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Pyrophosphate arthropathy — a literature review

ABSTRACT

Joint diseases associated with calcium pyrophosphate crystals (calcium pyrophosphate dihydrate deposition disease, CPPD) are classified as crystallopathies. They clinically present as chondrocalcinosis, acute or chronic arthritis. The main risk factors are age, injuries and degenerative changes in the joints. One or more joints may be affected. Knees, wrists and shoulders are the most commonly affected joints. CPPD may be primary or secondary, and may be associated with hemochromatosis, hyperparathyroidism, hypothyroidism, and hypomagnesemia. Treatment is mainly symptomatic, most commonly using non-steroidal anti-inflammatory drugs, colchicine, or glucocorticoids.

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KEY WORDS: crystals; calcium pyrophosphate; arthritis

INTRODUCTION

Calcium pyrophosphate dihydrate deposition disease (CPPD), along with gout, is one of the most common crystallopathies and involves the deposition of calcium pyrophosphate (CPP) crystals in cartilage and periarticular structures. It may be asymptomatic, or present as acute or chronic arthritis.

EPIDEMIOLOGY AND CLASSIFICATION OF CPPD

Joint diseases associated with calcium pyrophosphate crystals affect the elderly population and their risk of occurrence increases with age. The majority of patients with acute arthritis are over 65 years old, with 30–50% of patients over 85 years old [1]. In the British population, the incidence of CPPD in people aged 55–59 years is 3.7%, and in those aged 80–84 years, it is 17.5% [2]. No difference in incidence was found between men and women. There is an association between CPPD and osteoarthritis (OA), as advanced osteophytosis correlates with intra-articular deposition of CPP [3, 4]. CPPD comes in primary and secondary forms (generalized and localized). Primary CPPD may be familial and has an autosomal dominant inheritance pattern. Secondary, generalized form of CPPD may be associated with hemochromatosis, gout, hyperparathyroidism, alkaline phosphatase deficiency, hyper- or hypothyroidism, and hypomagnesemia [5]. Localized CPPD can develop in patients with joint instability or after meniscus removal surgery.

PATHOGENESIS OF CPPD

The pathogenesis of CPPD has been shown to be influenced by transglutaminases involved in extracellular matrix mineralization and affecting chondrocyte hypertrophy. A pathogenetic link with IL-8 is suggested, which causes chondrocyte hypertrophy through the CXCR1 receptor (CXC chemokine type 1 receptor). In familial CPPD, the association of two gene loci, CCAL1 (long arm of chromosome 8) and CCAL2, with the

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ANKH gene (short arm of chromosome 5) has been confirmed. The former is associated with a severe form of OA, while the latter encodes a protein that affects the transport of phosphorus across cell membranes and influences the activity of enzymes related to mineral metabolism. A change in the phenotype of chondrocytes near crystallization foci has also been demonstrated [6, 7]. The cause of CPPD in patients with hemochromatosis or alkaline phosphatase deficiency is unknown. Hypomagnesemia promotes CPP crystallization.

CLINICAL PRESENTATION OF CPPD

The clinical presentation of CPPD depends on its phenotype (Tab. 1). Joint diseases associated with calcium pyrophosphate crystals can take the form of:

— chondrocalcinosis;
— acute arthritis (pseudogout);
— chronic arthritis (pseudo-rheumatoid arthritis);
— pyrophosphate arthropathy associated with OA [7].

Pyrophosphate arthropathy most commonly affects weight-bearing joints: hips, knees, and shoulders. Crystal deposits accumulate mainly in fibrous and hyaline cartilage [8, 9].

Chondrocalcinosis is defined as the presence of calcium salt deposits (not just CPP) in articular cartilage, which have been detected by imaging or histological examinations. Chondrocalcinosis is the most common form of CPPD, and is usually asymptomatic [10].

Patients with acute arthritis have symptoms similar to an acute gout flare such as pain, swelling, and redness of the joint area. Unlike gout, symptoms build up more slowly. A pseudogout flare affects a single joint, most often the knee, followed by wrists, shoulders, ankles, and elbows. Sometimes the inflammation can involve ligaments, tendons, bursae, and spinal joints [11]. Half of the patients have general symptoms: subfebrile state, fatigue. Factors that induce the onset of acute pseudogout include: joint trauma, myocardial infarction, infections, treatment with thyroxine, bisphosphonates, intra-articular administration of hyaluronic acid.

