The crowned dens syndrome as a cause of neck pain: clinical and computed tomography study in patients with calcium pyrophosphate dihydrate deposition disease

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Abstract

Objective

To investigate the association between articular chondrocalcinosis and calcification of the atlantoaxial region on a cervical computed tomography (CT) scan and to explore the relation between such calcifications and neck pain.

Materials and methods

CT slices of the cervico-occipital junction were performed routinely in 49 consecutive patients (male/female ratio 28/21; mean age 70.4 yrs), diagnosed with calcium pyrophosphate dihydrate crystal deposition disease (CPPD). Of these, 35 met criteria for definite CPPD and 14 met the criteria for probable. The cervical CT scans were analyzed for the presence of periodontoid calcifications by 2 independent musculoskeletal radiologists. Both assessors were blinded to the disease status of the patients. Furthermore, conventional radiographs of the upper cervical spine were performed. An ad hoc designed protocol was used to register information at diagnosis, including age, sex, location of pain and stiffness, fever, presence of synovitis and its location.

Results

CT scan of the cervico-occipital junction showed periodontoid calcified deposits in 25 out of 49 patients (51%) with CPPD. In 10 of the 25 cases (40%) with periodontoid calcified deposits, CT scanning showed osseous abnormalities of the odontoid process, such as subchondral cysts or erosions. Conventional radiographs showed calcification behind the odontoid process in 17 patients (34.7%). Nine of CPPD cases (18.4%) presented with neck symptoms. In three patients, articular chondrocalcinosis was revealed only by an acute attack of neck pain with segmentary stiffness, fever, and an increased erythrocyte sedimentation rate; in one of them initial clinical examination found cervical stiffness with Kernig’s and/or Brudzinski’s sign. For the other two patients, impairment of general condition, occipito-temporal and mandible pain and weakness with inflammatory pain of the shoulder girdle was suggestive of giant cell arteritis (GCA) and/or polymyalgia rheumatica (PMR). In the six additional patients, questioning elicited a history of previous subacute or chronic neck pain, from one week to one year before their admission to our ambulatory or hospital.

Conclusions

These results suggest that CPPD deposition disease frequently involves the cervical spine. Although such calcification often remains asymptomatic, it may be associated with attacks of acute neck pain with segmentary stiffness, fever, and an increased erythrocyte sedimentation rate, sometimes mimicking PMR and/or GCA or neurological symptoms.

Key words

Crowned dens syndrome, neck pain, calcium pyrophosphate dihydrate crystal deposition disease, cervico-occipital junction, CT, radiographs.
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Introduction
Calcium pyrophosphate dihydrate (CPPD) crystal deposition disease is the second most common form of the crystal deposition disease that occurs most often in elderly patients (1). However, because of the marked heterogeneity in clinical syndromes associated with CPPD, its prevalence and incidence are difficult to define. Although most cases are idiopathic, there are rare familiar forms (2), and the condition has been observed in coincidence with other metabolic disorders (2, 3). CPPD crystal deposition disease is clinically associated with an acute episodic monocular or oligoarthritis, termed pseudogout, involving a large joint (including the knees, wrists, and ankles) or a chronic arthropathy manifesting as mild joint pain and stiffness of knees, wrists, metacarpophalangeal joints, elbows, and shoulders (4, 5). Less commonly, pyrophosphate deposits have been observed around peripheral joints and in the spine, including the intervertebral disc, posterior longitudinal ligament, facet joints, ligamentum flavum, and sacroiliac joint (6-10). In the cervical spine, calcified deposits in the ligamentum flavum, facet joints, lateral masses, and posterior longitudinal and atlantoccipital ligaments can remain asymptomatic or can be associated with periodic acute cervico-occipital pains with fever, neck stiffness and biological inflammatory syndrome (7, 11, 12). This clinical entity, termed crowned dens syndrome (CDS), should be better known (12, 16); it can mimic numerous diagnosis and be responsible for fever in the long course (17-24). The spectrum of CDS is widening. We would like to emphasize that other manifestations, such as meningism (evoking meningitis or spondylitis) (17, 18, 20, 22), cervicobrachial pain (with shoulder weakness and stiffness) and occipital and temporal headaches (evoking atypical polymyalgia rheumatica-PMR and/or giant cell arteritis-GCA) (17, 25) must be added to the classical acute feverish cervical pain. Some cases of prolonged evolution with relapses can mimic fever of unknown origin (17, 18, 24). The rapid diagnosis of CDS, based mainly on a cervical CT scan (7, 26-29), can prevent invasive, expensive and useless investigations as well as a long course of potentially dangerous and inadequate treatments, notably with cortisone, or prolonged hospitalization in elderly patients.

