Pseudogout of the temporomandibular joint: an uncommon cause of temporomandibular joint pain and swelling

Scott Sklenicka, DMD, MD,a Eric J. Dierks, DMD, MD,b Joe Jarmin,c and Cathy Miles, MD, d Jacksonville, FL, and Portland, OR
NORTH FLORIDA ORAL AND FACIAL SURGERY, OREGON HEALTH AND SCIENCE UNIVERSITY, AND LEGACY EMANUEL HOSPITAL

Background. Pseudogout, or calcium pyrophosphate deposition, is a rare cause of pain, swelling, and trismus of the temporomandibular joint (TMJ). Diagnosis and management of the lesion are discussed.

Case description. A 58-year-old female had a 2-month history of progressive swelling of right TMJ associated with trismus and facial pain. Imaging of the TMJ revealed a mixed radiolucent and radiopaque lesion associated with the right TMJ joint space. Surgical excision was performed successfully via preauricular approach. Pathology was consistent with calcium pyrophosphate deposition of the TMJ, also known as pseudogout. Surgical excision successfully treated her symptoms as expected. She is now disease free without recurrence.

Clinical implications. Pseudogout is a rare cause of TMJ pain, swelling, and trismus that should be included in the differential of joint pain and dysfunction. It can be treated successfully with surgery. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:709-714)

Calcium pyrophosphate dihydrate deposition disorder (CPPDDD) is a relatively rare condition that may affect the temporomandibular joints (TMJs). It is a systemic disease that results in crystal deposition within the joint space, resulting in pain, trismus, and preauricular swelling. It is difficult to diagnose and mimics many other neoplastic and infectious causes of TMJ symptoms. To date, fewer than 35 cases have been reported in the literature. The following is a case of extensive CPPDDD in both the TMJ as well as the surrounding tissues.

REPORT OF A CASE
A 58-year-old female was referred for evaluation of right preauricular mass. Her chief complaint was progressive swelling of right preauricular/TMJ area of 10 months’ duration. She first noticed swelling and pain in the area 2 years earlier when she underwent root canal therapy in a right posterior molar. After the procedure, she noted difficulty with her occlusion, requiring multiple occlusal adjustments. Ten months before presenting to clinic, she noted a painless, slowly enlarging mass overlying the right condylar area. She denied any history of regional trauma or previous TMJ disorders.

Her past medical history consisted of depression, for which she was on paroxetine. Previous surgical history was significant for bunionectomy, lower back surgery, and stapedectomy. Physical examination showed a mass overlying the lateral pole of the right mandibular condyle that was approximately 2 cm in diameter, with moderate pain to palpation (Fig. 1). Cranial nerve VII was intact. Otologic examination showed no abnormalities. Bilateral postauricular stapedectomy scars were well healed. Maximal incisal opening was 37 mm with significant deviation to the right upon opening. Her occlusion demonstrated a class 1 molar and canine relationship. Computed tomography (CT) showed a 1.7 × 3.5 × 1.8-cm well-defined mass interposed between the right glenoid fossa and condylar head. The condylar head was displaced inferiorly 7 mm with evident remodeling of the head at the medial aspect. The mass was felt to be consistent with a fibro-osseous lesion (Figs. 2 and 3).

Treatment consisted of excision of the mass under general anesthesia via a preauricular approach. Because of the depth of the lesion and medial extent of the mass, intraoperative navigation assistance was used, which was based on her preoperative CT scans. The medial extension of the mass limited surgical access and re-
quired temporary osteotomy of both the zygomatic arch and condylar head. The lesion was then fully visualized as a firm, encapsulated soft tissue mass emanating from the anterior portion of the articular disk, with significant displacement of the lateral pterygoid muscle. The mass was excised in 2 separate portions. A temporalis muscle flap was rotated into the defect to reconstruct the excised disk. The condyle and zygomatic arch were then replaced into their anatomic positions with titanium plate fixation.