Chronic arthritis associated with CPPD affects 11% of patients and is characterized by periods of exacerbation and remission. Periods of exacerbation occur asynchronously and most often affect the wrist and metacarpophalangeal (MCP) joints. The main symptoms are morning stiffness, joint pain and swelling, elevated ESR and CRP values.

Chronic arthropathy in the course of CPPD presents similarly to OA and often accompanies it. What distinguishes this form of CPPD from primary OA is the involvement of the wrist, shoulder, ankle, and elbow joints. Unlike OA without CPPD, the lesions are mainly symmetrical, and there is usually a narrowing of the lateral aspect of the knee joint gap and the development of valgus. It is not known whether chondrocalcinosis is the cause of OA or a consequence of the changes that occur in the articular cartilage during its course. The co-occurrence of both diseases significantly accelerates the progression of OA. CCP has been found in 25–43% of patients with advanced OA undergoing knee arthroplasty [12–14]. Pyrophosphate arthropathy can affect all structures of the spine, including facet joints, intervertebral disc cartilage, interspinous, supraspinous, yellow and posterior longitudinal ligaments. Accumulation of CPP in the fibrocartilage of the axial skeleton is a common phenomenon in patients undergoing spinal surgery, but symptomatic spinal involvement in CPPD is quite rare. Changes in spinal structures can cause acute pain syndromes, and more massive crystals can cause nerve compression, myelopathy, and symptoms of cauda equina syndrome. The cervical and lumbar spine are most commonly affected. Axial CPPD requires differentiation from septic arthritis of the spine and ankylosing spondylitis [15–17].

DIAGNOSIS OF CPPD

Joint fluid analysis and imaging are used in the diagnosis of CPPD. A reliable diagnosis of CPPD can be made by analyzing synovial fluid collected during arthrocentesis. During acute inflammation, the fluid is cloudy, slightly bloody, and inflammatory. Fluid analysis using polarized light microscopy reveals the presence of CPP crystals, which are characteristically rhomboid or rod-shaped and are mainly located in the cytoplasm of granulocytes/macrophages. CPP crystals are characterized by weakly positive birefringence [8, 18–23]. X-ray is the most commonly used diagnostic imaging method. Calcification of the hyaline cartilage of a joint, which appears in the form of narrow linear shadows, is the most characteristic trait. CPP deposits are also seen in tendons, ligaments, fascias, joint capsules, as well as in the

Table 1. Clinical presentations of CPPD [7]

Clinical presentation	Clinical symptoms
Chondrocalcinosis	Usually asymptomatic, typical radiological features
Acute arthritis	CPP deposits in articular cartilage and synovium; usually inflammation of one joint, mainly the knee
Chronic arthritis	Joint deformities caused by chronic CPP deposition
Pseudo-OA	Co-occurrence of CPPD and OA symptoms
Pseudo-RA	Symmetric polyarthritis, mainly PIP and MCP, morning stiffness, elevated inflammatory markers
Pseudo-neuropathic arthropathy	Radiological features of Charcot joints, without nervous system dysfunction

CPP — calcium pyrophosphate crystals; OA — osteoarthritis; CPPD — calcium pyrophosphate dihydrate deposition disease; MCP — metacarpophalangeal joints; PIP — proximal interphalangeal joints; RA — rheumatoid arthritis

meniscus (knee joints) or intervertebral discs (spine). A common radiologic sign of CPPD is isolated stenosis of the patellofemoral joint or degenerative changes in the metacarpophalangeal joints of the hands. X-rays also show cystic degeneration, bone and cartilage fragmentation. In patients with suspected CPPD, X-rays of knees, pubic symphysis, hips, and wrists are most often performed. The presence of characteristic X-ray changes may confirm CPPD, but their absence does not rule out the disease. Ultrasound is helpful in the early stages of the disease, as it shows synovitis and CPP deposits in cartilage in the form of hyperechoic bands or foci (monosodium urate crystals are present on the cartilage surface). Ultrasound has a higher sensitivity and specificity than X-ray. Magnetic resonance imaging also detects the presence of CPP with high accuracy. Despite the fact that computed tomography accurately shows calcification, it is not routinely used to diagnose pyrophosphate arthropathy [12, 15, 24–28]. Conventional radiography and computed tomography remain the gold standard in imaging diagnostics. MRI scans are of limited value [29].

