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CASE SERIES

Gout and pseudogout arthropathies spectrum of high-resolution ultrasonography (HRUS) findings – case series

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ABSTRACT
Gout and Pseudogoutarthropathiesare a group of disorders where various types of microcrystals are deposited in articular and periarticular tissues resulting in inflammation and damage. High Resolution Ultrasonography **(**HRUS) is rapidly growing in popularity in the evaluation of crystal-induced arthropathies because of its inherent high sensitivity to detect microcrystalline aggregates. HRUS provides a quick non-invasive tool to map crystal deposition. It also assists in local interventions like guidance for aspiration and local injection. HRUS was performed GE VOLUSON S8 ultrasound machines using a 3-13 MHz high-resolution linear array transducer. Both grayscale and power doppler were used to evaluate the involved joints. Here we demonstrate sonographic appearances in four patients of Gout, two cases of calcium pyrophosphate deposition disease. Familiarizing oneself with the typical sonographic appearances of gout and pseudogoutarthropathies allows for confident diagnosis. HRUS can also be used for suitable diagnostic and therapeutic procedures.

Keywords: Gout and Pseudogout Arthropathy, High Resolution Ultrasonography, Monosodium Urate, Calcium Pyrophosphate Deposition.

INTRODUCTION

Gout and Pseudogout arthropathies are a group of disorders where various types of microcrystals are deposited in articular and periarticular tissues resulting in inflammation and damage.[1]

Pathogenesis: A) GOUT is an inflammatory arthritis caused by the deposition of monosodium urate (MSU) crystals in joints and other tissues. Here is an overview of the pathogenesis of gout.**Hyperuricemia** is an elevated level of uric acid in the blood which is the primary risk factor. Uric acid is a product of purine metabolism. When uric acid levels exceed the solubility threshold, it can crystallize and form MSU crystals.**Crystal Formation** is seen in joints, particularly in cooler parts of the body like the big toe. Factors such as dehydration, rapid weight loss, alcohol consumption, and certain medications can precipitatecrystal formation. **MSU Crystal Deposition** are seen in the synovial fluid and surrounding tissues of the joints. **Asymptomatic hyperuricemia** where crystals can persist for years without causing symptoms.When crystals are released into the joint space, phagocytosed by resident macrophages and synovial cells. This initiates an **inflammatory response**, leading to the activation of the NLRP3 inflammasome. The **NLRP3 inflammasome** is a multiprotein complex which activates caspase-1. It cleaves pro-interleukin-1β (pro-IL-1β) into its active form, IL-1β.**Cytokine Release**such as IL-1β, along with other cytokines such as IL-6, IL-8, and TNF-α, is released into the joint space with this includes the recruitment of neutrophils to the site of inflammation, causing a cascade of inflammatory responses. **Theacute gout attack**results with the influx of neutrophils and the release of additional inflammatory mediators cause

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the acute symptoms of a gout attack such as intense pain, redness, warmth, and swelling of the affected joint.An acute gout attack typically resolves within a few days to weeks as the inflammatory response is downregulated and the crystals are cleared results in **resolution of acute gout**. However, repeated attacks can lead to **chronic gouty arthritis**, characterized by persistent inflammation, joint damage, and the formation of tophi (large aggregates of MSU crystals).Chronic hyperuricemia can lead to the **formation of tophi**, which are deposits of MSU crystals surrounded by granulomatous inflammation. Tophi can cause deformities and functional impairment in affected joints and tissues.**In Gouttherenal involvement**can also affect the kidneys, leading to urate nephropathy, nephrolithiasis (kidney stones), and chronic kidney disease (CKD) due to the deposition of urate crystals in the renal interstitium and tubules. [2, 4,7,10]

