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CASE REPORTS

Periarticular calcium pyrophosphate deposition disease in a young patient: a case report

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Abstract

Background. Calcium pyrophosphate deposition disease (CPPD) is an arthropathy that affects the synovium and periarticular tissues. More often, persons aged over 50 years old suffer from this disease. CPPD pathogenesis is not yet completely understood. In younger patients, the suspicion of familial predisposition or a metabolic disease is raised. Imaging tests and aspirate analysis from tendon in optical microscopy are essential for establishing an accurate positive diagnosis.

Case presentation. We report a case of a 45-year-old female patient, without significant personal pathological history, with atypical periarticular location of calcium pyrophosphate deposition in the supraspinatus tendon. This deposition was evidenced by X-ray and ultrasound, and then confirmed by the analysis of the aspirate from the tendon, in optical microscopy. The patient received nonsteroidal anti-inflammatory drugs, physiotherapy of the shoulder, local infiltration with betamethasone and lidocaine, with a favorable evolution.

Conclusions. This case is a rare one due to the following particularities: the patient has an age below the average age for this pathology; the atypical location of a single calcium pyrophosphate deposition in the supraspinatus tendon, a tendon that is usually correlated with hydroxyapatite deposition. The presented case highlights the importance of imaging examinations and aspirate analysis using optical microscopy in establishing the positive diagnosis of calcium pyrophosphate deposition disease.

Key words: calcium pyrophosphate deposition disease, supraspinatus tendon, imaging tests, optical microscopy, young patient

Background

Calcium pyrophosphate deposition disease (CPPD) is an arthropathy that affects the synovium and, more rarely, periarticular tissues (Rosales-Alexander et al., 2014). CPPD pathogenesis is not yet completely understood, but it is known that the first stage in the development of the disease is represented by the formation of calcium pyrophosphate crystals, especially in the cartilage pericellular matrix and to a lesser extent, in non-cartilaginous tissues (Rosenthal & Ryan, 2016).

CPPD is rarely found under the age of 50 (Neame, 2003). Studies have shown that aging is a major risk factor, so that after the age of 50, the disease incidence increases significantly. Under the age of 45, the suspicion of familial predisposition or a metabolic disease is raised (Felson, 1989).

The clinical presentation of CPPD includes four phenotypes: acute (self-limited synovitis, previously known as "pseudogout"), chronic, associated with arthrosis, and asymptomatic. The term "chondrocalcinosis" refers to cartilage calcification evidenced by imaging methods or histological examination (Zhang et al., 2011; Abhishek, 2016; Tedeschi et al., 2019). Periarticular location is more rarely reported in the literature, the described cases occurring in the tendons of the triceps,

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quadriceps, gastrocnemius muscles, in the Achilles tendon, and to a lesser extent, in the shoulder rotator cuff tendons (Steinbach, 2004).

CPPD diagnosis is confirmed by aspirate analysis which should evidence weakly positively birefringent crystals of rhomboid or rectangular shape, unlike the monosodium urate crystals in the form of needles with negative birefringence observed in gout (Rosales-Alexander et al., 2014; Iqbal et al., 2019).

Case presentation

A 45-year-old female patient, without significant personal pathological history, presented in April 2016 to the ambulatory service of the Clinical Rehabilitation Hospital for mixed pain in the left shoulder (at rest and during exercise), starting six weeks before. The patient had not performed sustained physical effort that might have been correlated with the development of symptoms, and had no trauma to the left shoulder. After administration of nonsteroidal anti-inflammatory drugs (NSAIDs) and analgesics, pain persisted and worsened towards the end of March.

On clinical examination, an increase in pain during movement and limited mobility were observed, with pain worsening when regaining the initial position, and internal and external rotation impossible to perform.

The patient was informed about her health condition, the medical interventions proposed and associated risks, as well as about diagnosis, treatment and prognosis. According to Romanian legislation, the patient's written informed consent was obtained.

Left shoulder X-ray evidenced the presence of periarticular calcifications anatomically corresponding to the supraspinatus tendon/subacromial-subdeltoid bursa (Fig. 1).