Gross pathologic examination demonstrated a 6.0 × 4.0 × 1.8-cm mass of bright white soft tissue with friable edges. Microscopic examination revealed nodules of birefringent crystalline material and calcifications associated with reactive chondroblasts and histiocytes (Fig. 4). The crystals showed no signs of degradation with processing. This was consistent with
calcium pyrophosphate crystal deposition, also known as pseudogout, of the TMJ.

The patient did well postoperatively with no facial weakness. On follow-up examination 4 months after surgery, maximal incisal opening had increased from 22 mm immediately postoperatively to 30 mm (Figs. 5 and 6). Rightward deviation of the mandible occurred only at maximum opening. Her occlusion was unchanged. Panoramic radiograph showed excellent realinement of the replaced condyle and zygomatic arch. Her pain and swelling had resolved.

DISCUSSION

Pseudogout, more accurately termed calcium pyrophosphate dihydrate deposition disorder (CPPDDD), is a rare disease originating from abnormally high concentrations of inorganic pyrophosphate (PPI) in the articular cartilage and synovial fluid. PPI crystals may form via precipitation within the joint space leading to goutlike symptoms, or they may enter the joint space by sloughing from the surrounding articular cartilage. Traditional gout is caused by urate crystal deposition in joint spaces, particularly the first metatarsophalangeal joint at the base of the big toe. However, CPPDDD is caused by calcium pyrophosphate dihydrate crystal formation and is often referred to as pseudogout because of the similarity of symptomatic presentation to that of actual gout. Urate tophi deposition is common in typical gout; however, in pseudogout, crystal tophi are rare. Many other terms have been used to describe the condition of pseudogout, including chondrocalcinosis and pyrophosphate arthropathy. CPPDDD encompasses the terms pseudogout, chondrocalcinosis, and pyrophosphate arthropathy. However, the terms pseudogout and CPPDDD are still often used interchangeably throughout the literature.

In 1958, Zitnan and Sitaj\(^1\) made the first radiographic identification of pseudogout in the hyaline and fibrocartilage of intervertebral joints. They coined the term “chondrocalcinosis” in reference to the appearance of articular cartilage calcification on radiograph. In 1962, CPPD crystals were first discovered in synovial fluid by McCarty et al\(^2\) and Kohn et al.\(^3\) Patients with synovial CPPD crystals presented with symptoms similar to those of gout, hence they coined the term “pseudogout” to describe the condition.

CPPDDD demonstrates a higher predilection for fibrocartilage than hyaline cartilage and most often occurs in the triangular ligament of the wrist, the meniscus of the knee, and the TMJ.\(^4\) It may also affect the ligamentum flavum and intervertebral disks as well.\(^5\) The articular surfaces of the TMJ are lined with fibrocartilage, and the articular disk is also fibrocartilage. It
would therefore seem that the TMJ would be prone to development of CPPDD disorders. However, there are surprisingly very few reported cases of pseudogout in the TMJ. It is currently unknown why PPI arthropathies display a predilection for fibrocartilaginous joints.

Common symptoms may include, but are not limited to, intermittent acute arthritic attacks, joint effusion, preauricular swelling, facial pain, trismus, mandibular deviation, otalgia, unilateral conductive hearing loss, and decreased joint mobility.\(^4\)\(^6\)\(^7\) It is also possible for CPPDDD to be completely asymptomatic, being discovered incidentally via radiography. It has been proposed that asymptomatic CPPDDD may actually be more common than symptomatic CPPDDD simply because of lack of diagnosis.\(^8\) Clinical symptoms of CPPDDD are variable and mimic other joint diseases, such as gout, osteoarthritis, rheumatoid arthritis, parotid gland neoplasms, cholesteatoma, synovial chondromatosis, TMJ neoplasms, degenerative joint disease, or neuropathic joint diseases.\(^5\)\(^8\) Therefore, CPPDDD can be difficult to diagnose from clinical symptoms alone.