B)CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD), commonly known as **pseudogout**, is characterized by the deposition of calcium pyrophosphate dihydrate (CPPD) crystals in the cartilage, synovium, and other periarticular tissues. Here is an overview of the pathogenesis of CPPD. **Crystal formation occurs by production pyrophosphate**(PPi)from chondrocytes in the cartilage. It is a byproduct of nucleotide triphosphate breakdown. Normally, pyrophosphate is kept in a soluble state by various regulatory mechanisms.**Crystal nucleation**when the balance between PPi production and degradation is disturbed, excess PPi combines with calcium ions to form CPPD crystals. Factors contributing to this imbalance can include aging, genetic predispositions, and metabolic abnormalities.**Predisposing Factors**a) Aging cartilage is more prone to developing crystal deposits due to decreased ability to degrade pyrophosphate.b) Genetic Factormutations, such as ANKH gene, which regulates PPi transport, can predispose individuals to CPPD.c) Metabolic disorderslike hyperparathyroidism, hemochromatosis, hypomagnesemia, and hypophosphatasia can increase the risk of CPPD by affecting calcium and phosphate metabolism. **Crystal Depositionin Cartilage and Fibrocartilage**are commonly deposited in articular cartilage (hyaline cartilage) and fibrocartilage (e.g., menisci, intervertebral discs). The deposition starts in the cartilage matrix and can extend into the synovial fluid.CPPD crystals can induce local tissue injury and inflammation. The mechanical stress on the cartilage and the metabolic activity of chondrocytes contribute to crystal formation. **Inflammatory responseoccurs** due to CPPD crystals are phagocytosed by synovial macrophages and other immune cells. The ingestion of CPPD crystals leads to activation of the NLRP3 inflammasome, similar to gout. This results in the production of **pro-inflammatory cytokines**, particularly interleukin-1β (IL-1β).The release of IL-1β and other inflammatory mediators, such as TNF-α and IL-8, attracts neutrophils and other inflammatory cells to the joint, causing acute inflammation.[3,5,6,9,10]
Most cases of crystal deposits are asymptomatic and represent incidental findings at imaging. In case of symptomatic arthropathies, imaging plays an important role in diagnosis, assessment of disease progression as well as extent of crystal deposits. Conventional radiography is the most common imaging modality and still remains essential to the workup.But High resolution ultrasound (HRUS), conventional computerized tomography (CT), dual-energy CT (DECT), and Magnetic resonance imaging (MRI) all play an increasing role. [2,3] HRUS is rapidly growing in popularity in the evaluation of Gout and Pseudogoutarthropathies because of its inherent high sensitivity to detect microcrystalline aggregates.[2] HRUS provides a quick non-invasive tool to map crystal deposition. It also assists in local interventions like guidance for aspiration and local injection.

AIMS AND OBJECTIVES

To familiarize Radiologists and other clinicians to the characteristic sonographic appearances of Gout and Pseudogout arthropathies. To evaluate the utility of HRUS in diagnosing and treating Gout and Pseudogout arthropathies.

MATERIALS AND METHODS

This study related cases were obtained from BLDE (DU), Shri B M Patil Medical College Hospital and Research Centre, Vijayapur, Karnataka, India HRUS was performed GE VOLUSON S8 ultrasound machines using a 3-13 MHz high-resolution linear array transducer. Both grayscale and power Doppler were used to evaluate the involved joints. Here we demonstrate sonographic appearances in four patients of Gout affecting the knee, elbow and 1st MTP joints; two cases of calcium pyrophosphate deposition disease involving metacarpophalangeal joint of hand and knee.

CASES ILLUSTRATIONS

Case 1: Tophaceous gouty arthropathy of 1stmetatarsophalangeal(MTP): A 40 years old male, presented with acute pain and swelling in the right 1st MTP since 3 days. Uric acid level 11 mg/dl. A) Long axis greyscale HRUS image of medial aspect of 1st MTP, showing a sharply defined erosion (thin arrows) echogenic focus within the 1st MTP joint (block arrow). B) Long axis greyscale HRUS image on medial aspect of 1st MTP, showing distended joint capsule (dashed line) and intra-articular echogenic material with multiple dotted bright foci related to urate crystals (giving a snowstorm appearance). C) Power Doppler US image shows mild internal vascularity.

