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# Calcium pyrophosphate dihydrate crystal deposition disease of the temporomandibular joint

**W Smolka[1], N Eggensperger[1], EJ Stauffer-Brauch[2], C Brekenfeld[3], T Iizuka[1]**

[1]*Department of Cranio-Maxillofacial Surgery;* [2]*Institute of Pathology, Department of Clinical Histopathology and Diagnostics;* [3]*Department of Neuroradiology, University of Berne, Berne, Switzerland*

**A case of a 74-year-old woman with calcium pyrophosphate dihydrate crystal deposition disease of the temporomandibular joint (TMJ) is presented. This disease rarely involves the TMJ and is not usually considered in the differential diagnosis of TMJ disorders. To our knowledge, only 23 cases have been reported in the literature and only four without any destructive changes of the condyle as in the present case.**
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## Introduction

Calcium pyrophosphate dihydrate (CPPD) crystal deposition disease is characterized by a crystal-induced synovitis caused by the accumulation of pyrophosphate dihydrate crystals in articular and periarticular tissues. Large joints like the knee, symphysis pubis and wrist as well as the intervertebral discs are most commonly affected. The deposition of CPPD crystals seems to have a definite predilection for fibrocartilage rather than hyaline cartilage (Bencardino and Hassankhani, 2003). Therefore it is surprising that the temporomandibular joint (TMJ), a joint in which fibrocartilage predominates, is rarely affected by CPPD crystal deposition disease. CPPD arthropathy of the TMJ has only been described in 23 cases in the literature (Pritzker *et al*, 1976; de Vos *et al*, 1981; Good and Upton, 1982; Zemplenyi and Calcaterra, 1985; Gross *et al*, 1987; Hutton *et al*, 1987; Kamatani *et al*, 1987; Mogi *et al*, 1987; Lambert *et al*, 1990; Magno *et al*, 1992; Chuong and Piper, 1995; Dijkgraaf *et al*, 1995; Ishida *et al*, 1995; Pynn *et al*, 1995; Kurihara *et al*, 1997; Onodera *et al*, 1997; Vargas *et al*, 1997; Aoyama *et al*, 2000; Osano *et al*, 2003).

In cases of CPPD crystal deposition disease of the TMJ, two kinds of clinical patterns can be found. *Pseudogout* is a term applied to an acute inflammatory attack – similar to a gout attack – causing a painful swelling of the TMJ. Often multiple joints are affected (pseudo-osteoarthritis) (de Vos *et al*, 1981; Hutton *et al*, 1987; Dijkgraaf *et al*, 1995). The second pattern, tumoral calcium pyrophosphate deposition disease (tophaceous pseudogout), occurs without history of acute attacks as preauricular swelling and occasionally malocclusion mimicking a tumor of the TMJ (Ishida *et al*, 1995; Kurihara *et al*, 1997).

Radiologically, calcification of the TMJ disc and joint space as well as destructive processes with erosive changes of the mandible condyle and mass formation in the joint space have been reported in most of the previous cases (Pritzker *et al*, 1976; de Vos *et al*, 1981; Good and Upton, 1982; Gross *et al*, 1987; Hutton *et al*, 1987; Kamatani *et al*, 1987; Mogi *et al*, 1987; Lambert *et al*, 1990; Magno *et al*, 1992; Chuong and Piper, 1995; Dijkgraaf *et al*, 1995; Ishida *et al*, 1995; Pynn *et al*, 1995; Kurihara *et al*, 1997; Osano *et al*, 2003). Only four publications did not report bony destruction of the condyle (Zemplenyi and Calcaterra, 1985; Onodera *et al*, 1997; Vargas *et al*, 1997; Aoyama *et al*, 2000).

We present a rare case of CPPD crystal deposition disease of the TMJ without destructive changes of the condyle. Furthermore, radiological findings were minimal compared with previously reported mass formations observed on computed tomography (CT) scans. In contrast to these minimal radiological findings, severe clinical symptoms occurred. Additionally, the TMJ was the only location affected by the disease.