CPPDDD may follow one of several common patterns of systemic presentation. First, the disorder may be completely asymptomatic. Second, pseudogout may present as a type of acute inflammatory arthritis. Third, it may present as a type of pseudo-osteoarthritis acting as a type of chronic degenerative arthritis. Fourth, it may present as a type of pseudorheumatoid arthritis acting as a type of chronic symmetric inflammatory polyarthritis. These 4 patterns most commonly occur in the knee and/or wrist and can be considered relatively mild compared with a fifth, more severe type of presentation called tophaceous pseudogout, which most commonly occurs in the TMJ.\(^9\)

There are 2 main clinical presentation patterns of CPPDDD of the TMJ.\(^10\) The first type of presentation involves acute inflammatory attacks causing painful preauricular swelling of TMJ. These attacks can also affect other joints throughout the body simultaneously with presentation in the TMJ. The second type of manifestation is called tophaceous CPPDDD. Tophaceous CPPDDD (also referred to as tumoral or massive CPPDDD) has an entirely separate manifestation when compared with other forms of pseudogout and presents with no history of acute attacks or preauricular swelling. Its presentation often mimics that of a TMJ tumor. Tophaceous pseudogout can be misinterpreted clinically and radiographically as benign (soft tissue chondroma, chondroblastoma) or malignant (chondrosarcoma, chondroid chordoma) cartilaginous lesions.\(^3\)

Tophaceous pseudogout is the rarest of the CPPDDD disorders; however, when it does occur, it occurs most commonly in the TMJ.\(^9\) Severe pain and dysfunction associated with the tophaceous form of pseudogout may lead to an earlier diagnosis when compared with milder forms of pseudogout. The skeletal distribution of tophaceous pseudogout differs from that of milder forms that tend to affect the knee and wrist. Tophaceous pseudogout has a clinical and radiographic presentation similar to that of synovial chondrosarcoma; therefore, it is essential to avoid misdiagnosis.\(^6\) Pritzker et al\(^11\) presented the first published case of tophaceous pseudogout of the TMJ in 1976. To our knowledge, 34 cases of tophaceous pseudogout have been published to date with a mean patient age of 58 years.\(^9\) According to Reynolds et al.,\(^9\) only 12% of chronic tophaceous CPPDDD had PPI deposits in joints other than the TMJ, whereas most reported cases of milder acute pseudogout had deposits in multiple joints.

CPPDDD disorders tend to display a female predominance with a male-to-female ratio of 1.0:1.9.\(^12\) It primarily affects those in late middle age and elderly individuals. Eighty percent of those affected are 60 years or older with levels of incidence increasing with age or history of trauma to the affected joints, and in patients suffering from other underlying metabolic abnormalities. Systemic metabolic issues should be considered if the patient is younger than 50 years.\(^13\) In addition, many systemic diseases are associated with CPPDDD disorders, including rheumatoid arthritis, various chronic arthropathies, gout, hypomagnesemia, hypothyroidism, amyloidosis, hypophosphatasia, hyperparathyroidism, hemosiderosis, hemochromatosis, familial hypocalciuria, and hypercalcemia.\(^10\)

CPPDDD disorders are believed to be caused by phosphate metabolism pathologies leading to increased levels of PPI in the affected joints; this pathology coupled with an abnormal cartilage matrix acting as a nucleation site can result in crystal precipitation. It has been hypothesized that symptoms typical of pseudogout may be the result of trauma to articular cartilage in the affected joints resulting in crystals being shed into joint space coupled with inflammation-induced cartilage degradation or localized infection.\(^4\) Pyrophosphate arthropathy is a pattern of structural joint damage particular to CPPDDD disorders. The resultant fibrocartilage damage may induce the hallmark symptoms of CPPDDD. However, it is unclear if it is the damaged fibrocartilaginous articular disk that causes the symptoms or if it is the damaged disk causing derangement of the articular fibrocartilaginous lining of fossa and condyle that leads to symptoms.\(^4\)

According to Aoyama et al., CPPDDD disorders can be classified into 4 main categories based on the etiology of disease: hereditary, sporadic, metabolic disease association, or traumatically or surgically induced. The exact pathogenesis of CPPD crystal deposition is poorly understood; however, several theories currently
exist. The first theory indicates that the increased PPi concentration in synovial fluid is the result of cell membrane proteins on the surface of articular cartilage chondrocytes in the TMJ, such as cartilage intermediate layer protein, that may exhibit ectoenzyme nucleotide triphosphate pyrophosphohydrolase (NTPPPH) activity. NTPPPH acts to hydrolyze extracellular adenosine triphosphate (ATP) in the synovial fluid to adenosine monophosphate and PPi, thus leading to increased concentrations of PPi.