The purpose of our study was to investigate the association between articular chondrocalcinosis and calcification of the atlantoaxial region on a cervical computed tomography (CT) scan and to explore the relation between such calcifications and neck pain.

Subjects and methods
Data collection and management
Forty-nine consecutive inpatients and outpatients diagnosed with CPPD deposition disease of peripheral joints were included. The evaluation of these patients was carried out by the same rheumatologist at diagnosis. A specifically designed protocol was used to register the information at diagnosis, including age, sex, associated conditions (metabolic diseases such as hyperuricemia and/or gout; hemochromatosis; ochronosis or Wilson’s disease; endocrinopathies including hypothyroidism and hyperparathyroidism; infections; neurologic diseases; rheumatic conditions including connective tissue diseases; tumors; and vasculitides, in particular GCA, location of pain and stiffness, fever, and presence of synovitis and its location.

At diagnosis, erythrocyte sedimentation rate (ESR, Westergren method), C-reactive protein (CRP, by nephelometry), and rheumatoid factor were determined. Synovial fluid was analyzed in 22 of the patients who presented with peripheral arthritis. Plain radiographs of the hands, pelvis, and knees were performed in all patients. Patients were diagnosed as having definite CPPD if calcium pyrophosphate dihydrate crystals were identified by compensated polarized light microscopy, and if typical radiographic calcifications (chondrocalcinosis) were also observed. When only 1 of these 2 criteria was present, patients were diagnosed as having probable CPPD (4, 30). Subsequently, a radiograph of cervical spine in lateral projection and a CT scan of the upper cervical spine were performed. Computed tomographies of the cervico-occipital junction were obtained by a Tomoscan 305
(14 patients) or a Tomoscan SR 7000 Philips (28 patients) without injecting a contrast agent, after each subject had given informed consent. Axial sections passing through the plane of C1 were performed using the following parameters: slice thickness 1.5 mm; contiguous slices; bone algorithm in each case [1600 Hounsfield units (HU)], complemented by an algorithm more adapted to soft tissues (800 HU). The cervical CT scans were graded for the presence of periodontoid calcifications by 2 independent musculoskeletal radiologists. Both radiologists were blinded to the disease status of the patients. Questionable cases were discussed by the two readers to obtain a consensus. The mean value of the 2 independent assessments was used for the calculations. Periodontoid calcified deposits were ranked into 4 stages: stage 1: thin calcifications (<1 mm); stage 2: thicker curvilinear deposits (>1 mm) in a single band; stage 3: in a double band; and stage 4: when the transverse ligament of the atlas (TLA) was ossified (Fig. 1).

All subjects gave informed consent to participate in the study, which was performed according to the Helsinki Declaration criteria and approved by the institutional review board for human research.