Due to the association of CPPD with metabolic diseases, the levels of calcium, phosphorus, magnesium, iron, alkaline phosphatase, ferritin, thyroid hormones, and ceruloplasmin should be determined in each patient with a recent diagnosis of CPPD [7, 30–32].

TREATMENT OF CPPD

Treatment of CPPD includes non-pharmacological and pharmacological therapies.

Non-pharmacological treatment includes reducing stress on the affected joint, applying cold compresses during acute inflammation, and controlling modifiable risk factors. There is no cure for the cause of pyrophosphate arthropathy. Unlike gout, no effective treatment has been found to eliminate calcium pyrophosphate crystal deposits. The goal of CPPD treatment is to reduce inflammation and compensate for metabolic abnormalities that could predispose to CPP deposition.

Asymptomatic CPPD does not require treatment [33, 34].

In the case of acute inflammation of one or two joints, glucocorticoids (GCs) are administered intra-articularly. When at least three joints are involved, systemic treatment is used: non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, and in the absence of improvement, oral or parenteral GCs at a gradually reduced dose [11, 35–36]. The use of NSAIDs and colchicine has been carried over from acute gout treatment. In many patients, these drugs should be used with great caution, keeping in mind that the vast majority are elderly with multiple comorbidities. Short courses of low-dose oral steroids are preferred in patients with polyarticular CPPD. Low-dose NSAIDs or colchicine (0.5–1 mg/day) can be administered as a preventive measure in frequent exacerbations of acute arthritis.

NSAIDs and/or colchicine (0.5–1 mg/day), or low-dose GCs, can be used in chronic arthritis [14].

If the above-mentioned drugs are ineffective, contraindicated or poorly tolerated, an alternative form of therapy is the use of methotrexate or hydroxychloroquine. However, studies have shown low efficacy of these drugs. There are isolated reports on the use of biologic drugs: anakinra and tocilizumab. The use of these drugs may be considered in patients for whom NSAIDs/colchicine/GCs are ineffective [37–40]. Intra-articular administration of hyaluronic acid should be avoided as it may induce acute arthritis. To date, the effect of diet on the occurrence of CPPD has

Table 2. Treatment of CPPD [7]

Conventional treatments	
NSAIDs	Low-dose naproxen/indomethacin. Effective in CPPD exacerbations, reduces the risk of exacerbations
GCs	Effective only in CPPD exacerbations. Oral/intramuscular GCs are preferred in polyarthritis; intra-articular GCs in mono- or oligoarthritis
Colchicine	Effective in CPPD exacerbations in combination with NSAIDs. Beneficial in the prevention of exacerbations
Alternative treatments	
Methotrexate	May be used in CPPD exacerbations if conventional treatment is ineffective/contraindicated. Prevents CPPD exacerbations
Hydroxychloroquine	Effective in chronic arthropathies in the course of CPPD
IL-1 receptor antagonists	May be used in CPPD exacerbations if conventional treatment is ineffective/contraindicated. Prevents CPPD exacerbations
Radiosynovectomy	Best treatment outcomes for hemophilia patients
Future treatments	
CPP-inhibiting drugs (e.g. probenecid)	Prevention of CPP formation

CPPD — calcium pyrophosphate dihydrate deposition disease; CPP — calcium pyrophosphate crystals; GCs — glucocorticoids; IL-1 — interleukin 1; NSAIDs — non-steroidal anti-inflammatory drugs

not been established. In the case of secondary CPPD, treatment of the underlying condition is necessary [2]. Table 2 presents the drugs used in the treatment of CPPD [7].

DIFFERENTIAL DIAGNOSIS OF CPPD

The diverse clinical presentation of CPPD requires extensive differential diagnosis.

Joint diseases associated with calcium pyrophosphate crystals require differentiation from gout (20% of CPPD patients have hyperuricemia), rheumatoid arthritis (10% of CPPD patients have a positive rheumatoid factor test), inflammatory spondyloarthropathy, OA, or septic arthritis [2, 11, 14]. Synovial fluid testing for the presence of CPP and X-ray/USG of the joints are very helpful in the differential diagnosis [41].