## Case report

A 74-year-old woman was referred to the Department of Cranio-Maxillofacial Surgery, University Hospital of Berne, Switzerland, complaining of an extremely painful preauricular swelling on the left side. The symptoms

Correspondence: W Smolka, Department of Cranio-Maxillofacial Surgery, University of Berne, Inselspital, CH-3010 Berne, Switzerland. Tel.: +41 31 632 3317; Fax: +41 31 382 0279; E-mail: wenko.smolka@insel.ch
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appeared for the first time in the patient's history. Recurrent meningitis caused by persistent cerebrospinal fluid rhinorrhea had been operated 3 years ago. However, the patient could not remember having had any cranio-facial trauma before. There were no metabolic disturbances such as hyperparathyoidism or diabetes.

On clinical examination there was marked painful preauricular swelling. Interincisal mouth opening was limited to 10 mm. Occlusion was normal. Physical examination showed generalized tenderness of the masticatory muscles on the left side. Non-steroidal anti-inflammatory medication had been used to treat the symptoms previously, without effect. Preoperative workup revealed a normal complete blood count and sedimentation, as well as a normal chemical profile.

In a panoramic radiograph both mandibular condyles showed a normal bony configuration (Figure 1). Magnetic resonance imaging showed a soft tissue swelling around the mandibular condyle of the left TMJ compared with the healthy right side (Figure 2). T2-weighted MR scan showed fluid collection anterior to the left condyle. Edema of the lateral pterygoid muscle was noticed and the muscle was slightly displaced medially by the fluid collection. No degenerative changes of the bony joint surface were observed. On high-resolution axial and coronal CT, the configurations of both the condyle and the glenoid fossa were found to be normal, with a slight anterior displacement of the condylar head. The CT scans revealed calcified mass in the joint space (Figure 3). There were no destructive changes in the bone.

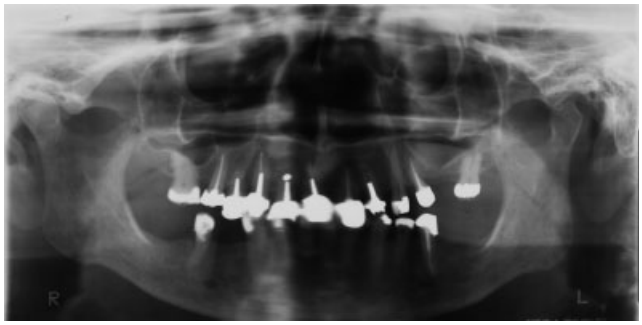

**Figure 1** Panoramic radiograph showing a normal bony configuration of both mandibular condyles

Excision of the lesion was performed under general anesthesia. The left TMJ was exposed via temporopreauricular incision. A gray and white, pus-like mass was removed from the anteromedial aspect of the upper joint space. Smaller portions of the lesion were also curetted from the inferior joint space. Additionally, biopsies were taken from the disc, the lateral joint capsule, and the lateral pterygoid muscle. The articular surface and the condylar head were covered with normal-looking fibrocartilage and the disc also appeared normal in color and texture. Therefore, discectomy was not performed.

The postoperative course was uneventful. The specimens were fixed in 4% formaldehyde and paraffin embedded. Macroscopically, the elastic specimen measured between $0.6 \times 0.4 \times 0.3$ and $1.6 \times 0.7 \times 0.3$ cm and presented a gray to white cut surface. Histological examination showed a chronic inflammation of the synovium and the fibrocartilage with a focal accumulation of birefringent crystal (interference microscopy). The crystal incited only minor cellular reaction (Figure 4). A foreign body giant-cell histiocytic reaction to the crystal was not observed. The routine procedure used in this report (fixation with 4% formaldehyde, parafine embedded and coloration) did not allow other special techniques as infrared spectrophotometry and X-ray diffraction or EDX analyser because of partial dissolution of crystal. The diagnosis of CPPD deposition was made based on the form, size and birefringence of the crystal elements.