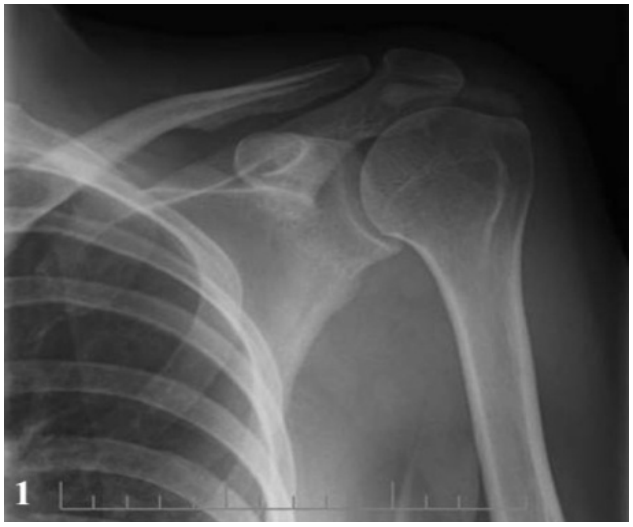

Fig. 1 – Left shoulder X-ray in anteroposterior view indicates periarticular calcification (a relatively well delimited, homogeneous mass, yet having a cloud-like appearance, supporting the subacute/chronic nature).

Left shoulder ultrasound of the supraspinatus tendon showed in longitudinal and transverse view a hyperechoic, inhomogeneous and well delimited area of 1.9 cm by 1.33 cm, with subacromial subdeltoid impingement syndrome. Power Doppler ultrasound indicated no vascularization. (Fig. 2).

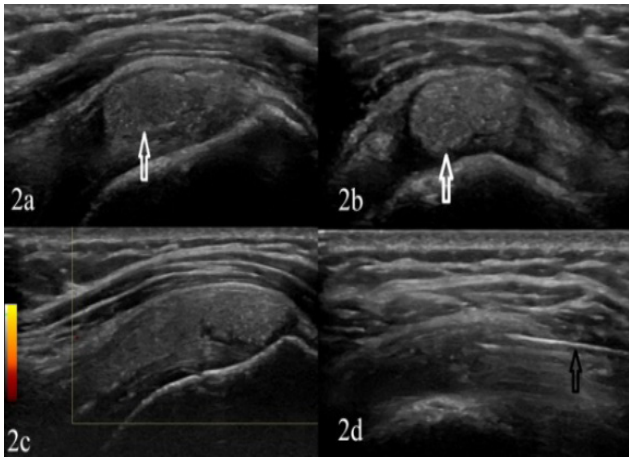

Fig. 2 – Ultrasound image of the supraspinatus tendon acquired in longitudinal and transverse view; **2a, 2b.** Hyperechoic, inhomogeneous, well-defined area; **2c.** Power Doppler ultrasound showing no vascularization; **2d.** The puncture needle during intratendinous calcification aspiration (black arrow).

Biologically, mild inflammatory syndrome was observed (1 h ESR = 20 mm/h, 2 h ESR = 38 mm/h). Laboratory tests did not identify a metabolic cause for CPPD.

Diagnosis was confirmed by the analysis of the aspirate from the supraspinatus tendon. Macroscopically, it had a white-yellowish, chalky, flocculent appearance (Fig. 3a). Microscopically, the material was processed by paraffin embedding. In routine staining, the material was formed by amorphous eosinophilic deposits, with small or even large dystrophic basophilic calcifications, without association of inflammatory infiltrate. In Congo red staining, no amyloid deposits were detected. Histological appearance suggested supraspinatus tendon chondrocalcinosis. The bacteriological examination of the aspirate was negative.

Polarized light optical microscopy using Alizarin red staining evidenced birefringent rectangular crystals (Fig. 3b), indicating the diagnosis of calcium pyrophosphate deposition disease. For this staining procedure, the following stages were performed: display of the aspirate on the slide, 10% formol fixation for 1 minute, application of 0.5% alizarin solution for 5-20 minutes, incubation of the slide at 40-50°, dehydration with acetone for 30 seconds and with a mixture of acetone and xylene in equal parts for 30 seconds. Transmission electron microscopy evidenced crystals about 0.5 μm long (Fig. 3c).