PROGNOSIS AND COMPLICATIONS OF CPPD

Pyrophosphate arthropathy is a chronic, self-limiting disease and the symptoms of acute inflammation usually disappear after a few days or weeks after the start of treatment. Long-term prognosis depends on the number of affected joints and the frequency and exacerbations, among other factors. Calcium pyrophosphate crystals can lead to the destruction of joint surfaces. Multiple exacerbations of CPPD promote the formation of palpable nodules that resemble gout nodules [42].

ARTICLE INFORMATIONS AND DECLARATIONS

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CONFLICT OF INTEREST

None.

References

1. Calcium pyrophosphate Deposition Disease. Encyclopedia of Diagnostic Imaging. 219, doi: 10.1007/978-3-540-35280-8_364.
2. Fliciński J, Prajs K. Choroba związana z odkładaniem kryształów dwuwodnego pirofosforanu wapniowego. Przegląd Reumatologiczny. 2011; 5-6(39): 3–5.
3. Stücker S, Bollmann M, Garbers C, et al. The role of calcium crystals and their effect on osteoarthritis pathogenesis. Best Pract Res Clin Rheumatol. 2021; 35(4): 101722, doi: 10.1016/j.berh.2021.101722, indexed in Pubmed: 34732285.
4. Abhishek A, Doherty M. Epidemiology of calcium pyrophosphate crystal arthritis and basic calcium phosphate crystal arthropathy. Rheum Dis Clin North Am. 2014; 40(2): 177–191, doi: 10.1016/j.rdc.2014.01.002, indexed in Pubmed: 24703342.
5. Williams CJ, Rosenthal AK. Pathogenesis of calcium pyrophosphate deposition disease. Best Pract Res