The second theory hypothesizes that increased concentrations of PPi may be related to the transmembrane protein ankyrin. Intracellular PPi is the by-product of numerous intracellular biosynthetic reactions. Ankyrin may play a role in the transmembrane transport of PPi, moving intracellular PPi into the extracellular environment. Mutations of the protein ankyrin or errors in the regulation of ankyrin may result in excess transport of PPi across the cellular membrane into the surrounding extracellular matrix, which can lead to the development of chondrocalcinosis (linear and punctate radiodensities in articular cartilage) typically seen in pyrophosphate arthropathies, such as asymptomatic CPPDDD, pseudogout, and tophaceous pseudogout. In addition, this may explain why CPPD crystals can be found in the extracellular matrix of articular and pre-articular structures, such as articular cartilage, the synovial membrane capsule, tendon, ligament, and blood vessels. In addition, CPPD crystals stimulate synovial lining cells to synthesize and secrete proteases, prostanoids, and cytokines that may be involved in the destruction of the cartilage matrix of the TMJ leading to destruction and derangement of the joint. In the case of tophaceous pseudogout, this destruction can be extensive and tophi may extend into the cranial fossa.

On gross histologic examination, the joint space is filled with numerous attached and free-floating nodules of friable, gritty granulomatous tissue in addition to filled with numerous attached and free-floating nodules containing cartilaginous material and chondrocyte clusters with multinucleated giant cells, thus leading to increased concentrations of PPi.

Imaging studies showing chronic destructive arthropathy with intra-articular calcification can help support a diagnosis; however, a definitive diagnosis can never be determined from just clinical or radiographic findings. Joint aspirate or histologic evaluation is necessary to definitively diagnose. Needle aspiration of the synovial fluid can be used to obtain a crystal sample. Compensated light microscopy can determine the crystals as weakly positively birefringent. However, other crystals demonstrate birefringence as well, such as calcium oxalate, synthetic steroids, and ethylenediaminetetraacetic acid. It is recommended that polarizing microscopic analysis be followed with radiographic diffraction and electron probe analyses to help differentiate from other possible crystal deposition diseases. Positive birefringence of CPPD crystals is the key to differentiating between gout and pseudogout crystals. Gout crystals demonstrate strong negative birefringence. In addition, x-ray diffraction of the obtained sample can be used to determine crystal composition and help provide a more definitive diagnosis. Quantitative analysis by electron probe micro analyzer can be used to determine the calcium and phosphate ratio, which is typically close to one. Again, a definitive diagnosis can be determined only from evaluation of joint aspirate containing CPPD crystal or an open biopsy followed by microscopic evaluation of resected specimens via histologic sections.

When taking a histologic section, it is essential not to decalcify the specimen. Decalcification dissolves CPPD crystals leaving behind metaplastic chondroid-type tissue (chondrometaplasia), i.e., dense, fibrous tissue with numerous enclosed nodules containing cartilaginous material and chondrocyte clusters with multinucleated giant cells. Chondrometaplasia because of CPPDDD can often be confused with chondroma and synovial chondromatosis. Metaplastic chondrocytes may demonstrate cytologic atypia, which can mimic malignant cartilage tumors and possibly lead to the misdiagnosis of chondrosarcoma. Recognition of the presence of CPPD crystal deposition within the tissue and the associated foreign body granulomatous reaction is essential to arriving at the proper diagnosis of CPPDDD disorders, especially tophaceous pseudogout.