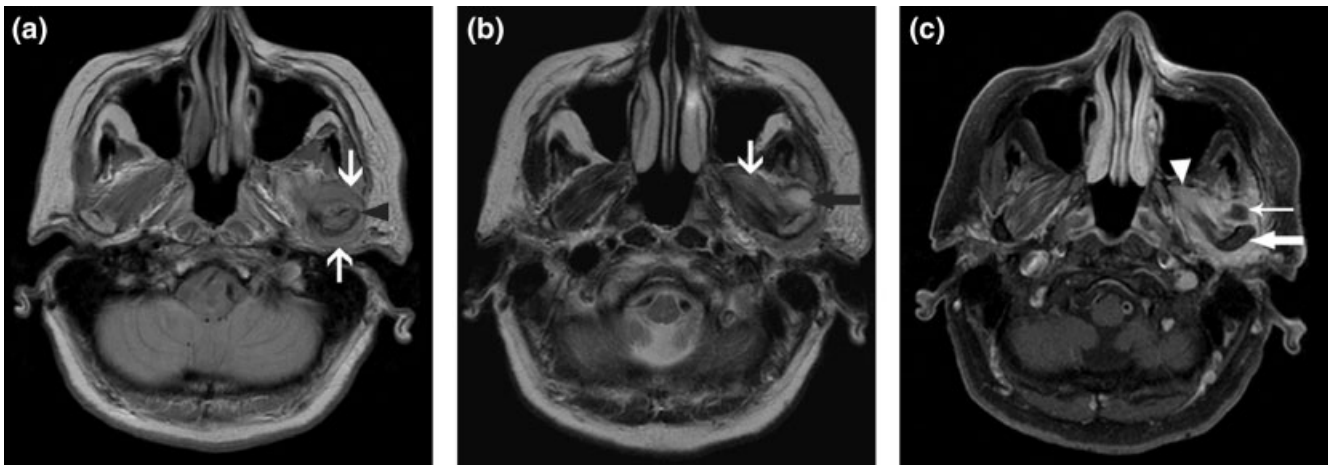


**Figure 2** Magnetic resonance image of axial plane (1.5 Telsa, Gradient-echo, TR 259 ms, TE 9 ms): (**a**) Proton density weighted axial MR scan. Note soft tissue swelling (white arrows) around the mandibular condyle (black arrow head) compared with healthy right side. (**b**) T2-weighted axial MR scan depicts fluid collection (black arrow) and edema of lateral pterygoid muscle (white arrow). (**c**) Contrast enhanced T1-weighted axial MR scan with fat suppression technique. Periarticular soft tissue swelling with strong enhancement that extends into the pterygoid muscles (arrow head) and encloses a fluid collection (small arrow). No bone edema of the condyle (thick arrow)