Clin Rheumatol. 2021; 35(4): 101718, doi: 10.1016/j.berh.2021.101718, indexed in Pubmed: 34696986.
6. Rosenthal AK, Ryan LM. Calcium Pyrophosphate Deposition Disease. N Engl J Med. 2016; 374(26): 2575––2584, doi: 10.1056/NEJMra1511117, indexed in Pubmed: 27355536.
7. Iqbal SM, Qadir S, Aslam HM, et al. Updated Treatment for Calcium Pyrophosphate Deposition Disease: An Insight. Cureus. 2019; 11(1): e3840, doi: 10.7759/cureus.3840, indexed in Pubmed: 30891381.
8. Rosales-Alexander JL, Balsalobre Aznar J, Magro-Checa C. Calcium pyrophosphate crystal deposition disease: diagnosis and treatment. Open Access Rheumatol. 2014; 6: 39–47, doi: 10.2147/OARRR.S39039, indexed in Pubmed: 27790033.
9. Bencardino JT, Hassankhani A. Calcium pyrophosphate dihydrate crystal deposition disease. Semin Musculoskelet Radiol. 2003; 7(3): 175–185, doi: 10.1055/s-2003-43228, indexed in Pubmed: 14593559.
10. Tausche AK, Aringer M. [Chondrocalcinosis due to calcium pyrophosphate deposition (CPPD). From incidental radiographic findings to CPPD crystal arthritis]. Z Rheumatol. 2014; 73(4): 349–57; quiz 358, doi: 10.1007/s00393-014-1364-5, indexed in Pubmed: 24811359.
11. Higgins PA. Gout and pseudogout. JAAPA. 2016; 29(3): 50–52, doi: 10.1097/01.JAA.0000475472.40251.58, indexed in Pubmed: 26914781.
12. Ea HK, Lioté F. Diagnosis and clinical manifestations of calcium pyrophosphate and basic calcium phosphate crystal deposition diseases. Rheum Dis Clin North Am. 2014; 40(2): 207–229, doi: 10.1016/j.rdc.2014.01.011, indexed in Pubmed: 24703344.
13. Ferrone C, Andracco R, Cimmino MA. Calcium pyrophosphate deposition disease: clinical manifestations. Reumatismo. 2012; 63(4): 246–252, doi: 10.4081/reumatismo.2011.246, indexed in Pubmed: 22303531.
14. Zimmermann-Górska I. Choroby wywołane przez kryształy pirofosforanu wapnia. Medycyna Praktyczna, Interna — Mały Podręcznik. 2022.
15. Duran Tİ, Özgen M. Two cases of calcium pyrophosphate deposition disease (CPPD) presented with spondylodiscitis. Eur J Rheumatol. 2020; 7(2): 84–87, doi: 10.5152/eurjrheum.2020.19180, indexed in Pubmed: 32644929.
16. Greca I, Ben Gabr J, Perl A, et al. Trauma Induced Calcium Pyrophosphate Deposition Disease of the Lumbar Spine. Case Rep Rheumatol. 2020; 2020: 3218350, doi: 10.1155/2020/3218350, indexed in Pubmed: 32095306.
17. Tausche AK, Reuss-Borst M. [Crystal arthropathies]. Dtsch Med Wochenschr. 2019; 144(15): 1055–1060, doi: 10.1055/a-0857-0916, indexed in Pubmed: 31350748.
18. Filippou G, Filippucci E, Mandl P, et al. A critical review of the available evidence on the diagnosis and clinical features of CPPD: do we really need imaging? Clin Rheumatol. 2021; 40(7): 2581–2592, doi: 10.1007/s10067-020-05516-3, indexed in Pubmed: 33231775.
19. Sirotti S, Gutierrez M, Pineda C, et al. Accuracy of synovial fluid analysis compared to histology for the identification of calcium pyrophosphate crystals: an ancillary study of the OMERACT US Working Group - CPPD subgroup. Reumatismo. 2021; 73(2): 106–110, doi: 10.4081/reumatismo.2021.1403, indexed in Pubmed: 34342211.
20. Zamudio-Cuevas Y, Martínez-Nava GA, Martínez-Flores K, et al. Synovial fluid analysis for the enhanced clinical diagnosis of crystal arthropathies in a tertiary care institution. Clin Rheumatol. 2021; 40(8): 3239–3246, doi: 10.1007/s10067-021-05610-0, indexed in Pubmed: 33598809.
21. Lehmann B, Betsch-Bischof B, Horn R. [Arthrocentesis in the Emergency Department]. Ther Umsch. 2020; 77(5): 213–217, doi: 10.1024/0040-5930/a001178, indexed in Pubmed: 32870099.
22. Kaneyama H, Morishita Y, Kawano O, et al. Acute Attack of Pseudogout with the Wide Lesion in Lumbar Spondylolytic Spondylolisthesis. Case Rep Orthop. 2020; 2020: 4512695, doi: 10.1155/2020/4512695, indexed in Pubmed: 32802536.
23. Zell M, Aung T, Kaldas M, et al. Calcium pyrophosphate crystal size and characteristics. Osteoarthr Cartil Open. 2021; 3(1), doi: 10.1016/j.ocarto.2020.100133, indexed in Pubmed: 34386778.
24. Jacques T, Michelin P, Badr S, et al. Conventional Radiology in Crystal Arthritis: Gout, Calcium Pyrophosphate Deposition, and Basic Calcium Phosphate Crystals. Radiol Clin North Am. 2017; 55(5): 967–984, doi: 10.1016/j.rcl.2017.04.004, indexed in Pubmed: 28774457.
25. Filippou G, Scanu A, Adinolfi A, et al. Criterion validity of ultrasound in the identification of calcium pyrophosphate crystal deposits at the knee: an OMERACT ultrasound study. Ann Rheum Dis. 2021; 80(2): 261–267, doi: 10.1136/annrheumdis-2020-217998, indexed in Pubmed: 32988839.
26. Cai K, Tedeschi SK. Review: Outcome measures in calcium pyrophosphate deposition. Best Pract Res Clin Rheumatol. 2021; 35(4): 101724, doi: 10.1016/j.berh.2021.101724, indexed in Pubmed: 34799278.
27. Ziegeler K, Diekhoff T, Hermann S, et al. Low-dose computed tomography as diagnostic tool in calcium pyrophosphate deposition disease arthropathy: focus on ligamentous calcifications of the wrist. Clin Exp Rheumatol. 2019; 37(5): 826–833, indexed in Pubmed: 31025927.
28. Nowak P. [Hemochromatosis related Arthropathy]. Ther Umsch. 2018; 75(4): 235–239, doi: 10.1024/0040-5930/a000994, indexed in Pubmed: 30468115.
29. Tedeschi SK, Becce F, Pascart T, et al. Imaging Features of Calcium Pyrophosphate Deposition Disease: Consensus Definitions From an International Multidisciplinary Working Group. Arthritis Care Res (Hoboken). 2023; 75(4): 825–834, doi: 10.1002/acr.24898, indexed in Pubmed: 35439343.
30. Cadiou S, Le Gruyer A, Giguet B, et al. Calcium pyrophosphate deposition (CPPD) in a liver transplant patient: are hypomagnesemia, tacrolimus or both guilty? A case-based literature review. Rheumatol Int. 2022; 42(6): 1105–1112, doi: 10.1007/s00296-021-04828-0, indexed in Pubmed: 33709178.
31. Catelli A, Venetucci P, Castaldo A, et al. Calcium pyrophosphate deposition disease: The role of imaging in their detection and in differential diagnosis of crystal arthropathies. Radiol Case Rep. 2020; 15(10): 1773–1776, doi: 10.1016/j.radcr.2020.07.012, indexed in Pubmed: 32774579.
32. Cipolletta E, Di Matteo A, Filippucci E, et al. Calcium Pyrophosphate Deposition Disease in a Patient with Familial Hypokalemia-Hypomagnesemia (Gitelman's-Syndrome): A Case Report - CPPD in Gitelman's syndrome. Ultraschall Med. 2020; 41(6): 695–697, doi: 10.1055/a-0990-9960, indexed in Pubmed: 31434112.
33. Stack J, McCarthy G. Calcium pyrophosphate deposition (CPPD) disease - Treatment options. Best Pract Res

