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CPPD crystal deposition disease of the cervical spine: A common cause of acute neck pain encountered in the neurology department

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ABSTRACT

Background: Calcium pyrophosphate dihydrate (CPPD) crystal deposition disease is one of the most common forms of crystal-associated arthropathy in the elderly. However, CPPD deposition on the cervical spine is less well known, and only a limited number of cases have been reported to date. Here, we report our recent clinical experience with CPPD crystal deposition disease of the cervical spine and describe the clinical features of this disease.
Methods: Fourteen patients with clinically diagnosed CPPD crystal deposition disease of the cervical spine at our department during the period from January 2005 to December 2008 were analyzed retrospectively.
Results: Patients ranged in age from 54 to 92 (mean ± SD, 77.5 ± 8.5). Chief symptoms of patients were acute posterior neck pain and fever. All patients had markedly restricted neck rotation. Serum CRP level was highly elevated in all patients (10.16 ± 5.35 mg/dL). Computed tomography of the cervical spine demonstrated linear calcific deposits in the transverse ligament of atlas (crowned dens syndrome) in all patients. Calcific deposits were also found in other periodontoid structures and the ligamenta flava in some patients. Posterior neck pain, fever, and increased serum inflammatory indicators were relieved within 1 to 3 weeks by nonsteroidal antiinflammatory drugs (NSAIDs) or a combination of NSAIDs and prednisolone. Most of the patients were misdiagnosed as having other diseases before consultation.
Conclusions: CPPD crystal deposition disease of the cervical spine is one of the most common underrecognized causes of acute neck pain in the neurology department, especially in elderly patients.

1. Introduction

The crystal-associated arthropathies form a group of metabolic diseases in which crystals, such as calcium pyrophosphate dihydrate (CPPD), basic calcium phosphate (*e.g.*, hydroxyapatite and octacalcium phosphate), and monosodium urate, are deposited in and around joints, leading to inflammatory and destructive lesions. Pseudogout is one of the most common forms of crystal-associated arthritis associated with CPPD deposition in the joints and periarticular tissues [1–3]. The prevalence of CPPD deposition is extremely high and it is reported that knee chondrocalcinosis, which is assumed to be due to CPPD deposition, is found in 9.6% of individuals older than 50 years old, and this incidence increases with age [4,5]. Attacks of pseudogout can be either monoarticular or oligoarticular, and the most commonly affected joints are the knees, followed by the shoulders, wrists, and ankles [2]. CPPD crystal deposition also induces arthritis mimicking rheumatoid arthritis (pseudorheumatoid arthritis) or osteoarthritis (pseudoosteoarthritis). However, CPPD crystal deposition on the cervical spine is less well known and only a limited number of cases of this condition have been reported to date [6–14].

Here, we report our recent clinical experience with 14 patients with CPPD crystal deposition disease of the cervical spine manifested by acute severe posterior neck pain. Acute neck pain is a common complaint among patients in the neurology department; however, it is sometimes difficult to make a precise diagnosis. Although a small number of patients have previously been reported, our recent clinical experience with 14 patients suggests that CPPD crystal deposition disease of the cervical spine is one of the most common underrecognized causes of acute neck pain.

2. Patients and methods

Data from 14 patients with clinically and radiologically diagnosed CPPD crystal deposition disease of the cervical spine at our department

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Table 1
Summary of patients with CPPD crystal deposition disease of the cervical spine.

