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RESEARCH

Steroid or pseudogout? Analysis of white deposits in tissues during surgery

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Abstract

Introduction Pseudogout is characterized by the deposition of calcium pyrophosphate crystals in the pericellular matrix of chondrocytes. Pseudogout flares can present similar to gout, osteoarthritis, septic arthritis, or prosthetic joint infection, potentially complicating post-surgical outcomes. With a high prevalence among patients undergoing arthroplasty, appropriate awareness is essential to mitigate misdiagnosis and inappropriate treatment. This study reviews a series of eight patients in whom white deposits are identified intraoperatively and seeks to guide identification, patient education, and future treatment for pseudogout.

Methods Patients undergoing surgical intervention were assessed for the presence of an intraarticular white substance. When the substance was identified, a sample was sent for assessment by a pathologist. The patients' age, sex, pertinent history, surgery, site of biopsy, and pathologist findings were documented.

Results Of the eight patients included in the study, the average age was 67.9 years (range 62–75). Five (62.5%) were male and three (37.5%) were female. Six (75%) were found to have CPPD crystals. Out of these six, one had a steroid injection 5 months prior and another 7 months prior. One patient who had a steroid injection 4 months prior to surgery had a scant amount of white substance that was identified as "acellular material" by the pathologist. Only a single patient of these six had a standing diagnosis of pseudogout prior to surgery. Intraoperatively, the white substances were visually similar in all cases.

Conclusions There is a high prevalence of pseudogout in patients over the age of 65 and with concurrent arthritis. Presentation of pseudogout can range from asymptomatic to mimicking septic arthritis. Unidentified white substances noted intraoperatively should be sent to pathology for identification. In patients with pseudogout, it is important to educate the patient and consider prophylactic treatment to minimize risk of recurrence and damage to other joints.

Keywords Pseudogout · Intraoperative substance identification · Chondrocalcinosis · CPPD

Introduction

Pseudogout, also known as calcium pyrophosphate dihydrate (CPPD) deposition disease, is a form of arthropathy characterized by the deposition of calcium pyrophosphate crystals in the pericellular matrix of chondrocytes [1–4]. These deposits, seen radiologically as chondrocalcinosis, clinically manifest as an array of symptoms resembling gout and numerous other pathologies [1, 3]. The occurrence of pseudogout is often sporadic with no substantial genetic cause due to its metabolically-based etiology, though it exhibits a strong association with age and major joint pathologies such as osteoarthritis [1, 5–8].

CPPD arthritis is the third most common inflammatory arthritis behind rheumatoid arthritis and gout. The prevalence of chondrocalcinosis is estimated to range from 3 to

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17.5% in elderly populations and can be as high as 53% in individuals also experiencing osteoarthritis [1, 5, 6]. However, this likely severely underestimates the true prevalence, as chondrocalcinosis is difficult to visualize radiographically in patients with severe cartilage degeneration [9].

Additionally, pseudogout poses a longstanding diagnostic challenge due to its varied clinical presentation [5]. Pseudogout can present in the knees (most common), ankles, wrists, intervertebral disks, and spinal ligaments. Symptoms may mimic gout, rheumatoid arthritis, osteoarthritis, meningitis, sepsis, or malignancies [3, 5, 8, 10]. Of particular concern is its impact on post-surgical outcomes for major joint procedures. Pseudogout often manifests with symptoms of warmth, erythema, pain, and swelling in the affected joint, which clinically resembles septic arthritis or prosthetic joint infection [1, 2, 10]. Additionally, patients may have elevated inflammatory markers and low-grade fevers, further complicating the diagnosis. Misdiagnosis can result in unnecessary long-term antibiotic therapy and additional surgical intervention, including the explantation of orthopaedic implants. Given its high prevalence among patients with arthritis and arthroplasty, appropriate awareness and consideration are essential to mitigate misdiagnosis and associated adverse consequences.

Occasionally, a white substance is identified in a joint undergoing surgery for arthritis. The repeated dogma is that this substance is residue from prior steroid injections. However, this substance has also been found in joints that do not typically undergo steroid injection, such as metatarsophalangeal joints. This study reviews a series of eight patients in whom the white substance is noted and seeks to guide identification, patient education, and future treatment.

