonance imaging findings of pigmented villonodular synovitis and differential diagnosis of atraumatic hemarthrosis

PVNS	
Possible US findings	**Possible MRI findings**
Joint effusion	
Anechoic or hypoechoic depending on the stage of blood content	Joint effusion with possible "hematocrit effect"
Synovial proliferation	
Heterogeneous hypoechoic projections	Well-demarcated mass lesion with signal characteristics based on components of hemosiderin, lipids, and inflammatory fibrosis Lipid-laden macrophage or hemorrhage as high-signal areas on T1 Inflammatory fibrotic synovial linings as low-signal capsule on T1 Intense enhancement postgadolinium is common
Focal or diffuse distribution	Focal or diffuse distribution
Synovial hyperemia	
Increased signal under Doppler	
Hemosiderin deposition	Hemosiderin as low signal on T1 and "blooming effect" low signal in gradient echo sequences
Bone erosions	
Extra-articular bone can be identified	Both extra-articular and intra-articular bone erosion may be identified
Intra-articular bone erosion may not be seemed due to blockage of ultrasound	
Clinical relevance	
A tool for fast and early differential diagnosis	Current "gold standard" image diagnosis
Guidance of aspiration and monitoring tool	
Other differential diagnoses of atraumatic hemarthrosis	
Hemophilia	Drug related
Hemangioma	Other synovial tumors
Osteoarthritis	Septic arthritis

PVNS: Pigmented villonodular synovitis, US: Ultrasonography, MRI: Magnetic resonance imaging

gold standard of imaging diagnosis. In MRI, the proliferative synovium has low signal in T1 and T2 sequences. In gradient echo sequence, scattered hemosiderin granules in the synovium show further decrease in signal intensity due to the magnetic susceptibility of hemosiderin.[4] This is called the "blooming effect" and aids in the diagnosis of PVNS in MRI. Imaging features of PVNS and a summary of other causes of atraumatic hemarthrosis are listed [Table 2]. Another common diagnosis of hemarthrosis is hemophilia. Recent studies had advocated US scoring systems be used as a part of comprehensive periodic monitoring.[7] The essential US screening items are similar for hemophilia and PVNS. Both diseases would cause proliferating synovial tissue, but currently, we are not certain if there is any specific US sign to differentiate these two diseases.

CPPD features intra-articular CPP dihydrate deposits in cartilage, synovium, joint capsule, and ligaments.[2] It is the third most common inflammatory arthritis and a major cause of acute monoarticular arthritis in the elderly. Synovial fluid CPPD crystal showing weak-positive birefringence is diagnostic. Characteristic chondrocalcinosis may be demonstrated by US and radiography but is mostly nonspecific [Figure 2].[8]

Both PVNS and CPPD may attribute to the clinical manifestations of this case. Dual-antiplatelet treatment may be another possible contributor of hemarthrosis. To our understanding, this is the first case reported in the English literature of concurrent PVNS and CPPD and the first report discussing the image features of PVNS under US and MRI.

Ethical statement

This study was approved by IRB of Mackay Memorial Hospital (approved no. 19MMHIS150e obtained on Sep. 16th, 2019) and informed consent was waived by IRB.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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