Case 2: Gouty olecranon bursitis: A 32 years old male, presented with gradually increasing painful swelling over the right elbow since 2 weeks. Uric acid

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level 35 mg/dl. A) Clinical photograph showing swelling over the elbow. B) HRUS image showing large echogenic tophus in the subcutaneous plane within the olecranon bursa (asterisk). C) Long-axis grayscale US showing 21G needle within the tophus. D) High power wet mount microscopic image showing needle shaped crystals indicative of Monosodium Urate crystals.

Case 3: Gouty arthropathy of knee:A 40 years old male, with acute pain and swelling in the right 1st MTP x 3 days. Tophaceous Gouty deposit in Patellar (A), Semimembranosus tendons (B) and Double contour sign (C) involving trochlear cartilage.

Case 4: Gouty arthropathy of knee: A 50 years old male, with pain and swelling in the right knee. Diffuse tophaceous gout in Patellar tendon causing rupture. B) Diffuse infiltration of Gouty tophus within the patellar tendon (white asterisk) and double contour sign over the trochlear cartilage (white arrows).

Case 5: CPPD kneejoint:A 45 years old male, presented with pain and swelling both knees since 6 months. A) Frontal X ray showing calcifications in meniscal (thin arrows) and trochlear fibrocartilage (thick arrow). B) Grayscale USG image showingechogenic calcification within the trochlear fibrocartilage (arrow). C) Echogenic calcification within the extruded medial meniscal fibrocartilage (arrow). Polarized light microscopy (not shown) axis parallel direction to birefringence of CPPD crystals. Features are consistent with CPPD disease.

Case 6: CPPD MCPwrist: A 53 years old female, presented with pain and swelling right wrist and both knees since 3 months. A) Frontal X ray of MCP joints showing calcifications in the fibrocartilage at 2nd, 3rd, 4th and 5th MCP joints (arrows). B) & C) USG images showing echogenic calcifications in the fibrocartilage (arrows) of 2nd and 3rd MCP joints. D) Frontal X ray of wrist showing calcifications in the triangular fibrocartilage (TFC) (arrow). E) USG images along ulnar aspect of wrist showing echogenic calcifications in the TFC (arrow) D) Polarized light microscopy axis parallel direction to birefringence of CPPD crystals. Consistent with CPPD disease.

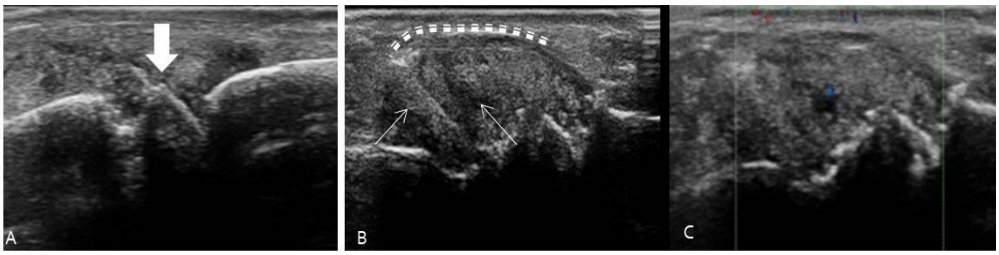

FIGURE 1: Tophaceous Gouty Arthropathy of 1st MTP A) Long axis greyscale HRUS image of medial aspect of 1st MTP, showing a sharply defined erosion (thin arrows) echogenic foci within the 1st MTP joint (block arrow) B) Long axis greyscale HRUS image on medial aspect of 1st MTP, showing distended joint capsule (dashed line) and intra-articular echogenic material with multiple dotted bright foci related to urate crystals (giving a snowstorm appearance). C) Power Doppler US image shows mild internal vascularity.