Patient no.	Age	Sex	Inflammation markers			Calcifications in the cervical spine		Suspected diagnosis before consultation
			CRP	ESR	WBC	Periodontoid str.	Lig. flava	
1	83	F	18.02	n. e.	9620	+	+ (C3–7)	Occipital neuralgia
2	82	M	13.70	n. e.	7920	+	+ (Th1)	Tension-type headache
3	78	M	11.67	n. e.	11,500	+	+ (C4)	Subarachnoid hemorrhage
4	75	M	2.05	n. e.	9120	+	−	
5	92	F	12.31	97	9170	+	+ (C2–6)	Collagen disease
6	76	F	n. e.	n. e.	5600	+	−	
7	54	M	n. e.	n. e.	7300	+	−	
8	80	M	n. e.	n. e.	n. e	+	+ (Th1–2)	
9	78	F	15.96	87	8030	+	−	Polymyalgia rheumatica
10	71	M	11.00	n. e.	11,000	+	−	Cervical spondylosis
11	85	F	3.60	n. e.	6800	+	+ (C5)	
12	79	F	13.17	n. e.	7960	+	−	Meningitis
13	78	M	6.20	57	7970	+	−	Bacterial spondylodiscitis
14	74	F	4.03	80	9160	+	−	Epidural abscess
Mean	77.5		10.16	80.3	8550			
SD	8.5		5.35	20.8	1623			

CRP, serum C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood-cell count; Periodontoid str., Periodontoid structure; Lig. flava, Ligamentum flava; n. e., not examined.

during the period from January 2005 to December 2008 were analyzed retrospectively. The following data were collected from the medical records of the patients: gender; age; clinical course; inflammatory indicators, such as white blood-cell count (WBC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level; radiological findings; and outcome.