Methods

This case series was retrospectively collected with Institutional Review Board approval from our institution. All patients provided informed consent prior to their participation in the study, in accordance with ethical guidelines and Institutional Review Board approval. Adult patients undergoing surgical intervention for joint pathology were assessed for the presence of intraarticular white substances. These substances were identified intraoperatively based on visible deposition on soft tissues and were systematically sampled for pathological evaluation, as is standard for the senior surgeon. All patients between the ages of 18–90 with the presence of an intraarticular white substance and biopsy results were included. The substances biopsied were heterogenous in appearance between some patients, but all were included. The patients' age, sex, pertinent medical history, prior steroid injections, surgical history, biopsy site, and pathologist findings were documented (Table 1).

Table 1 Patient information

Patient	Age/Sex	History	Surgery	Location	Findings
1	69 M	Multifocal arthritis, steroid injection 5 months prior	R 1st MTP fusion	R 1st MTP	CPPD crystal deposits are present within the synovium
2	62 F	Steroid injection 4 months prior	L 3rd webspace neuroma excision	L 3rd webspace	Acellular material
3	62 M	R great toe and plantar MT head ulcers, prior TKA PJI	R great toe IP disarticulation, tibial sesamoidectomy	R 1st MTP	Fragments of benign fibrocartilage and acellular debris
4	71 F	Multifocal arthritis	L 1st MTP fusion	L 1st MTP	Calcium pyrophosphate crystal deposition within synovium (pseudogout)
5	64 M	Severe R progressive collapsing foot deformity, multifocal arthritis; nephrolithiasis	R flatfoot correction	R posterior tibial tendon	Fibrocartilaginous tissue with calcium pyrophosphate crystal deposition (pseudogout)
6	75 M	Pseudogout	R 1st MTP fusion, 2nd weil osteotomy and flexor tenotomy	R 1st and 2nd MTP	Calcium pyrophosphate crystal deposition within synovium (pseudogout)
7	74 M	Bl knee arthritis, steroid injection 7 months prior	L medial UKA	L knee	Calcium pyrophosphate dihydrate (CPPD) crystal deposits within the fibrous tissue
8	66 F	Bl hallux rigidus	R great toe cheilectomy	R 1st MTP	Calcium pyrophosphate crystal deposition (pseudogout)

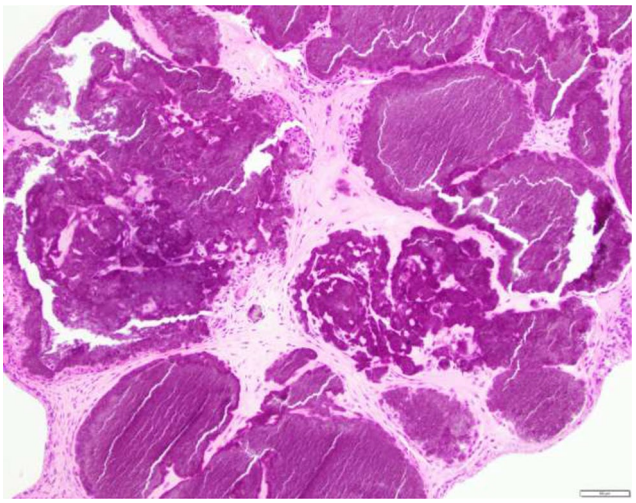

Fig. 1 Dense deep purple deposits of CPPD with associated histiocytic reaction within the synovium

