Case Report

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Others Section

Calcium Pyrophosphate Deposition Disease in the Craniovertebral Junction: An Unusual Cause of Neck Pain

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ABSTRACT

Crowned Dens Syndrome (CDS) is a rare manifestation of Calcium Pyrophosphate Deposition (CPPD) disease characterised by calcification around the odontoid process in the atlantoaxial joint. It manifests as intense neck pain with signs of systemic inflammation, including elevated acute phase reactants. Thus, it can simulate other causes of neck pain and diagnosis can be challenging. Moreover, CPPD disease can be asymptomatic and observed as radiological finding. Here in, two cases of spinal CPPD disease with distinct presentations are reported. The first of 83-year-old woman describes CDS that was misdiagnosed as Polymyalgia Rheumatica (PMR) whereas in the second case of 70-year-old female calcification around the odontoid process was incidentally found in a patient with acute cervical spine fracture. These two reported cases highlight the spectrum of manifestations of spinal CPPD disease and support the notion that careful discrimination of the cause of neck pain is essential for improving outcomes.

Keywords: Cervical spine, Chondrocalcinosis, Ligament calcification, Odontoid process

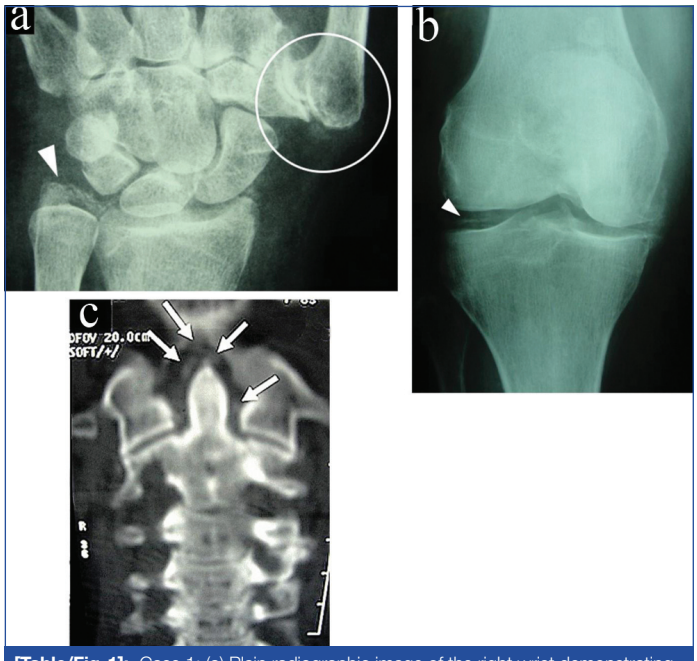
CASE REPORT

Case 1

An 83-year-old female, with diabetes mellitus and hypothyroidism presented with intense pain and increasing morning stiffness lasting at least one hour involving neck, shoulders and interscapulovertebral area since two weeks. She complained of limited cervical range of motion, but with slight improvement during the day. She had no fever, weight loss, headache, jaw claudication, visual complaints, or arthritis, or similar previous episodes of neck pain. Clinical examination revealed local tenderness in occipital region and posterior area of the neck along with severe global restriction of cervical spine movements.

Laboratory tests evidenced Erythrocyte Sedimentation Rate (ESR) 120 mm/h, C-Reactive Protein (CRP) 14.5 mg/dL, creatinine 1.68 mg/dL and Blood Urea Nitrogen (BUN) 65 mg/dL. Complete blood count, glucose, calcium, phosphorus, magnesium, parathormone, ferritin, liver enzymes, plasma protein electrophoresis and thyroid function were normal. Magnetic Resonance Imaging (MRI) of spine showed only degenerative structural changes, some disc protrusions, without evidence of nerve compression, tumor lesions or higher intensity areas in soft tissue around the vertebrae in T2 image. Age adjusted cancer screening results negative, including mammography, oncotic colpocytology, upper digestive endoscopy, colonoscopy, thyroid ultrasound and chest and abdomen Computed Tomography (CT) scans. The diagnosis was PMR based on clinical characteristics keeping in mind the factors like advanced age and neck and shoulder girdle pain associated with increased ESR without any other apparent cause. Prednisone was started at a dose of 20 mg (0.5 mg/kg) once daily.