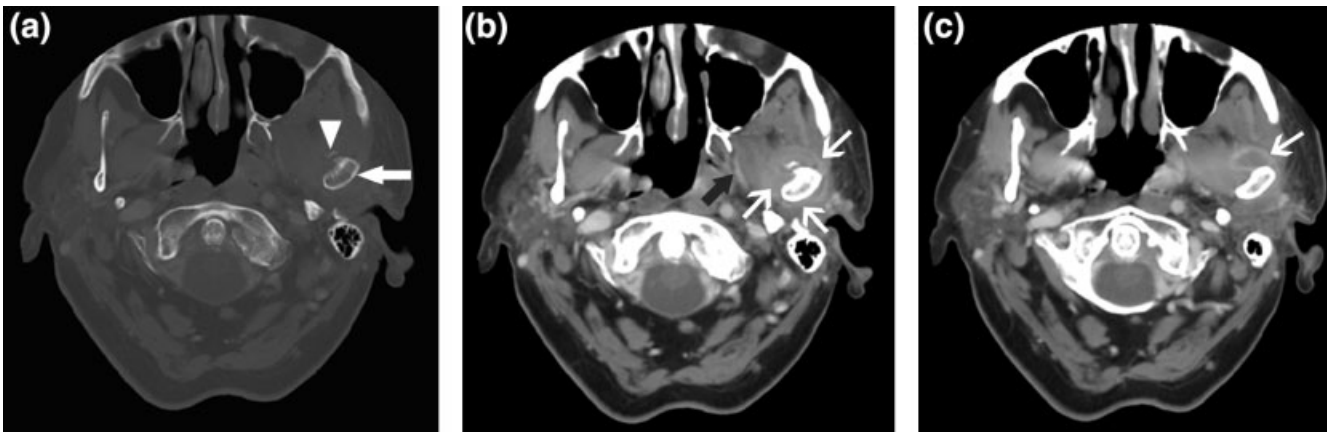


**Figure 3** Computed tomography (CT) of axial plane: (**a**) Axial CT scan of the temporomandibular joint. Bone window depicts soft tissue calcifications (arrow head) ventromedial to the mandibular condyle (arrow) that shows no signs of bone destruction but a ventral osteophyte. (**b**) Axial CT scan at the same level as (**a**). Soft tissue mass (white arrows) around the mandibular condyle with edema of the pterygoid muscles (black arrow). (**c**) Axial contrast enhanced CT at the next level to (**a**) and (**b**). Ring enhancing fluid collection (arrow) ventral to the mandibular condyle

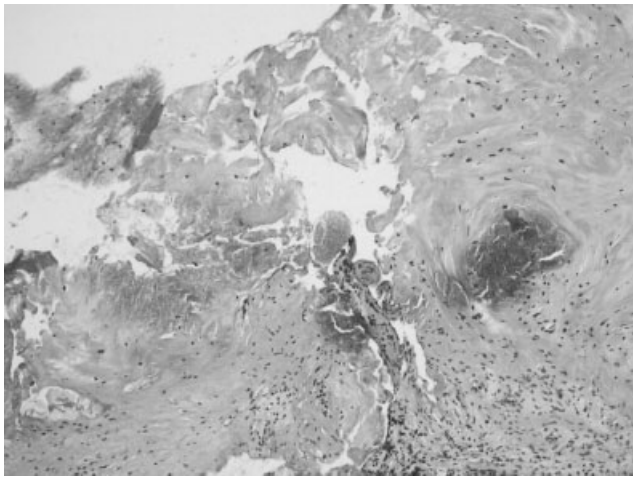

**Figure 4** Histologic section showing aggregations of crystals embedded into fibrocartilage tissue and chronic inflammation (hematoxylin-eosin, original magnification ×10)

Postoperative clinical examination of the other joints, especially the knees and wrists, showed no abnormalities. Radiographs of the extremities and the vertebral column were planned, but did not take place because of the patient's poor compliance. At the 12-month follow-up, no evidence of recurrence at the TMJ was observed. Clinically, mouth opening was 45 mm without any mandibular deviation. No pain, swelling, or clicking or crepitation of the TMJ were evident in the latest follow-up.

## Discussion

A variety of systemic diseases have been associated with CPPD crystal deposition disease, including rheumatoid arthritis and other chronic arthritides, gout, hypomagnesemia, hypothyroidism, amyloidosis, hypophosphatasia, hyperparathyroidism, hemosiderosis, hemochromatosis, and familial hypocalciuric hypercalcemia (Bencardino and Hassankhani, 2003). Furthermore, CPPD crystal deposition disease occurs commonly in elderly women. Decreased sex hormone levels after menopause are suggested to play a causal role in the pathogenesis of pseudogout of the TMJ (Onodera *et al*, 1997). A general correlation between CPPD and localized trauma has also been proposed (Chuong and Piper, 1995). However, the pathogenesis of crystal formation in CPPD crystal deposition disease and its precipitation remain unclear.

It is indicated that synovial fluid inorganic pyrophosphate (PPi) concentrations are consistently elevated in patients with CPPD crystal deposition disease. Articular cartilage chondrocytes uniquely elaborate large amounts of extracellular PPi. Chondrocyte cell membrane proteins, such as cartilage intermediate layer protein, may exhibit activity of the ecto-enzyme nucleotide triphosphate pyrophosphohydrolase (NTPPPH). NTPPPH hydrolyses extracellular adenosine triphosphate (ATP) into monophosphate esters and extracellular PPi. It is suggested that extracellular PPi involved in CPPD crystal formation in joints is derived from hydrolysis of extracellular ATP by NTPPPH. Transforming growth factor $\beta$1 (TGF $\beta$1) has been shown to stimulate extracellular PPi production, whereas insulin-like growth factor 1 (IGF 1) inhibits it.