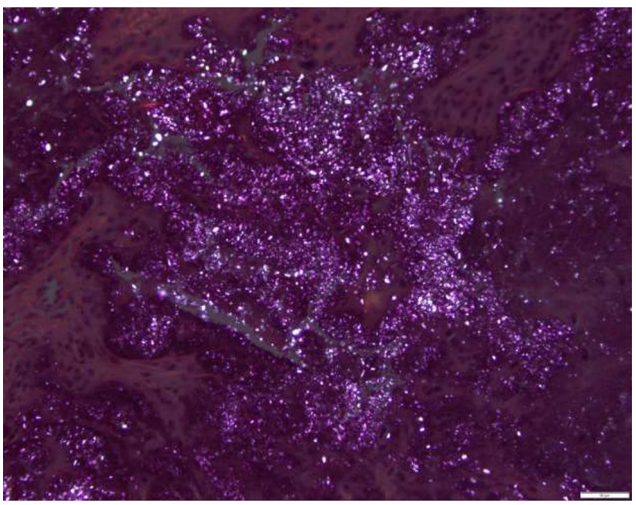

Fig. 2 Rhomboid shape crystals are present under polarized light

Results

Eight patients were included in the study, with an average age of 67.9 years (range 62–75). Five patients (62.5%) were male and three (37.5%) were female. Pathology identified CPPD crystals in six patients (75%) (Figs. 1 and 2). Of these six, three patients had steroid injections prior to surgery. One patient had a steroid injection five months prior and another seven months prior. Both of these patients had pseudogout identified intra-operatively. The third patient, who received a steroid injection four months prior to surgery, had a scant amount of white material intraoperatively, which was later identified as "acellular material" on pathology. Another patient, who had not received a steroid injection, had a similar-appearing white substance in an infected

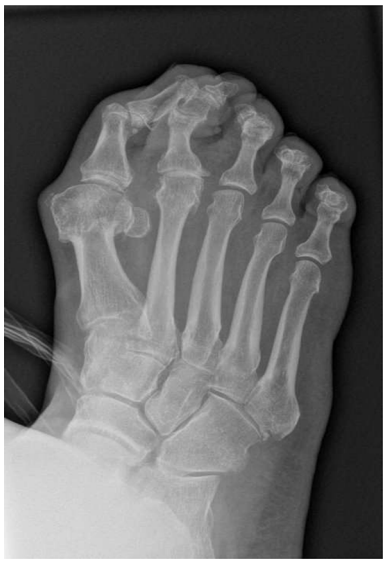

Fig. 3 Preoperative oblique X-Ray of right foot displaying first and second metatarsophalangeal joint space narrowing

region, which was identified as "fragments of benign fibrocartilage and acellular debris.

Of the six patients with pseudogout identified, three had multifocal arthritis and two had arthritis in the same joint bilaterally. One patient with identified pseudogout crystals postoperatively had a standing diagnosis of pseudogout prior to surgery. All patients received radiographs preoperatively (Figs. 2 and 3). Two patients had results with clear chondrocalcinosis visible on preoperative radiographs of the operative joint (See Fig. 4).

Intraoperatively, the white substance appeared visually similar in most cases, described as chalky and easily extricated from soft tissues (Figs. 5 and 6). None of the material was embedded in the cartilage. In the case of acellular material in the patient with a steroid injection four months prior, the amount was much less as compared to those who had pseudogout. Conversely, in the patient with an infection, there were copious amounts of the white substance within the joint and surrounding tissues.

The patient with a prior diagnosis of pseudogout was not undergoing any chronic treatment. He had a recent flare prior to surgery and was prescribed prednisone for symptomatic management.

In the patient with pseudogout identified within the posterior tibial tendon, it may be hypothesized that the collection within the tendon led to its degeneration. Additionally, a combination of CPPD deposition and altered stresses throughout the rest of the foot contributed to its progressive collapse. He had excellent deformity correction postoperatively. However, four months postoperatively, he suddenly had severe swelling, erythema, and pain throughout the foot. He had waxing and waning, low-grade fevers that worsened

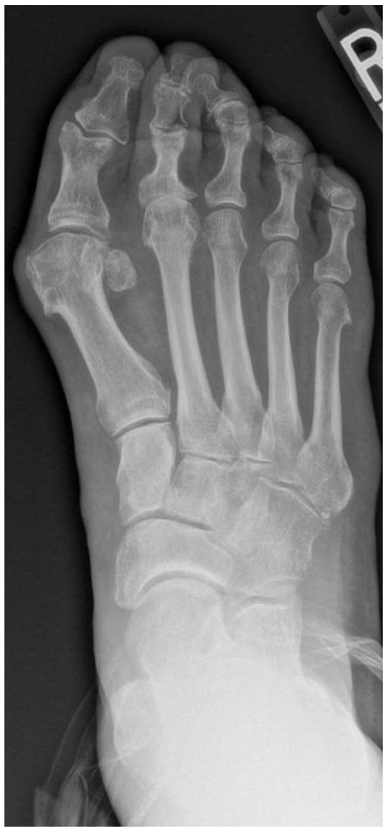

Fig. 4 Preoperative anterior-posterior X-Ray of right foot displaying first and second metatarsophalangeal joint space narrowing