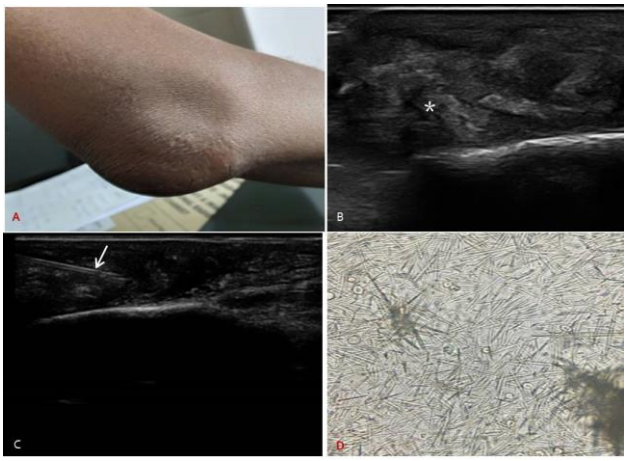

FIGURE 2: Gouty Olecranon Bursitis A) Clinical photograph showing swelling over the elbow. B) HRUS image showing large echogenic tophus in the subcutaneous plane within the olecranon bursa (asterisk) C) Long-axis grayscale US showing 21G needle within the tophus. D) High power wet mount microscopic image showing needle shaped crystals indicative of Monosodium Urate crystals.

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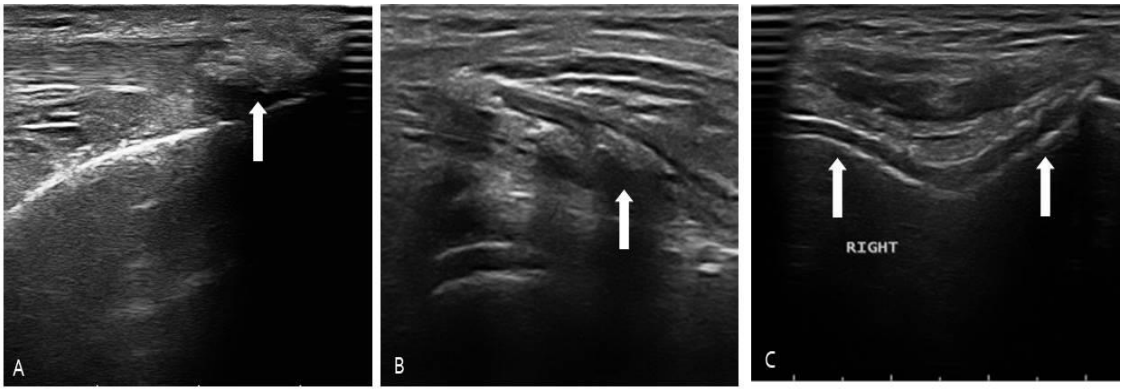

FIGURE 3: Tophaceous Gouty deposit in Patellar (A), Semimembranosus tendons (B)and Double contour sign (C)involving Trochlear cartilage.

