

Calcium Pyrophosphate Dihydrate (CPPD) Crystal Deposition Disease, Crowned Dens Syndrome (CDS) and Its Mimicries: Case Report

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ABSTRACT

Headache is one of the most encountered presentations worldwide. Hence, the approach in which practitioners take in investigating, diagnosing and managing it is crucial given the high complication rates from secondary causes seen more commonly in the elderly population. We discuss a case of a patient with chronic headaches, features of occipital neuralgia and neck pain who was eventually diagnosed with Crowned Dens Syndrome (CDS). We intend to highlight this unique presentation of Calcium Pyrophosphate crystal deposition (CPPD) disease in the spine and the need to consider a broad range of differentials especially in an elderly individual presenting with headaches.

Keywords: Acute Headaches, Headaches in Elderly, Calcium Pyrophosphate Dihydrate Crystal Deposition, Crowned Dens Syndrome, Cervical Arthropathy

Introduction

An elderly lady presented to her geriatrician with chronic headaches, occipital neuralgia and neck pain. Headache is a relatively common presentation and it is key to rule out common secondary causes (infection, cerebrovascular accidents, rheumatological and malignancies) before considering rarer differentials such as CDS (Kaniecki and Levin, 2019). CDS involves the deposition of CPPD crystals around the odontoid process which leads to inflammation within the joint (Bouvet *et al.*, 1985).

Case

An 88-year-old lady presented with chronic headaches. Her co-morbidities include short term memory deficits, systolic hypertension, aortic regurgitation, osteoarthritis and recurrent syncopal episodes secondary to orthostatic hypotension. Over the last 2-3 weeks, she noticed a worsening of her chronic headaches and reported sharp throbbing pains which began in the occipital region. It radiated to the frontal region and was also accompanied by neck pain. She denied pain radiating to the arm, sensory

or motor deficits. Aggravating factors included activities which require a forward flexion of the neck (e.g., reading and knitting). She reported no other neurological or constitutional symptoms (fever, loss of weight or a loss of appetite). There was also no trauma to the surrounding region, history of malignancy or infections. She denied joint stiffness, muscle weakness or a history of inflammatory arthritis.

On physical examination, she was alert and orientated (Glasgow Coma Scale of 15) with a normal inspection of the cervical spine region. Palpation of the cervical paravertebral region elicited tenderness, especially around the C2-C5 region. A normal cervical spine range of motion was established with occasional crepitus and no pain on movement. A Spurling's test was negative and no neurological deficits (motor or sensory) were identified including negative Kernig and Brudzinski signs.

Laboratory investigations were almost normal with an Erythrocyte Sedimentation Rate (ESR) of 12 mm/h and a borderline elevated C-Reactive Protein (CRP) of 5 mg/dL. The initial imaging of choice included a Magnetic Resonance Imaging (MRI) scan and carotid ultrasonography, both of which were reported as normal. However, a Computed Tomography (CT) scan of her spine demonstrated calcification of the periodontal transverse ligament, posterior longitudinal ligament and ligamentum flavum at the region of C2/C3 and C3/C4 consistent with CPPD disease. There were minor degenerative changes and osteophytes reported in the C4-C7 region with narrowing of the left C6 neural foramen causing impingement (Fig. 1 and Fig. 2).



Figure 1: Non-contrast Coronal CT demonstrating CPPD deposition of the ligaments in a circular or crowned appearance (green arrow) consistent with CDS.

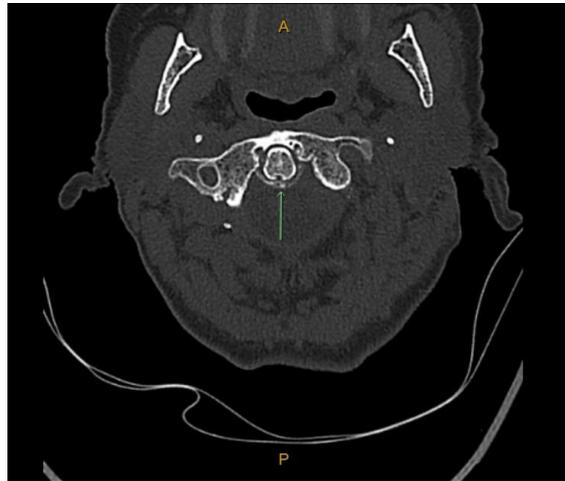


Figure 2: Axial CT showing transverse ligament calcification (green arrow) consistent with CPPD disease.

Management included pain relief (Nonsteroidal anti-inflammatory drugs (NSAIDs) and Paracetamol) and heat packs. Thereafter, she reported good improvement of her symptoms with a reduction in pain scores and an improved quality of sleep. She was then referred on to the physiotherapist for commencement of neck mobility exercises.

Discussion

Headache is a common complaint seen in any healthcare setting. When approaching a presentation of such, especially acutely, it is important to rule out red flags such as infections (meningitis, epidural abscesses and osteomyelitis), cerebrovascular accidents, rheumatological causes (giant cell arteritis or polymyalgia rheumatica), primary musculoskeletal degenerative conditions or worse yet malignancies (primary or metastatic) before making a diagnosis of primary headaches (Kaniecki and Levin, 2019). Despite the fact that primary headaches remain $\frac{2}{3}$ of the cause, elderly individuals are 12 times more likely to have serious underlying pathologies which may present differently as compared to the younger population (Kaniecki and Levin, 2019). Other less common differentials, such as crystal deposition, should be considered once life-threatening causes have been ruled out.