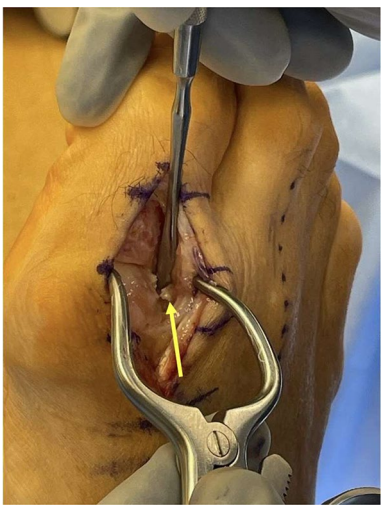

Fig. 6 Surgical incision visualizing first metatarsophalangeal joint of the right foot with intraarticular white substance (arrow)

with activity. Arthrocentesis showed CPPD crystals and no bacteria. He was hospitalized, placed on intravenous antibiotics, and underwent multiple surgical debridements. Given the concern for possible postoperative infection, steroid treatment was never initiated. He noted some symptomatic improvement from oral anti-inflammatory use. No infection

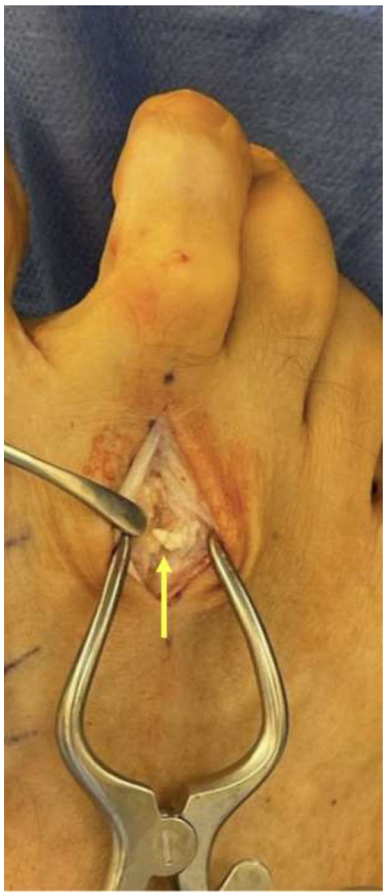

Fig. 5 Surgical incision visualizing first metatarsophalangeal joint of the right foot with an intraarticular white substance (arrow)

was ever identified, but all symptoms immediately resolved following removal of all foreign implants.

Discussion

With continual ambiguity in the literature on pseudogout prevalence, treatment, appearance, and presentation, this retrospective case series aimed to determine pseudogout prevalence and diagnostic criteria to provide a framework of identification to guide surgeons. Unlike gout, which can be diagnosed with laboratory analysis of bloodwork, pseudogout requires invasive arthrocentesis and polarized light microscopy or visible chondrocalcinosis on radiographs for diagnosis. Additionally, while there are acute and preventative treatments for gout, the most appropriate treatment for pseudogout remains debated. The first line treatment for acute pseudogout flare is intraarticular corticosteroid. However, given the differential diagnosis of septic arthritis, this treatment is frequently avoided [5, 6].

Within our cohort of eight patients, six were found to have CPPD deposition in the operative site. Although our

study has a limited sample size, the frequency with which the white substance was identified to be CPPD rather than steroid residue is much higher than expected, even in patients who received prior steroid injections.

Our results demonstrate that the deposition of white debris in an operative site may be steroid (acellular material), degenerative tissue, or CPPD crystals. We observed that acellular material presents in very small quantities while calcium pyrophosphate deposition or degenerative tissue both manifest with much larger quantities of debris. Given the frequency with which patients opt for corticosteroid injections preoperatively, acellular white debris found intraoperatively inside arthritic joints may be misconstrued as remnants of corticosteroid. Instead, this study accentuates the major possibility that the white debris is indicative of calcium pyrophosphate crystal deposition. Typically, surgical intervention after an intraarticular steroid injection is delayed at least three months to minimize the risk of infection. During this time, the steroid is absorbed and degraded by the body and is unlikely to result in significantly appreciable residue.