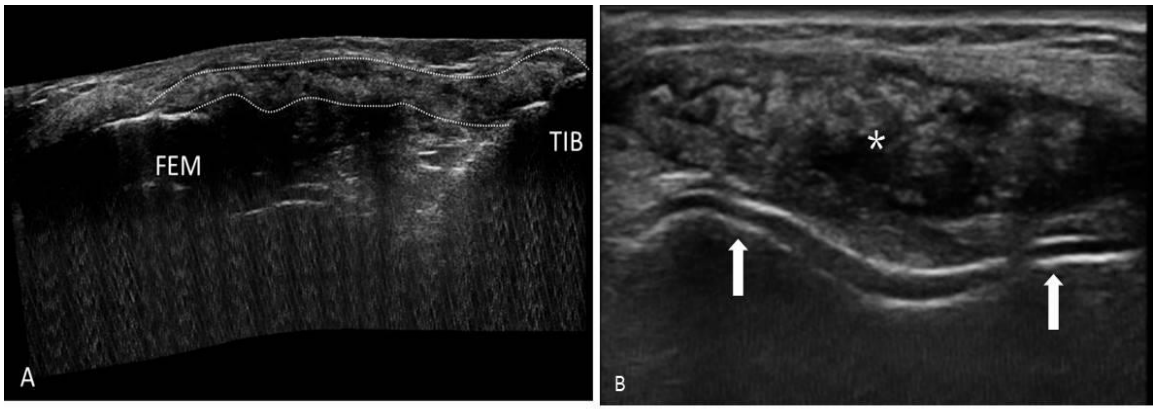

FIGURE 4:Gouty Arthropathy of knee A) Diffuse tophaceous gout in Patellar tendon causing rupture. B) Diffuse infiltration of Gouty tophus within the patellar tendon (white asterisk) and double contour sign over the trochlear cartilage (white arrows).

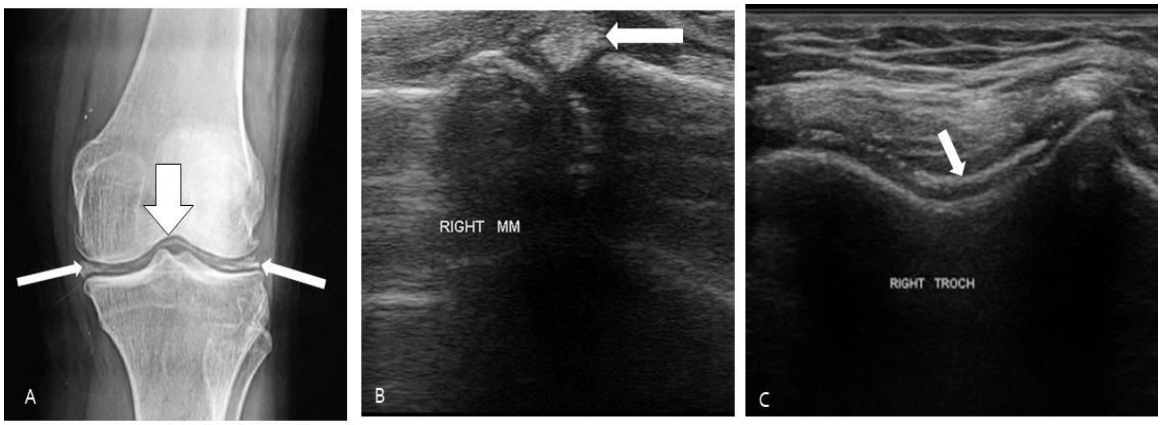

FIGURE 5:CPPD kneejoint A) Frontal X ray showing calcifications in meniscal (thin arrows) and trochlear fibrocartilage (thick arrow). B) Grayscale USG image showingechogenic calcification within the trochlear fibrocartilage (arrow). C) Echogenic calcification within the extruded medial meniscal fibrocartilage (arrow). Polarized light microscopy (not shown) axis parallel direction to birefringence of CPPD crystals. Features are consistent with CPPD disease.