Crystal arthropathy of the spine is less commonly heard of as deposition is mostly seen in the peripheries. The reason behind its deposition in the spine is still not well established and has been attributed to tissue changes such as necrosis, injuries or degeneration (Hsu *et al.*, 2002). Additionally, de novo deposition is relatively common in individuals >65 years old (Mikhael *et al.*, 2013). Examples of crystal arthropathies of the joint and soft tissue include gout which is caused by monosodium urate (MSU), CPPD, calcium oxalate and basic calcium phosphate (Rubenstein and Pritzker, 1989). Gout is said to more commonly affect the lumbar spine while CPPD deposits in the thoracic region. Presentations of both could vary from minimal (cervical myelopathy and radiculopathy) to severe (spinal stenosis and

cauda equina syndrome) (Lam *et al.*, 2007). To date, there have been no reports of basic calcium phosphate deposition in the spine. Ideally, the diagnosis of spinal gout is made by identifying negatively birefringent MSU crystals on fine needle aspiration cytology or biopsy as imaging findings may be non-specific and could mimic infections and metastasis (Jegapragasan *et al.*, 2014; Chan *et al.*, 2009) There has been emerging evidence on the use of Dual Energy Computed Tomography (DECT) scans in diagnosing gout peripherally; however, there is no validated data regarding its use in regions such as the shoulders, hip, spine and pelvis (Chou *et al.*, 2017).

Several case reports of gout and pseudogout in the spine have demonstrated clinical (acute onset of fever, back pain and neurological deficits), laboratory (elevated inflammatory markers) and radiological findings which closely mimic infections such as pyogenic spondylitis (Mikhael *et al.*, 2013, Bridges *et al.*, 2017). Although osteomyelitis typically presents acutely, it is important to be mindful of chronic and tuberculous osteomyelitis which is slow and indolent (Yoshikawa and Cunha, 2002).

First described by Bouvet. *et al.* in 1985, CDS, as the name implies, is a crowned shaped deposition of CPPD crystals around the odontoid process (ligaments, synovial membrane and articular capsule) causing inflammation within the joint (Bouvet *et al.*, 1985; Goto *et al.*, 2007). A retrospective study looking into incidental calcium deposition on CT scans showed that odontoid calcifications were present in 15.9% of patients. However, only 12.5% were symptomatic (Sano *et al.*, 2018).

CPPD arthropathy is commonly seen in patients of increasing age, prior injuries and surgeries. It is also associated with osteoarthritis, chronic kidney disease and endocrine disorders (haemochromatosis, hypomagnesemia, hyperparathyroidism, hypophosphatemia, Wilson's disease and familial hypocalciuric hypercalcemia) (Rosenthal, 2020). The above mentioned should be screened for in patients aged <60 years who present with florid polyarticular CPPD. Although there are hereditary predispositions to CPPD arthropathy, the most common is the sporadic form (Rosenthal and Ryan, 2016).

In acute CPPD arthritis, patients typically present with mono- or oligoarthritis, inflammatory and constitutional symptoms mimicking gout or septic arthritis. It commonly affects the lower (knee) and upper limbs (wrist). However, axial manifestations involving the temporomandibular joint and spine (intervertebral disc, facet joints, neural foramen and ligaments) are possible (Rosenthal, 2020, Naqvi *et al.*, 2008).

Chronic CPPD arthritis, which is more common, presents with chronic polyarticular joint involvement resembling osteoarthritis, rheumatoid arthritis and polymyalgia rheumatica (Rosenthal, 2020). With that being said, both osteo- and CPPD arthritis are common in older patients and have similar

risk factors (e.g., increasing age and previous injuries) (Zhang *et al.*, 2011). Studies have shown that 1/3 of patients with osteoarthritis undergoing knee arthroscopy had CPPD deposition (Macmullan and McCarthy, 2012). Although there have been associations described, it is of no surprise that it could occur by chance (Rosenthal, 2020).

A diagnosis of CPPD arthropathy is made by identifying positively birefringent crystals in synovial fluid analysis and/or the presence of radiographic evidence (Rosenthal, 2020). In CDS, an unenhanced CT of the cervical region is the preferred modality of imaging. It demonstrates CPPD deposition in a 'crown-like' shape surrounding the dens apex or ligaments (transverse or flavum) (Rosenthal, 2020). As reported, there is still a limited use for DECT in diagnosing CPPD disease (sensitivity of 55% and specificity of 92%). Other modalities reported a (sensitivity and specificity) as follows: ultrasound (91% and 92%), conventional radiography (36% and 90%) and suspected clinical diagnosis (82% and 88%) (Kravchenko *et al.*, 2021). MRI is usually not helpful in assessing CPPD deposition, as seen in the case above, due to the absence of signals from the calcifications (Rosenthal and Ryan, 2016).

Management of CPPD arthropathy includes the use of NSAIDs which is said to provide relatively quick pain relief. Other treatment options include colchicine, corticosteroids (i.e., intra-articular or systemic) or even combinations of the two (Rosenthal and Ryan, 2016). Although there have been trials, evidence is still lacking surrounding the use of disease modifying agents (Rosenthal and Ryan, 2016). CDS generally carries a good prognosis, although physicians should be mindful of the rare neurological complications (e.g., myelopathy of the cervical spine and spinal stenosis) due to large crystal depositions (Goto *et al.*, 2007).

Conclusion

CPPD disease, as described, has multiple clinical mimics and associations hence posing a challenge of diagnosis. We are therefore hoping to increase awareness of this medical phenomenon amongst the elderly population hence reducing the need for unnecessary interventions (e.g., imaging and antimicrobial use).

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