Although intracellular PPi is a byproduct of many synthetic intracellular reactions, the multipass transmembrane protein Ankyrin is proposed to be an important factor in transport of PPi across the cell membrane and may control egress of intracellular PPi. Therefore it may play a role in CPPD crystal formation. CPPD crystals initiate or amplify cartilage destruction by stimulating mitogenesis of synovial lining cells as well as synthesis and secretion of proteases, prostanoids, and cytokines that have been implicated in cartilage matrix degeneration. This process will end up in bony destruction of the joint (Hirose *et al*, 2002). Destructive changes of the mandible condyle have therefore been described in most previous reports (Pritzker *et al*, 1976; de Vos *et al*, 1981; Good and Upton, 1982; Gross *et al*, 1987; Hutton *et al*, 1987; Kamatani *et al*, 1987; Mogi *et al*, 1987; Lambert *et al*,

1990; Magno *et al*, 1992; Chuong and Piper, 1995; Dijkgraaf *et al*, 1995; Ishida *et al*, 1995; Pynn *et al*, 1995; Kurihara *et al*, 1997; Osano *et al*, 2003). A case without joint destruction such as the present case is rare (Zemplenyi and Calcaterra, 1985; Onodera *et al*, 1997; Vargas *et al*, 1997; Aoyama *et al*, 2000). In all four cases without joint destruction previously reported, the TMJ was the only location of CPPD expression.

The mechanism for mass formation in CPPD crystal deposition disease also remains unclear. However, the presence of masses in CPPD crystal deposition disease of the TMJ is common (Pritzker *et al*, 1976; de Vos *et al*, 1981; Zemplenyi and Calcaterra, 1985; Gross *et al*, 1987; Kamatani *et al*, 1987; Mogi *et al*, 1987; Lambert *et al*, 1990; Magno *et al*, 1992; Chuong and Piper, 1995; Ishida *et al*, 1995; Onodera *et al*, 1997; Vargas *et al*, 1997). The case presented here shows only a small region of calcified material in the joint space.

Although systemic diseases are often associated with CPPD crystal deposition disease, none were observed in the present case. Nor was there a history of trauma which might have triggered the pseudogout of the TMJ. The radiological findings were minimal and no destructive changes of the joint were observed. The TMJ was also the only affected joint. Compared with the previous reports, these findings are extremely uncommon. As the time from onset to definite diagnosis is usually long in CPPD crystal deposition disease of the TMJ, lasting anywhere from several years up to 20 years (Kamatani *et al*, 1987; Mogi *et al*, 1987; Lambert *et al*, 1990; Chuong and Piper, 1995; Ishida *et al*, 1995; Onodera *et al*, 1997), the early identification of the disease might explain the discrete radiological findings in our patient, and the case is suggested to represent an early stage of CPPD crystal deposition disease of the TMJ. The localized TMJ pain and normal findings in panoramic images can mimic internal derangement disease. However, the swelling of the preauricular region easily differentiated the inflammatory disease in our patient from internal derangement.

There are differing opinions about how to treat the disease in the literature. Spontaneous resolution of symptoms of TMJ-CPPD crystal deposition disease without any therapy or with non-operative treatment using non-steroidal anti-inflammatory medications has been reported (Hutton *et al*, 1987). According to an extensive literature review (Aoyama *et al*, 2000), however, the most common therapy is temporomandibular arthrotomy. Although conservative treatment of CPPD crystal deposition disease is possible (Alcantara *et al*, 1998), an open biopsy is necessary for definite diagnosis. When only the TMJ is involved and there is no destruction of the joint structure, as in the case reported here, a careful removal of the lesion seems to be a suitable treatment option.

## References

Alcantara J, McDaniel JW, Plaugher G, Alcantara J (1998). Management of a patient with calcium pyrophosphate deposition disease and meniscal tear of the knee: a case report. *J Manipulative Physiol Ther* **21:** 197–204.

Aoyama S, Kino K, Amagasa T, Kayano T, Ichinose S, Kimijima Y (2000). Differential diagnosis of calcium pyrophosphate dihydrate deposition of the temporomandibular joint. *Br J Oral Maxillofac Surg* **38:** 550–553.

Bencardino JT, Hassankhani A (2003). Calcium pyrophosphate dihydrate crystal deposition disease. *Semin Musculoskelet Radiol* **7:** 175–185.