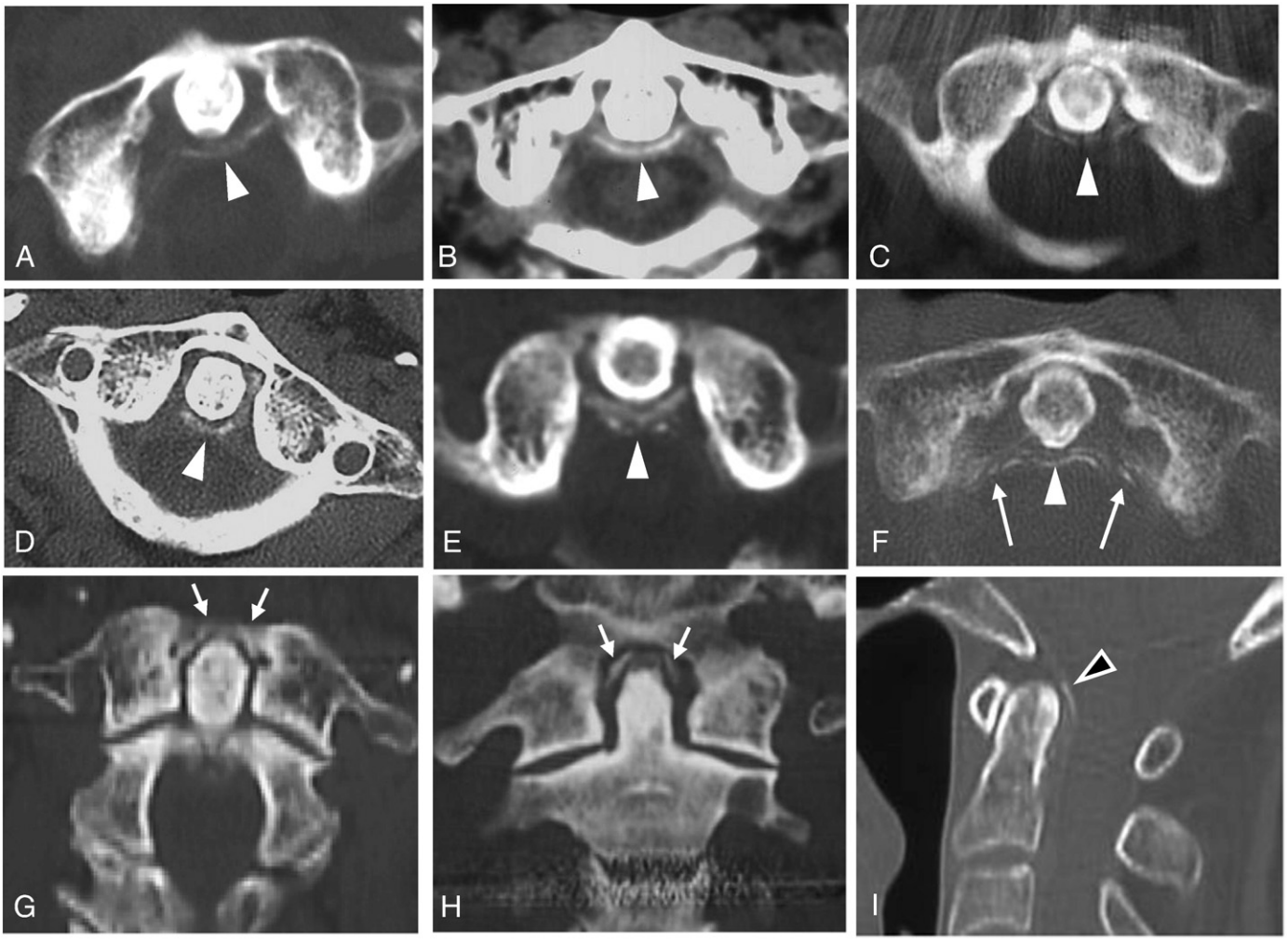

Fig. 1. Axial (A–F), coronal (G, H), and sagittal (I) views of the cervical CT scan at the C1/C2 level showed linear calcifications of the transverse ligament (A–F; arrowheads), alar ligament (F; long arrows), apical ligament (G, H; short arrows), and superior longitudinal fibres of the cruciate ligament (I; black arrowhead) suggesting CPPD deposition. (A) Patient 2. (B) Patient 4. (C) Patient 5. (D) Patient 7. (E) Patient 8. (F) Patient 11. (G) Patient 10. (H) Patient 13. (I) Patient 11.