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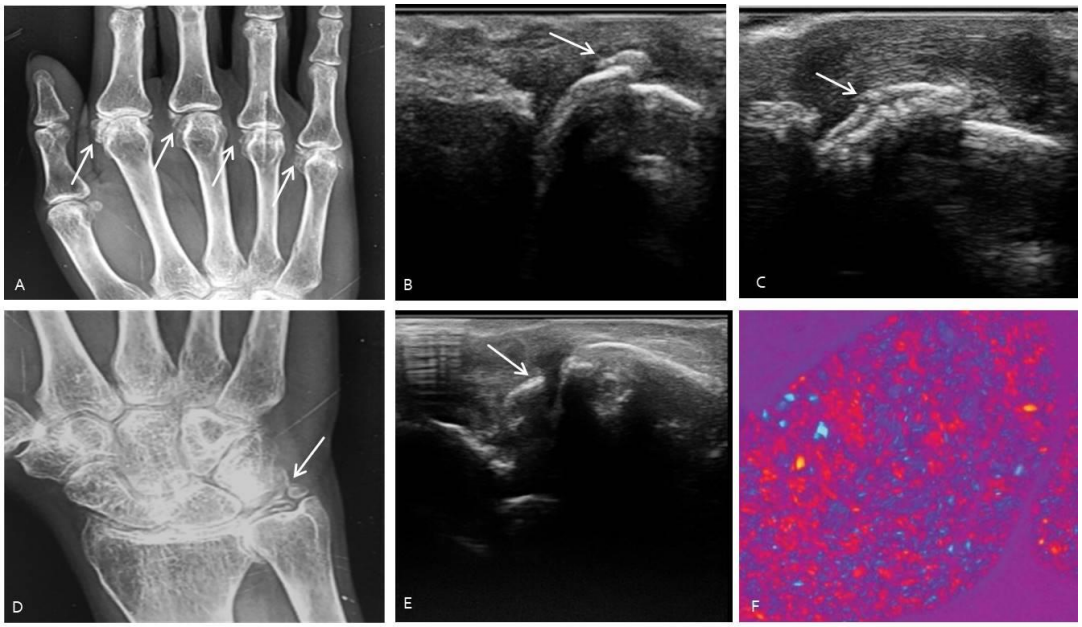

FIGURE 6:CPPD MCPwristA) Frontal X ray of MCP joints showing calcifications in the fibrocartilage at 2nd, 3rd, 4th and 5th MCP joints (arrows). B) & C) USG images showing echogenic calcifications in the fibrocartilage (arrows) of 2nd and 3rd MCP joints. D) Frontal X ray of wrist showing calcifications in the triangular fibrocartilage (TFC) (arrow). E) USG images along ulnar aspect of wrist showing echogenic calcifications in the TFC (arrow) D) Polarized light microscopy axis parallel direction to birefringence of CPPD crystals.

DISCUSSION

Gout and Pseudogoutarthropathies are a group of disorders where various types of microcrystals are deposited in articular and periarticular tissues resulting in inflammation and damage. Ultrasound is an imaging technique that is safe, noninvasive, inexpensive, real time and well accepted by patients, allowing the detection of a wide spectrum of morphostructural abnormalities in joint, periarticular and soft tissues resulting from both nonspecific and specific signs created by Gout and Pseudogoutarthropathies.[1,3,5] The finding of crystal deposits is an incidental finding in asymptomatic patients. They can cause acute or chronic arthropathy. There are many causes or types of crystal arthropathies, our aim of this case series is to describe the monosodium urate and CPPD induced Gout and Pseudogoutarthropathies.

Gouty arthropathy results secondary to abnormal purine metabolism, uric acid which is the end product of purine metabolism, combined with overproduction of uric acid or under excretion, resulting in sustained hyperuricemia. Hyperuricemia above the local solubility, can lead to monosodium urate (MSU) crystal deposition in joints, on the surface of the hyaline cartilage and within periarticular soft tissues. Gout predominantly affects the peripheral joints, but the axial skeleton may also be affected. [3,4,7]**Radiographic finding**, acute phase soft tissue swelling / nodules (tophaceous gout), joint effusion, well-defined punched-out erosion with overhanging edges, with preservation of joint space and expansive intraosseous erosions. Chronic phase (also called tophaceous gout) includes asymmetric articular, juxta-articular, or periarticular soft tissue nodules, corresponding to tophi. Ultrasound is a valuable imaging modality for diagnosing and assessing gouty arthropathy. It helps in visualizing the deposition of monosodium urate (MSU) crystals and the associated inflammatory changes in the joints. Key ultrasound findings in gouty arthropathy include **1) Double Contour Sign**The double contour sign is a pathognomonic feature of gout. It appears as a hyperechoic (bright) line parallel to the subchondral bone, representing MSU crystal deposits on the surface of the articular cartilage.This sign helps differentiate gout from other types of arthritis where no such deposition occurs. 2) **Tophi** are collections of MSU crystals that appear as heterogeneous, hyperechoic nodules or masses. They can be seen within the joint, in the periarticular soft tissues, or along tendons. Identification of tophi helps confirm chronic gout and assess the burden of crystal deposition. 3) **Synovitis and Effusion** ultrasound may show signs of active inflammation, including synovial thickening (synovitis) and joint effusion (excess fluid within the joint).These findings indicate an active gout flare and help differentiate it from other causes of joint swelling and pain. 4) **Erosions** Gout can cause bony erosions, which appear as cortical breaks with an irregular contour on ultrasound.Erosions indicate chronic and advanced disease, often associated with recurrent gout attacks and significant tophi formation. 5) **Crystal "Snowstorm" Appearance**Intra-articular MSU crystals can appear as hyperechoic foci with a "snowstorm" pattern,