Results

Our study population included 49 patients [male/female ratio 28/21; mean age 70.4 yrs, standard deviation (SD) 6.4, range 60-88], with CPPD features who fulfilled the classification criteria proposed by McCarty (4). Of these, 35 met criteria for definite CPPD and 14 met criteria for probable CPPD. In 46 patients, articular chondrocalcinosis was revealed by clinical symptoms in peripheral joints: there were 28 patients with a degenerative chronic arthropathy mainly of the knees, the wrists and the hips, 15 with a pseudogout profile [an attack of acute arthritis of the knees (eight patients), the wrists (three), the ankles (one)], and three with an acute or subacute pseudopolyarthritis pattern. Nine of these 49 CPPD cases (18.4%) (male/female ratio 4/5; mean age 72.1 yrs, SD 5.1, range 65-79), presented neck symptoms (Table I). In three patients, articular chondrocalcinosis was revealed only by an acute attack of neck pain with segmentary stiffness, fever, and an increased ESR (more than 50 mm/1st h); in one of them initial clinical examination found cervical stiffness with Kernig’s and/or Brudzinski’s sign. In this case, infectious meningitis was the diagnosis made. A lumbar puncture was performed and the cerebrospinal fluid was normal. For the other two patients, impairment of general condition, occipito-temporal and mandible pain and weakness with inflammatory pain of the shoulder girdle was suggestive of GCA and/or PMR, leading to temporal artery biopsy and steroid treatment at the initial dosage of 50 mg of prednisone (Table I) in one of them. In the six additional patients, questioning elicited a history of previous subacute or chronic neck pain, from one week to one year before their admission to our ambulatory or hospital. Systematic axial CT scan of the cervico-occipital junction revealed periodontoid calcified deposits in 25 out of 49 patients (51%). The calcifications were found in all nine patients with evidence of present or past acute or subacute neck pain (Table I), but was also revealed by our routine CT scans in another 16 asymptomatic patients (32.6%) (Fisher’s exact test; p=0.04). Among the 25 CPPD cases, the extent of the cervical calcifications was as follows: stage 1 (9 patients, 36%); stage 2 (11 patients, 44%); stage 3 (2 patients, 8%); and stage 4 (3 patients, 12%). The median extent of calcifications was of stage 2 in symptomatic patients as compared to stage 1 in the asymptomatic cases (Wilcoxon signed-rank test: p<0.01). Analysis by kappa statistics showed a good agreement (k=0.763) between observers. CT images showed osseous abnormalities of the odontoid process, such as subchondral cysts or erosions, in 10 of the 25 cases (40%) with periodontoid calcified deposits (Figs. 2 and 3). Conventional radiographs showed calcification behind the odontoid process in 17 patients (34.7%).
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Discussion

Neck pain due to calcifications surrounding the odontoid process were described by Bouvet et al. in 1985 and termed CDS (13). The deposition of CPPD crystals is known to occur within various soft tissues, which include cartilage, joint capsules, synovium, bursae, tendons, and ligaments (6, 8-10). One of the ligaments that may be involved by CPPD crystal deposition is the TLA, which is a thick, strong band of collagen fibers that arches behind the odontoid process and maintains contact between the odontoid process and the anterior arch of C1 (6, 26, 32). When disrupted, atlantoaxial subluxation may result (6, 33, 34). The calcification observed in the TLA may be curvilinear, stippled, or mixed (6, 7). Although the mixed appearance was common in our cases, curvilinear calcium deposits in the retroodontoid region are strongly suggestive of CPPD crystal deposition in the transverse ligament of the atlas (6, 7, 26, 35-39).

We studied 49 patients with CPPD deposits in peripheral joints for signs of CPPD involvement of the cervical spine and for symptoms of the neck. We found that CT of the cervico-occipital junction revealed atlantoaxial calcified deposits in 51% of these CPPD cases. These results are belo with those of Constantin (26) and Finckh (7), who found 66% and 69%, respectively, of calcifications on cervical CT scan, but higher than results of Dirheimer (40), who reported 44% of calcifications on radiotomography, a less sensitive technique. Clinical relevance of the high prevalence of CPPD deposition in the cervical spine is not well established. In our study, 9 of the 49 CPPD cases (18.4%), presented with neck symptoms. In three of these patients, articular chondrocalcinosis was revealed only by an acute attack of neck pain with segmentary stiffness, fever, and an increased ESR (more than 50 mm/1st h); in one of them initial clinical examination found cervical stiffness with Kernig’s and/or Brudzinski’s signs, mimicking meningitis. For the other two patients, impairment of general condition, occipito-temporal and mandible pain and weakness with in-
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Inflammatory pain of the shoulder girdle was suggestive of GCA and/or PMR. In the six additional patients, questioning elicited a history of previous subacute or chronic neck pain, from one week to one year before their admission to our ambulatory or hospital.