Clin Rheumatol. 2021; 35(4): 101720, doi: 10.1016/j.berh.2021.101720, indexed in Pubmed: 34756508.
34. Sidari A, Hill E. Diagnosis and Treatment of Gout and Pseudogout for Everyday Practice. Prim Care. 2018; 45(2): 213–236, doi: 10.1016/j.pop.2018.02.004, indexed in Pubmed: 29759121.
35. Rigsbee CA, Sizemore TC, Lohr KM. Severe calcium pyrophosphate dihydrate deposition disease of the metacarpophalangeal joints. BMJ Case Rep. 2018; 2018, doi: 10.1136/bcr-2018-226132, indexed in Pubmed: 30269092.
36. Sivera F, Andrés M, Pascual E. Current advances in therapies for calcium pyrophosphate crystal arthritis. Curr Opin Rheumatol. 2016; 28(2): 140–144, doi: 10.1097/BOR.0000000000000252, indexed in Pubmed: 26780424.
37. Altomare A, Corrado A, Maruotti N, et al. The role of Interleukin-1 receptor antagonist as a treatment option in calcium pyrophosphate crystal deposition disease. Mol Biol Rep. 2021; 48(5): 4789–4796, doi: 10.1007/s11033-021-06457-z, indexed in Pubmed: 34075537.
38. Andrés M, Sivera F, Pascual E. Therapy for CPPD: Options and Evidence. Curr Rheumatol Rep. 2018; 20(6): 31, doi: 10.1007/s11926-018-0739-z, indexed in Pubmed: 29675606.
39. Parperis K, Papachristodoulou E, Kakoullis L, et al. Management of calcium pyrophosphate crystal deposition disease: A systematic review. Semin Arthritis Rheum. 2021; 51(1): 84–94, doi: 10.1016/j.semarthrit.2020.10.005, indexed in Pubmed: 33360232.
40. Cipolletta E, Di Matteo A, Scanu A, et al. Biologics in the treatment of calcium pyrophosphate deposition disease: a systematic literature review. Clin Exp Rheumatol. 2020; 38(5): 1001–1007, indexed in Pubmed: 32359034.
41. Krekeler M, Baraliakos X, Tsiami S, et al. High prevalence of chondrocalcinosis and frequent comorbidity with calcium pyrophosphate deposition disease in patients with seronegative rheumatoid arthritis. RMD Open. 2022; 8(2), doi: 10.1136/rmdopen-2022-002383, indexed in Pubmed: 35701012.
42. Shen G, Su M, Liu B, et al. A Case of Tophaceous Pseudogout on 18F-FDG PET/CT Imaging. Clin Nucl Med. 2019; 44(2): e98–e9e100, doi: 10.1097/RLU.0000000000002308, indexed in Pubmed: 30325826.