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especially when observed in a joint effusion. This appearance supports the diagnosis of gout, particularly during an acute flare. 6) **Tendon Involvement**MSU crystals can deposit along tendons, causing tenosynovitis, which appears as hyperechoic linear deposits along the tendon sheath. Tendon involvement helps in assessing the extent of crystal deposition and associated inflammation.Treatment of gout is nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, anti-gout agents and xanthine oxidase inhibitors. [2,4,7,8,9,10]

Calcium pyrophosphate deposition disease (CPPD) disease is the second leading cause of crystal arthropathy and appears to affect 4-7% of the adult population in Europe and the United States.[2,6] CPPD aggregates range from tiny circumscribed hyperechoic spots to extended deposits with or without acoustic shadow and can be detected in various tissues including fibrocartilage, hyaline cartilage, tendons and entheses.[2,6] Diagnosis in the acute phase, analysis of synovial fluid still constitutes the gold standard. The role of diagnostic imaging is very important for both diagnosis and percutaneous treatment. Although in the acute phase there are no classical imaging signs, but specific imaging signs may require in the detection and differential diagnosis of chronic crystal arthropathies. Radiologically CPPD usually have a mono or polyarticular distribution like knees, pubic symphysis, and wrist, the deposits are often articular usually involves hyaline cartilage, fibrocartilage, synovium, capsules, and ligament and have point or linear morphology.[2,6] The US is widespread in the area, because of low costs, real time, allows to evaluate in detail the characteristics as well as the deposits, also the structural conditions of the ligaments, tendons, bursa as well as some intraarticular components. Furthermore, it also allows to evaluate and quantify the intra-articular fluid. The power doppler study help to identify the degree of hyperemia of the tissues involved. It allows to investigate the cortical profile. CT helps to allow to identify the location, density and morphology of the crystal deposits by means of volumetric reconstructions. Magnetic resonance imaging can show serious inflammatory changes and the correlation with radiographs or CT should help distinguish crystalline arthropathies. Treatment is that to provide symptomatic relief include systemic or intra-articular therapy with non-steroid anti-inflammatory drugs (NSAIDs) or corticosteroids, ice, temporary rest, and joint aspiration. Although the progression of this condition may vary between individuals, many of the patients will experience recurrent symptomatic episodes. Despite the incurable nature of this condition, the prognosis is good, as long as symptoms are controlled and patients are monitored that can be treatable and preventable.[6,8,10]

CONCLUSION

Familiarizing oneself with the typical sonographic appearances of various joints involvement features of Gout and Pseudogout arthropathies allows for confident diagnosis.

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We all express our gratitude to the referring clinicians and patients who were involved in this analytic study. Also Department of Pathology for providing the histopathology images and legends.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent.

CONFLICTS OF INTEREST

There are no conflicts of interest.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

ABBREVATIONS:

HRUS- High Resolution Ultrasonography
US / USG- Ultrasonography
MSU- Monosodium Urate
CPPD- Calcium Pyrophosphate Deposition
MTP-Metatarsophalangeal
MCP- Metacarpophalangeal
TFC- Triangular Fibrocartilage

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