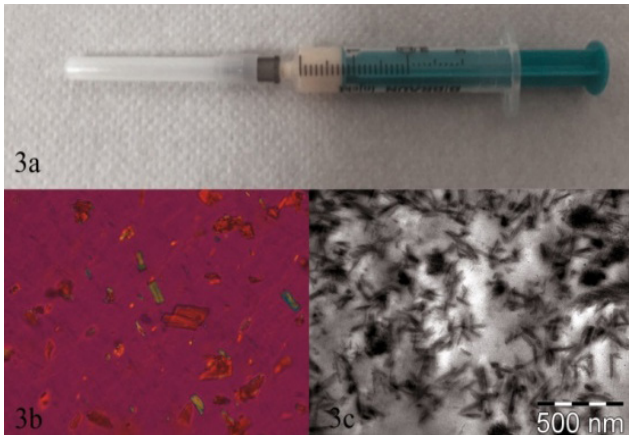

Fig. 3 – 3a. Macroscopic white-yellowish, chalky appearance of the aspirate; 3b. Polarized light optical microscopy using Alizarin red staining evidences positively birefringent rectangular crystals; 3c. Electron microscopic image with crystals of variable sizes (TEM x 80,000).

Locally, betamethasone and lidocaine were concomitantly administered. In addition, the patient received nonsteroidal anti-inflammatory injections, physiotherapy of the shoulder, kinesiotherapy and massage of the paravertebral cervical spine and left shoulder.

Evaluation of the patient after one month evidenced improvement of pain (on the visual analogue scale from the initial value of 8 to 3) and of shoulder range of motion (active abduction improved from 55 degrees to 110 degrees).

Discussion

It is known that CPPD is rare among persons younger than 50 years of age; its presence under the age of 45 raises the possibility of familial predisposition or a metabolic disease (hemochromatosis, hyperparathyroidism, hypomagnesemia, Wilson's disease, hypothyroidism, gout, acromegaly) (Joshi et al., 2017**).** Given that laboratory tests were negative for a metabolic cause in a patient without a suggestive family history, the presented case can be included in the category of sporadic, rare cases in the literature (Zhang et al., 2011).

In the second place, periarticular involvement is rarely found in the case of CPPD. The literature describes the involvement of the triceps muscle tendons and Achilles tendon (Steinbach, 2004), as well as of the quadriceps and gastrocnemius muscles (Yang et al., 1996). A particularity of the case is therefore the location in the supraspinatus tendon, usually correlated with hydroxyapatite deposition (Chiou et al., 2009; Pereira et al., 2015).

The presented case highlights the importance of imaging examinations and aspirate analysis in establishing the diagnosis of CPPD. Compared to the nodular appearance of the calcium hydroxyapatite deposition, intratendinous calcification with calcium pyrophosphate deposition disease is linear or punctate (Steinbach, 2004). The imaging characteristics of this case are however particular compared to the ones found in the literature, also considering that ultrasound assessment detected hyperechoic spots in the supraspinatus tendon of other patients with CPPD disease (Filippucci et al., 2013; Filippou et al., 2018).

Since the aspirate contained tissue (supraspinatus tendon), Alizarin red staining was used to identify calcium pyrophosphate crystals. Routine hematoxylin-eosin staining has a low probability of evidencing birefringent crystals because of the reagent dissolution of the crystals. Studies have proven that using Alizarin red staining does not affect crystals (Yamakawa et al., 2003).

The primary "take-away" lesson from this case presentation is that CPPD can occur in rare locations, such as the supraspinatus tendon, in young patients, despite the absence of a familial predisposition or a metabolic disease; imaging tests and aspirate analysis are essential for establishing an accurate positive diagnosis.

Conclusions

1. In the case of atypical localization of calcifications, we should not exclude the calcium pyrophosphate deposition disease.
2. In this case, paraclinical investigations proved to be highly useful in establishing the etiopathogenetic diagnosis and the therapeutic conduct.

Conflicts of interest

There are no conflicts of interest.

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