Chuong R, Piper MA (1995). Bilateral pseudogout of the temporomandibular joint: report of case and review of literature. *J Oral Maxillofac Surg* **53:** 691–694.

Dijkgraaf LC, Liem RS, de Bont LG, Boering G (1995). Calcium pyrophosphate dihydrate crystal deposition disease: a review of the literature and a light and electron microscopic study of a case of the temporomandibular joint with numerous intracellular crystals in the chondrocytes. *Osteoarthritis Cartilage* **3:** 35–45.

Good AE, Upton LG (1982). Acute temporomandibular arthritis in a patient with bruxism and calcium pyrophosphate dihydrate deposition disease. *Arthritis Rheum* **25:** 353–355.

Gross BD, Williams RB, DiCosimo CJ, Williams SV (1987). Gout and pseudogout of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol* **63:** 551–554.

Hirose J, Ryan LM, Masuda I (2002). Up-regulated expression of cartilage intermediate-layer protein and ANK in articular hyaline cartilage from patients with calcium pyrophosphate dihydrate crystal deposition disease. *Arthritis Rheum* **46:** 3218–3229.

Hutton CW, Doherty M, Dieppe PA (1987). Acute pseudogout of the temporomandibular joint: a report of three cases and review of literature. *Br J Rheumatol* **26:** 51–52.

Ishida T, Dorfman HD, Bullough PG (1995). Tophaceous pseudogout (tumoral calcium pyrophosphate dihydrate crystal deposition disease). *Hum Pathol* **26:** 587–593.

Kamatani Y, Tagawa T, Hirano Y, Nomura J, Murata M (1987). Destructive calcium pyrophosphate dihydrate temporo-mandibular arthropathy (pseudogout). *Int J Oral Maxillofac Surg* **16:** 749–752.

Kurihara K, Mizuseki K, Saiki T, Wakisaka H, Maruyama S, Sonobe J (1997). Tophaceous pseudogout of the temporomandibular joint: report of a case. *Pathol Int* **47:** 578–580.

Lambert RG, Becker EJ, Pritzker KP (1990). Case report 597: calcium pyrophosphate deposition disorder (CPPD) of the right temporomandibular joint. *Skeletal Radiol* **19:** 139–141.

Magno WB, Lee SH, Schmidt J (1992). Chondrocalcinosis of the temporomandibular joint: an external ear canal pseudotumor. *Oral Surg Oral Med Oral Pathol* **73:** 262–265.

Mogi G, Kuga M, Kawauchi H (1987). Chondrocalcinosis of the temporomandibular joint. Calcium pyrophosphate dihydrate deposition disease. *Arch Otolaryngol Head Neck Surg* **113:** 1117–1119.

Onodera K, Ichinohasama R, Saito M, Ooya K (1997). A case of the calcium pyrophosphate dihydrate (CPPD) deposition disease without condylar destruction of the temporomandibular joint. *Pathol Int* **47:** 622–626.

Osano H, Matsumoto K, Kusama M (2003). Calcium pyrophosphate dihydrate arthropathy with condylar destruction of the temporomandibular joint. *J Oral Sci* **45:** 223–226.

Pritzker KP, Phillips H, Luk SC, Koven IH, Kiss A, Houpt JB (1976). Pseudotumor of temporomandibular joint: destructive calcium pyrophosphate dihydrate arthropathy. *J Rheumatol* **3:** 70–81.

Pynn BR, Weinberg S, Irish J (1995). Calcium pyrophosphate dihydrate deposition disease of the temporomandibular joint. A case report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **79:** 278–284.

Vargas A, Teruel J, Trull J, Lopez E, Pont J, Velayos A (1997). Calcium pyrophosphate dihydrate crystal deposition disease presenting as a pseudotumor of the temporomandibular joint. *Eur Radiol* **7:** 1452–1453.

de Vos RA, Brants J, Kusen GJ, Becker AE (1981). Calcium pyrophosphate dihydrate arthropathy of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol* **51:** 497–502.

Zemplenyi J, Calcaterra TC (1985). Chondrocalcinosis of the temporomandibular joint: A parotid pseudotumor. *Arch Otolaryngol* **111:** 403–405.