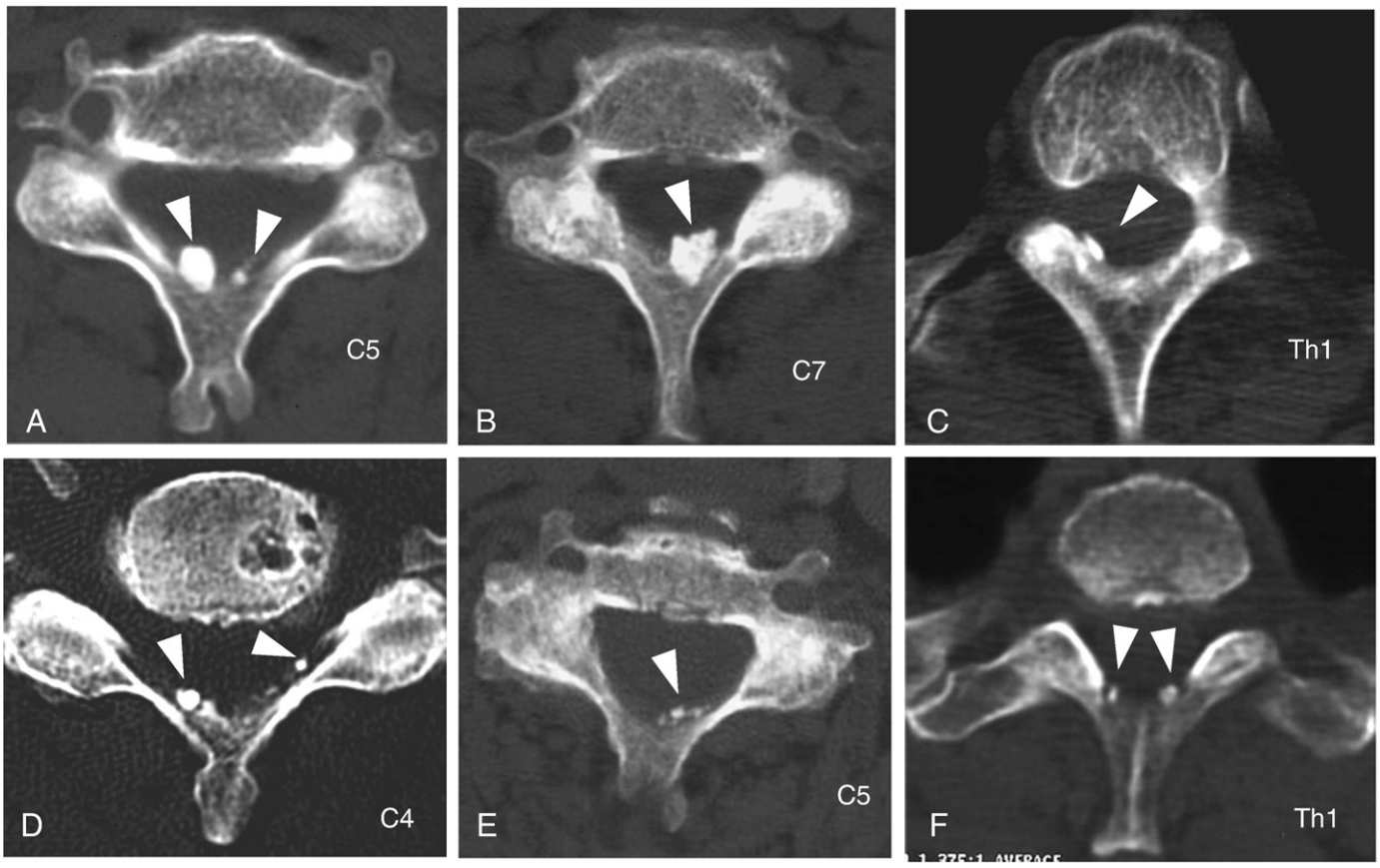

Fig. 2. Axial view of the cervical CT scan showed nodular calcifications of the ligamenta flava. (A, B) Patient 1. (C) Patient 2. (D) Patient 3. (E) Patient 4. (F) Patient 8. The levels of the spine are indicated at the bottom right corner of each figure.

3. Results

3.1. Clinical findings

The data for the 14 patients are summarized in Table 1. The male-to-female ratio was 1.0 (7:7), and patients ranged in age from 54 to 92 with a mean ± SD of 77.5 ± 8.5. Thirteen patients (93%) were older than 70 years of age. None of the patients was previously diagnosed as having pseudogout or other crystal-associated arthropathies, although two patients had histories of severe neck pain attacks. The patients' chief symptoms were acute severe posterior neck pain (100%) and fever (79%). Nine (64%) patients were referred from general practitioners, orthopedic surgeons, neurosurgeons, or neurologists from other hospitals with suspected diagnoses of meningitis, epidural abscess, subarachnoid hemorrhage, bacterial spondylodiscitis, cervical spondylosis, occipital neuralgia, tension-type headache, polymyalgia rheumatica, and collagen disease. The pain spread mostly from the suboccipital region to the posterior part of the neck on both sides without specific points of tenderness and abnormal superficial sensation. Characteristically, all patients had markedly restricted neck motion, particularly in rotation.

3.2. Laboratory data

Serum level of CRP was markedly elevated in all patients (mean ± SD, 10.16 ± 5.35 mg/dL; range, 2.05–18.02 mg/dL). ESR was also increased in all patients (mean ± SD, 80.3 ± 20.8 mm/h; range, 57–97 mm/h). Leukocytosis was relatively unremarkable and mild elevation of WBC was observed in 38% of patients (mean ± SD, 8550 ± 1623 cells/mL; range, 5600–11,500 cells/mL) (Table 1). All patients were negative for rheumatoid factor. No other abnormal findings were observed on routine blood examination, including parathyroid function. Lumbar punctures were performed in 2 patients, showing normal opening pressure, cell count, protein, and glucose level of cerebrospinal fluid.

3.3. Radiological findings

There were no remarkable findings on roentgenograms or magnetic resonance imaging (MRI) of the cervical spine. However, computed tomography (CT) imaging of the cervical spine demonstrated linear calcific deposits in the transverse ligament of atlas in all patients (Fig. 1A–F). Calcific deposits were also found in other periodontoid structures, including alar ligaments (Fig. 1F), apical ligament (Fig. 1G, H), and superior longitudinal fibres of the cruciate ligament (Fig. 1I). Punctate or nodular calcifications in the ligamenta flava at the level of C2–Th2 were observed in 6 (43%) patients (Fig. 2).