Pseudogout is one of the most common types of inflammatory arthritis and it has a strong correlation with age and previous trauma, making it particularly prevalent in elderly patients with arthritic changes [5, 6, 8, 11]. Pseudogout mimics other pathologies due to its diverse symptom presentation, making diagnosis difficult. Specifically, it often clinically presents similarly to prosthetic joint infection or septic arthritis, which requires further surgical intervention [2]. In our series, one patient had a postoperative complication due to a pseudogout flare and underwent intravenous antibiotic treatment, multiple surgical debridements, implant explanation, and revision surgery. On one hand, misdiagnosing pseudogout as an infection can lead to unnecessary antibiotic and surgical treatment, both of which can be fraught with complications [2, 12]. On the other, misdiagnosing infection as pseudogout would lead to improper treatment and severe harm to the patient, particularly if immunosuppressive treatment were administered. As such, a proper diagnosis must be established. In patients who have biopsy proven pseudogout within the operative joint, chronic prophylactic treatment may be appropriate. This is especially true in those who have frequent flares and multifocal arthropathies to minimize the risk of recurrent flares and acute treatment uncertainty.

The mainstay of pseudogout treatment strategies is directed toward reducing the body's natural inflammatory response to crystal formation [11]. The goal of this method is to reduce symptom presentation and frequency of severity of CPPD episodes. Strategies for lowering inflammation acutely include colchicine, NSAIDs, and steroids [5, 14, 15]. Unlike gout, there are no definitive treatments for directly decreasing the crystal burden of pseudogout or completely arresting the progression [6, 8, 13]. Current literature suggests potential avenues to explore for chronic pseudogout prophylaxis include biologic agents such as anakinra and tocilizumab [14, 16]. Additionally, intraarticular glycosaminoglycan polysulphate, hyaluronic acid, and yttrium may be beneficial [14].

While primary pseudogout occurs sporadically, secondary pseudogout can occur as a result of underlying metabolic disorders such as hyperparathyroidism, hypomagnesemia, hypophosphatasia, and hemochromatosis [4–6, 8]. Secondary pseudogout accounts for 20% of all cases [6]. When the primary cause is treated, its symptoms can be improved and the secondary pseudogout can be successfully abated. Patients who have CPPD crystals identified intraoperatively should have blood work tested for intact parathyroid hormone, calcium, phosphorous, thyroid-stimulating hormone, magnesium, ferritin, iron transferrin, and alkaline phosphatase (Fig. 7). Treatment is recommended for any associated diseases.

The limitations of this study are primarily its retrospective nature and limited sample size. Additionally, because pseudogout may be relatively asymptomatic, formal diagnosis and treatment are not typically pursued, even if it is identified on radiographs. In our patient cohort, we did not order testing for secondary metabolic disorders that may belie the pseudogout diagnosis. Patients with biopsies positive pseudogout were informed and recommended to follow up with rheumatology. To our knowledge, no patients were started on chronic prophylaxis.

Ultimately, this study aims at the importance of standardizing intraoperative biopsy of suspicious debris to facilitate faster and more accurate diagnosis of pseudogout. By routinely collecting and analyzing intraoperative debris, surgeons can ensure earlier identification of pseudogout, reducing the need for invasive procedures or unnecessary antibiotic treatments in postoperative patients. Prompt diagnosis also enables timely referrals to rheumatology or primary care, ensuring better symptom management and evaluation for underlying metabolic disorders.