On microscopic histologic examination, small deposits of intensely basophilic calcified crystalline material containing needle-shaped rodlike rhomboid crystals can be visualized within the articular fibrocartilage, i.e., chondrocalcinosis. These crystals have an appearance similar to urate crystals; however, under polarizing microscopy, PPi crystals are weakly birefringent, whereas urate crystals are not birefringent. A consistent foreign body granulomatous reaction to the CPPD crystals is evident involving histiocytes along with foreign body type multinucleated giant cells surrounding the calcified areas in highly cellular tissues. Fewer cellular tissues demonstrate metaplastic chondroid-type tissue (chondrometaplasia), i.e., dense, fibrous tissue with numerous enclosed nodules containing cartilaginous material and chondrocyte clusters with multinucleated giant cells. Chondrometaplasia because of CPPDDD can often be confused with chondroma and synovial chondromatosis. Metaplastic chondrocytes may demonstrate cytologic atypia, which can mimic malignant cartilage tumors and possibly lead to the misdiagnosis of chondrosarcoma. Recognition of the presence of CPPD crystal deposition within the tissue and the associated foreign body granulomatous reaction is essential to arriving at the proper diagnosis of CPPDDD disorders, especially tophaceous pseudogout.
Recognizing the presence of CPPD crystals is essential to properly diagnosing CPPDD disorders. CPPD crystals can be identified microscopically with conventional hematoxylin and eosin (HE) staining.

A pseudogout differential diagnosis may include Wilson’s disease, hemochromatosis, hemophilia, hypothyroidism, arthritis (rheumatoid, infectious, traumatic, and degenerative), amyloidosis, acromegaly, diabetes mellitus, ochronosis, and gout. A tophaceous pseudogout differential diagnosis may include synovial chondromatosis, infectious arthropathies, cholesteatoma, acute otitis, osteoma of the mandible, and parotid neoplasms, as well as malignant lesions, such as chondrosarcoma and chondroidchordoma, and benign lesions, such as chondromas and chondroblastomas. It is essential to rule out chondroid chordoma, benign lesions, and malignant lesions, such as chondrosarcoma and chondroidchordoma, and benign lesions, such as chondromas and chondroblastomas. It is essential to rule out tophaceous pseudogout from the differential diagnosis to avoid unnecessary radical treatment for malignant conditions.

Treatment for pseudogout depends on the clinical manifestation of the condition and the severity of the symptoms. Steroids, colchicines, nonsteroidal anti-inflammatory drugs (NSAIDs), triamcinolone, and acetylsalicylic acid can provide symptomatic relief for acute attacks of pseudogout that involve only the synovium. It has been reported that colchicine can also be used as a prophylactic agent to help prevent acute exacerbations. Arthrocentesis may be used to reduce joint pressure resulting from synovial inflammation as well as to lavage CPPD crystal and inflammatory agents out of the joint space for patients with more severe symptoms. However, the gold standard treatment for tophaceous pseudogout wherein large deposits and mass destruction of peri-articular structures are involved requires surgical excision with copious amounts of irrigation to lavage away any residual CPPD crystals. Residual crystals predispose the patient to recurrence. Mass resections may require grafting or prosthetic devices to reconstruct the joint. Early detection of CPPD crystals greatly improves prognosis as well as decreasing the extent of future surgeries. Proposed treatment for pseudogout is not without some controversy, however. Meul et al and Asconi et al both indicate that the use of NSAIDs as a management tool for pseudogout is contraindicated. However, neither elucidate further on their reasoning for the contraindication.

Pseudogout is an important, although uncommon, systemic disease entity that can affect the temporomandibular joint. Its presentation and management should be considered by those who manage diseases involving the temporomandibular articulation.

REFERENCES

Reprint requests:
Eric Dierks, DMD, MD
Oral and Maxillofacial Surgery Service
Legacy Emanuel Hospital and Health Center
1849 NW Kearney, Suite 300
Portland, OR 97209
eric.dierks@gmail.com.