The diagnosis of CDS is based on the association of clinical, biological, radiological and therapeutic signs: acute periodic attacks of cervico-occipital stiffness and feverish pains with biological inflammatory syndrome, radiological identification of periodontal calcifications due to microcrystalline deposits on the retro-odontoid ligament and dramatic resolution of symptoms under treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) or colchicine. This typical description was reported for the first time in 1980 (18). Authors have described acute attacks of pain in high cervical areas that are different from the chronic or subacute manifestations of microcrystalline deposition in the lower part of the cervical or dorsal and lumbar spine, which are often confused with common degenerative processes. The triad of headaches, fever and cervical morning stiffness evokes either infectious meningitis leading to lumbar puncture, or of cervical metastatic spondylitis in the case of a medical history of cancer. As illustrated by our patient, CDS can mimic and lead to misdiagnosis of meningitis or cervical spondylitis. When cervical stiffness is associated with pain in the shoulder girdle and jaw claudication, CDS can mimic PMR and/or GCA (41). Dieppe et al. (5) reported 8 individuals with presumed PMR from a series of 105 patients with pyrophosphate arthropathy, suggesting that either CPPD might present with polymyalgic symptoms or that the steroid treatment prescribed to these patients with PMR features might predispose to the development of chondrocalcinosis (5). In addition, 3 patients with CDS and chondrocalcinosis of the wrist and knee who were misdiagnosed as having PMR have been described (17). More recently, a prospective study on a large series of patients who meet the diagnostic criteria for CPPD (4, 30) and PMR (42) demonstrate that eighty-two of the 118 patients with PMR manifestations were diagnosed as having pure PMR, and 36 met the diagnostic criteria for both PMR and CPPD (41). The best predictive factors for the occurrence of this atypical pattern of CPPD in a patient presenting with polymyalgia rheumatica features were the age at diagnosis and the presence of tibiofemoral osteoarthritis, tendinous calcifications, and ankle arthritis (41).

Conventional radiographs are useful in the detection of chondrocalcinosis in the appendicular skeleton, however, in our clinical patients, periodontoid

Fig. 2. Cervical computed tomography (CT). Coronal multiplanar reconstruction showing crown-like calcium deposits surrounding the odontoid process (arrows) and multiple subchondral erosions suggesting CPPD (arrowheads). There is also discal chondrocalcinosis involving both the annulus and the nucleus pulposus (empty arrowhead).
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CPPD crystal deposition was either subtle or undetectable with routine radiography because of superimposition of adjacent osseous structures. CT is the technique of choice for the detection of CPPD crystal deposition adjacent to the odontoid process (6, 7, 11, 26-29, 35, 43). CT focusing on C1/C2 is the gold standard of the diagnosis of CDS. Another useful aspect of CT technique is the ability to rule out differential diagnoses of CDS such as unrecognized odontoid fractures or cervical cord compression. Massive CPPD crystal deposits with subchondral cysts or bone erosion involving the cervical vertebrae have been reported previously (43). In our study, CT showed osseous abnormalities of the odontoid process, such as subchondral cysts or erosions, in 10 of the 25 cases (40%) with periodontoid calcified deposits. This feature is interesting, because conspicuous subchondral cyst formation or bone erosion has not been reported as a dominant feature of CPPD crystal deposition disease in the peripheral joints and is generally considered a finding that suggests an alternative diagnosis (e.g., rheumatoid arthritis) (44, 45). Kakitsubada et al. (43), however, suggest that CPPD crystal deposition in the TLA can be associated with erosion of the odontoid process that may weaken the odontoid process and predispose it to subsequent fracture.

Our study has two major limitations. First, the number of cases that we evaluated was limited, so defining the relationship among articular chondrocalcinosis and calcification of the atlantoaxial region will require a larger study. Another limitation is the cross-sectional design, without control subjects, and without histologic proof in all cases, where CPPD and neck pain were assessed at the same time. However, since the presence of CPPD deposits is a relatively stable condition in time, we could use the presence of CPPD on the CT scan as a proxy for prior exposure to CPPD crystals to make longitudinal inferences about the effect of this exposure and neck symptoms. We chose to report our experience at this time in the hope of prompting recognition – and further study – of this potentially debilitating injury in patients with CPPD crystal deposition disease.

References
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