After eight days, the patient still reported moderate pain and the rheumatology team was asked to reassess the diagnosis. At the rheumatologic clinic, physical examination showed severe limitation of neck rotation, in addition to partially decreased range of motion of the shoulders due to pain, including resisted movements. Also, coarse crackles and synovitis in the knees, Heberden and Bouchard nodes and synovitis in wrists were observed. There were no sensory or motor abnormalities, cranial nerves dysfunction or meningeal irritation signs. Peripheral radiographs showed signs of tibiofemoral osteoarthritis (Kellgren-Lawrence grade III), bilateral exuberant degenerative changes of first carpometacarpal joints, with involvement of proximal and distal interphalangeal joints and bilateral hallux valgus. Furthermore, there were linear calcifications of the triangular fibrocartilage in wrists and in cartilage of both knees [Table/Fig-1a,b]. A CT scan of the cervical spine, with 3D reconstruction of C1-C2, revealed calcifications in the atlantoaxial joint, surrounding the odontoid, with more continuous crystal deposits in cruciform ligament [Table/Fig-1c], in addition to degenerative structural changes like those seen in the MRI. Rheumatoid factor and anti-cyclic Citrullinated Peptide (CCP) antibodies were negative. Thus, the acute onset of pain, significant



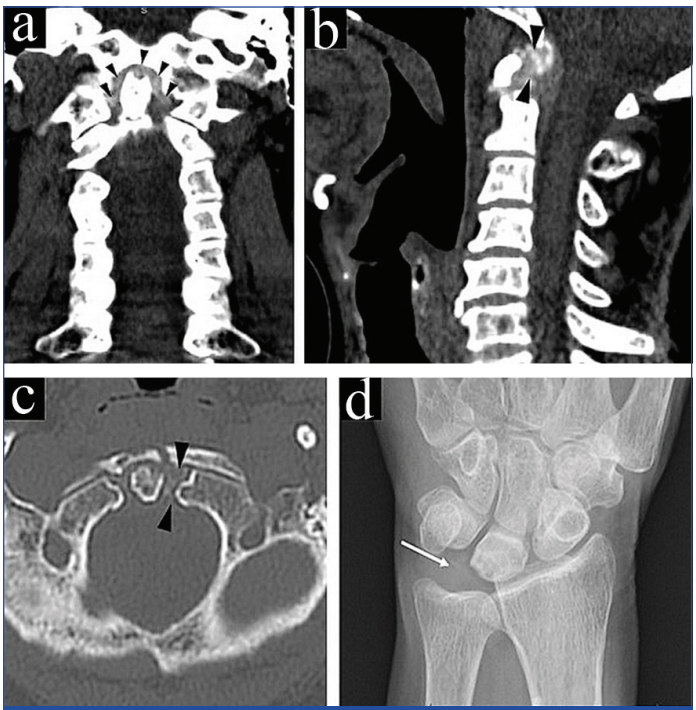
[Table/Fig-1]: Case 1: (a) Plain radiographic image of the right wrist demonstrating the presence of linear deposits of calcium pyrophosphate crystals in the carpal triangular ligament (white arrowhead) and exuberant rhizoarthrosis (white circle); (b) Linear calcification in the knee (white arrowhead); (c) Computed Tomography of the cervical spine showing deposits of calcium pyrophosphate crystals around the odontoid process (white arrows).

loss of cervical spine rotation and peripheral arthritis in the presence of radiographic calcifications forwarded the rheumatology team to review the diagnosis. Therefore, symptoms were attributed to these findings and CDS was diagnosed. Prednisone was maintained, and colchicine 0.5 mg twice daily was added. Pain was diminished and the cervical spine mobility was recovered to be in a normal range. After five days, there was complete resolution of symptoms.

Case 2

A 70-year-old female with no co-morbidities or spine pain was admitted to the hospital due to direct neck trauma from falling down a ladder two days ago. The patient reported severe neck pain with no complaints. Osteoarticular examination showed only Heberden nodes. Deficits in sensory and motor systems were not detected on neurological examination. Age adjusted ESR and CRP levels were not elevated (1.96 mg/dL and ESR 22 mm/h, respectively). No other abnormalities on basic laboratory tests, including blood count, renal function and electrolytes, were detected. Spine CT showed fractures of the anterior C1 arch and odontoid process. In addition, there were periarticular calcifications surrounding the dens, but no signs of acute inflammation [Table/Fig-2a-c]. Because of these findings on CT scan, radiographs of the hands, wrists and knees were obtained. These examinatons revealed calcifications in the carpal triangular fibrocartilages [Table/Fig-2d], although the patient had no history of arthritis. Spine MRI revealed bone oedema close to the fractured area, suggesting acute lesion, as well as degenerative changes, without spinal cord injury. Also, there was no evidence of synovitis, joint effusion, or soft tissue oedema. No surgical treatment of fracture was indicated after orthopaedic evaluation.

Patient was treated with dipyrone 1 g Q6h, tramadol 100 mg Q8h and cyclobenzaprine 5 mg once a day, with significant pain relief. Thus, pain was attributed to the fracture, whereas CPPD was probably just a radiological finding in cervical spine. The patient was discharged from the hospital five days after admission with recommendation for the use of cervical collar, analgesics, and physical rehabilitation. At the follow-up visit three months later, she had little residual pain and minimal limitation of cervical movements.