3.4. Outcome

Posterior neck pain, fever, and increased serum inflammatory indicators were relieved within 1 to 3 weeks by nonsteroidal antiinflammatory drugs (NSAIDs) or a combination of NSAIDs and prednisolone. Restricted neck motion was also improved; however, mild to moderate restriction of neck motion, particularly in rotation, remained even after disappearance of inflammation.

4. Discussion

Disease caused by CPPD crystal deposition was first described by McCarty et al. in 1962 [1]. CPPD deposition disease is a pathological process of crystal formation classically within articular, hyaline, and

fibrocartilaginous structures, and can also be found in periarticular structures such as the joint capsule, tendons, and ligaments. This pathological process is especially common in the elderly [4,5]; however, there have been relatively few reports regarding CPPD deposition on the cervical spine. CPPD deposition on the cervical spine can be associated with both cervical spondylarthritis [6–8] and even cervical radiculomyelopathy when the deposition builds up and compresses the spinal cord [9–13]. The most commonly reported cervical sites of CPPD crystal deposition are the transverse ligament of the atlas and ligamenta flava.

All patients presented here developed cervical spondylarthritis induced by CPPD crystal deposition. On the other hand, none of the patients developed compressive radiculomyelopathy, although nodular calcifications in the ligamenta flava were observed in some cases (Fig. 2). Our patients shared a number of common clinical findings, such as acute onset of severe posterior neck pain, restricted range of neck rotation, fever, and elevation of serum CRP, suggesting spondylarthritis involving the atlantoaxial joint. Indeed, all patients described here showed calcifications around the odontoid process, such as the transverse ligament, alar ligaments, apical ligament, and superior longitudinal fibres of the cruciate ligament (Fig. 1). This condition has been termed the "crowned dens syndrome" [6], a clinical and radiographic entity characterized by acute neck pain and evidence of calcium deposits around the odontoid process on radiographs.

As illustrated in our patients and in those reported previously [7,8,14], crowned dens syndrome can mimic and lead to misdiagnosis of meningitis, epidural abscess, rheumatoid arthritis, polymyalgia rheumatica, giant cell arthritis, cervical spondylitis, or metastatic bone tumors. However, based on our experience in 14 patients, the distribution and character of the pain (*i.e.*, mostly from the suboccipital region to the posterior part of the neck on both sides without specific points of tenderness and abnormal superficial sensation) and restricted neck motion, particularly in rotation, are strongly suggestive of crowned dens syndrome. As described previously [7,8,14,15], CT imaging of the cervical spine was superior to MRI in confirming CPPD crystal deposition in our patients, especially when calcifications were small. Ideally, CT should be analyzed multidirectionally using reconstruction images, as the axial view is useful for detecting calcification of the transverse ligament, ligamenta flava, and alar ligament; the coronal view is useful for detecting calcification of the apical ligament; and the sagittal view is useful for detecting calcification of the longitudinal fibres of the cruciate ligament (Figs. 1 and 2). Careful physical examination and characteristic radiological findings can lead to correct diagnosis and reduce the need for hospitalization, invasive procedures (*e.g.*, temporal artery biopsy), and unnecessary therapy (*e.g.*, antibiotics) in most patients, although lumbar puncture may be necessary in some patients to exclude meningitis. Although the pathophysiology of crystal formation in CPPD deposition disease, as well as specific therapies that could prevent crystal accumulation in this condition, are unknown, NSAIDs or a combination of NSAIDs and prednisolone are effective for symptom relief.

CPPD crystal deposition disease of the cervical spine is more common than previously recognized [14] and it should be considered in the differential diagnosis of acute neck pain, especially in elderly patients. Therefore, neurologists must understand and be aware of the clinical features of this disease.

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