Conclusion

There is a high prevalence of pseudogout in patients over the age of 65 with concurrent arthritis who undergo surgery for arthritic conditions. Due to the diverse presentation, pseudogout should be included in the differential of a postoperative painful joint and proper work up should be completed to identify the diagnosis, which can include sending intra-operative samples of tissue. When pseudogout is identified, prophylactic treatment should be provided to

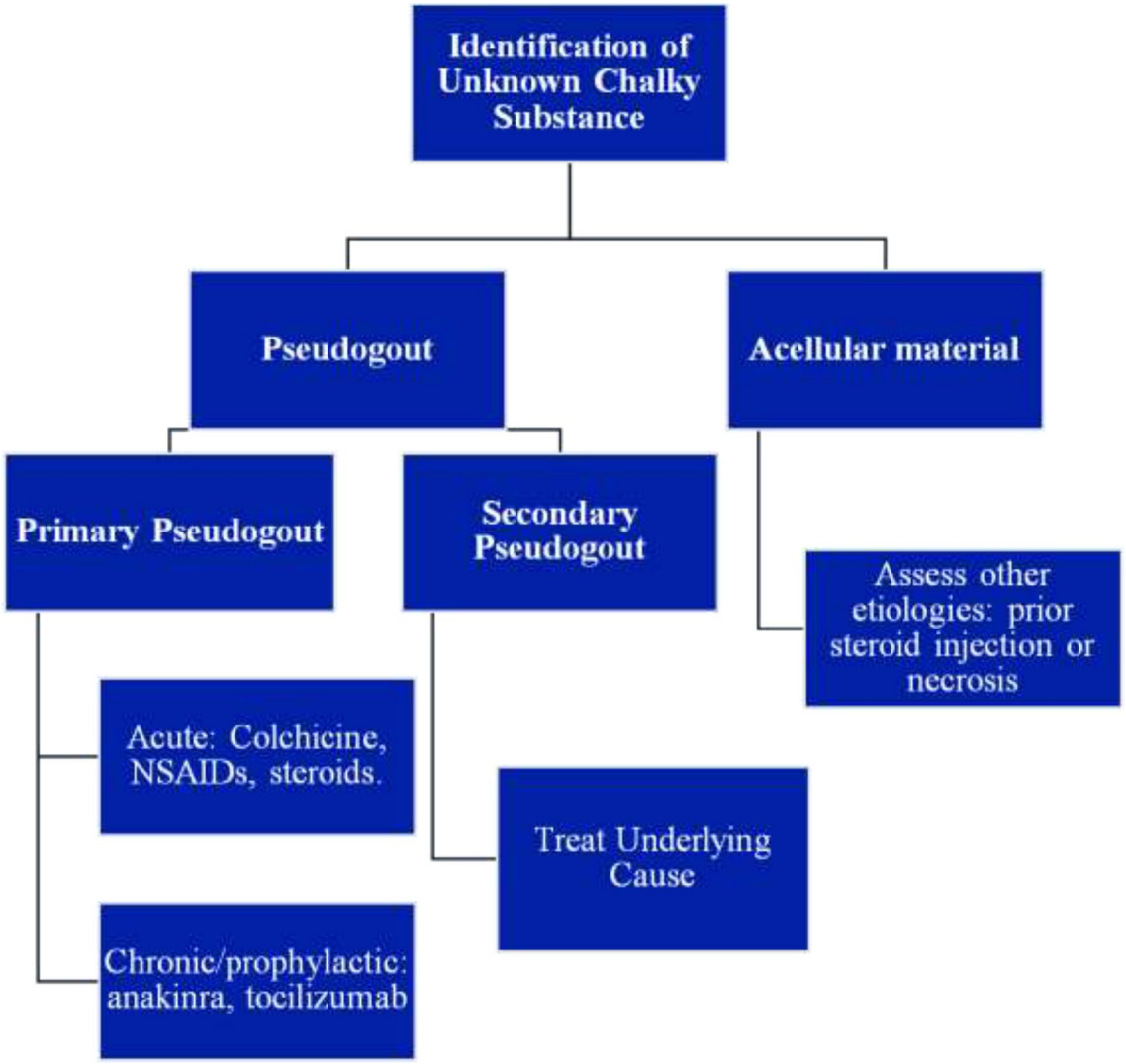

Fig. 7 Flowchart of treatment strategies based on pathological analysis

the patient to mitigate the risk of degeneration of multiple joints. If clinically prudent, the patient should be worked up for primary metabolic disorders that can cause secondary pseudogout or consider chronic prophylactic treatment to prevent recurrent flares.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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