[Table/Fig-2]: Case 2: (a-c) Computed tomography of the cervical spine depicting calcifications in the atlantoaxial joint, surrounding the odontoid process in coronal (a), sagittal (b) and axial (c) planes (black arrowheads). Fracture of the odontoid process and of the anterior C1 arch (c); (d) Plain radiographic image of the right wrist with chondrocalcinosis in the carpal triangular ligament (white arrow).

DISCUSSION

The CDS is characterised by acute neck or shoulder pain and stiffness due to calcification in structures surrounding the odontoid process caused by crystal deposition, mostly calcium pyrophosphate dihydrate but also hydroxyapatite. It usually affects individuals aged over 50 years and is more common in females [1]. The diagnosis is a challenge because symptoms can mimic other diseases, such as PMR (as in the first case), meningitis, ankylosing spondylitis [2], Giant Cell Arteritis (GCA) [2,3], osteomyelitis [4], rheumatoid arthritis [5], gout [6] and metastatic bone disease [7].

Most subjects with CDS have cervical pain lasting a few days to years before diagnosis [2,3,8]. Elevated acute phase reactants were a frequent finding in these patients [2,3,8]. In a recently published series of 24 cases, elevated inflammatory markers were observed in 19 cases (79%) [8]. In many reports, ESR is reported to reach values close to 100 mm/h [2,3,8], like the first case presented here.

Differentiating CDS from GCA or PMR can be challenging since these share similar features, such as age of onset, presence of new onset headache, shoulder pain, constitutional symptoms, and peripheral arthritis [2,3,8-10]. However, absence of visual complaints, jaw claudication, or pain upon temporal artery palpation, especially in the presence of peripheral radiological evidence of chondrocalcinosis, are more suggestive of CPPD disease than other diagnosis [1,2,8]. The occurrence of relapses in PMR patients could be the opportunity to look for cervical CPPD, if not firstly detected. A study showed cervical CPPD predictors in patients with PMR-like symptoms: age over 70 years at diagnosis, arthritis (especially ankles), tibiofemoral osteoarthritis and tendinous calcifications, most commonly in the rotator cuff tendons and the quadriceps tendon [3]. In addition, neck rotation is remarkably restricted because this is the main role of the atlantoaxial joint [3]. The woman in the first case had advanced age, peripheral arthritis with radiological evidence of calcifications, and advanced osteoarthritis, as well as severe restricted neck rotation, fitting the high risk profile for atlantoaxial CPPD. In addition, since PMR commonly presents with a subacute or insidious onset of pain and there is usually prompt improvement of symptoms within 24-72 hours after starting glucocorticoid, the acute pattern of pain and the absence of rapid clinical response to prednisone in the first patient supports other diagnosis rather than PMR. The patient noticed substantial improvement of the symptoms after longer use of prednisone (more than 3-5 days) combined to colchicine.

However, as in other sites of CPPD, spine calcifications can be an incidental image finding in patient without pain or with pain due to other causes [1,11]. Hereby, authors reported a female with spinal ligament calcifications found in image scans upon admission to neurosurgical ward due to acute spine fracture. In a series of 554 subjects submitted to CT at admission to a neurosurgical ward, odontoid calcifications were found in 15.9%. Only 12.5% of those with calcifications developed CDS [11]. It suggests that CPPD is usually asymptomatic in the spine.

Therefore, chondrocalcinosis in imaging studies does not rule out other diseases. In the first case reported, main causes of neck pain were ruled out and the symptoms could be properly attributed to CPPD. In the second case, despite of calcifications, the cause of neck pain must have been the traumatic vertebral fracture.

The CT imaging at the C1-C2 level is superior to MRI to identify calcifications, especially when they are small, as observed in the reported cases. Typical findings of calcification surrounding the dens are radiopaque densities in the shape of halo or crown [11,12]. However, MRI can add important information for diagnosis, such as presence of synovitis/arthritis and soft tissue oedema in the atlantoaxial joint, which are relevant signs to reinforce the

CDS diagnosis. In the second case, MRI was fundamental for the correct diagnosis of the patient, since it did not demonstrate the joint inflammation, but only bone oedema surrounding the traumatic injury which allowed to characterise acute fracture.

CONCLUSION(S)

The CPPD disease of the spine may have entirely different clinical presentations, from asymptomatic radiological finding to intense neck pain associated with elevation of inflammatory markers. It must be considered in the differential diagnosis of neck pain in elderly patients, especially in the presence of severe restriction of neck rotation along with peripheral chondrocalcinosis or advanced osteoarthritis. The two cases reported here, highlight the spectrum of manifestations of spinal CPPD disease and supports the notion that careful discrimination of the cause of neck pain is essential for improving outcomes.

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