Frequency of Atlantoaxial Calcium Pyrophosphate Dihydrate Deposition at CT[1]

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Purpose: To determine *(a)* the prevalence of atlantoaxial calcium pyrophosphate dihydrate (CPPD) crystal deposition in a population of patients undergoing computed tomography (CT) for acute trauma and *(b)* the association between atlantoaxial CPPD crystal deposition and retro-odontoid soft-tissue thickness.

Materials and Methods: This HIPAA-compliant study was approved by the institutional review board, and the requirement to obtain informed consent was waived. In 513 consecutive patients, CT scans of the cervical spine obtained for acute trauma were retrospectively reviewed for the presence of atlantoaxial CPPD crystal deposition, and the maximal thickness of the retro-odontoid soft tissues was measured. The relationships among imaging findings, age, and sex were assessed with the *t* test, the χ^2 test, Spearman correlation, and logistic and linear regression models as appropriate.

Results: The overall prevalence of atlantoaxial CPPD crystal deposition was 12.5% (64 of 513 patients), and prevalence increased with age ($P < .0001$, logistic regression coefficient). In patients aged 60 years and older, the prevalence of CPPD crystal deposition was 34% (58 of 170 patients). In patients aged 80 years and older, the prevalence of CPPD crystal deposition was 49% (37 of 75 patients). There was a positive correlation between age and retro-odontoid soft-tissue thickness (Spearman $\rho = 0.48$, $P < .0001$). The mean retro-odontoid soft-tissue thickness in patients with CPPD crystal deposition was greater than that in patients without CPPD crystal deposition (3.4 mm vs 2.2 mm, respectively; $P < .0001$, *t* test).

Conclusion: CPPD crystal deposition in the cervical spine is seen with a higher prevalence than previously reported. CPPD crystal deposition shows a positive correlation with age and retro-odontoid soft-tissue thickening.

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Calcium pyrophosphate dihydrate (CPPD) crystal deposition can occur in cartilage (hyaline cartilage or fibrocartilage), ligaments, tendons, bursae, and joint capsules (1). CPPD crystal deposition is associated with many diseases, including inherited or acquired metabolic diseases such as hemochromatosis and hyperparathyroidism (2,3). In addition, there is a strong association with increasing age (4–6).

Although studies have been performed on the epidemiology of CPPD crystal deposition, they have focused on articular cartilage in the extremities—with radiographic determination of calcium deposition as a diagnostic criterion (4,7,8). In the literature to date, there has been a focus on associated complications such as inflammation (the so-called "crowned dens" syndrome, which is predominantly due to CPPD but also hydroxyapatite crystals) (9–14), mass effect causing compression on the cervicomedullary junction (15,16), or an association with odontoid fractures (17). In patients with radiographically evident peripheral articular chondrocalcinosis, the prevalence of CPPD crystal deposition in the atlantoaxial region has been reported to range from 44% to 66% (18,19). This has led some authors to conclude that spinal involvement is far less common than extremity involvement (15,20,21).

The true prevalence of CPPD crystal deposition remains uncertain and likely varies depending on which body part or structure is studied. We have noticed in our practice that these previously reported numbers seemed conservative.

Advances in Knowledge

- The prevalence of atlantoaxial calcium pyrophosphate dihydrate (CPPD) crystal deposition is higher than previously recognized.
- The prevalence of atlantoaxial CPPD crystal deposition increases with age.
- Retro-odontoid soft-tissue thickening is greater in patients with atlantoaxial CPPD crystal deposition.

The purpose of this study was to determine *(a)* the prevalence of atlantoaxial CPPD crystal deposition in a population of patients undergoing CT for acute trauma and *(b)* the association between atlantoaxial CPPD crystal deposition and retro-odontoid soft-tissue thickness.

Materials and Methods

Study Population

Institutional review board approval was obtained for this retrospective Health Insurance Portability and Accountability Act–compliant study. The requirement to obtain informed consent was waived. Using our picture archiving and communication system, we searched the medical records of all patients who presented to our level I trauma center (by means of either trauma triage or the emergency room) between January 1, 2010, and March 31, 2010. As part of our search criteria, we identified patients who had undergone CT of both the cervical spine and head. Of note, CT of both the cervical spine and head is included as part of our routine trauma protocol, regardless of symptomology or where in the body the trauma occurred. This search yielded 521 patients. Five patients were excluded because the patient age was not documented and three were excluded owing to metallic artifact that precluded adequate visualization of the retro-odontoid region. In total, 513 patients were included in our study.

Image Acquisition and Analysis

Patients underwent imaging from the occiput to T4 with either a 64–detector row (CT750 HD; GE Healthcare, Waukesha, Wis) or 16–detector row (LightSpeed, GE Healthcare) CT scanner with 0.625-mm or 2.5-mm collimation, respectively. Sagittal and coronal reformations were reconstructed with 3.0-mm-thick sections. Images were viewed on a picture archiving and communication system and interpreted in consensus by two board-certified musculoskeletal radiologists (E.Y.C. and W.Y.L., with 2 years and 1 year of experience, respectively) who were blinded to patient demographics during interpretation.

The soft-tissue algorithm images in the axial plane were used for characterization. For this study, CPPD crystal deposition was determined to be present if there were linear, curvilinear, or discrete mottled foci of high-attenuation material (Fig 1) perceived to be greater in attenuation than that of other surrounding soft tissues in an anterior, posterior, or lateral atlantoaxial region—similar to that previously described in the literature (18,22,23).

In addition, the axial section that best corresponded to the expected center of the transverse ligament was selected and the retro-odontoid soft tissues were magnified. Electronic calipers were used to measure the length between the posterior osseous margin of the odontoid process and the posterior edge of the retro-odontoid soft tissues (Fig 2).

Statistical Analysis

Statistical analyses were performed with software (R, version 2.15.1 [2012]; R Foundation for Statistical Computing, Vienna, Austria). The study sample was described, and the relationship between age and sex was assessed with the *t* test. The relationship among atlantoaxial

Implication for Patient Care

- Atlantoaxial CPPD crystal deposition is a very common finding in elderly patients, and its presence is associated with thicker retro-odontoid soft tissues.

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Abbreviation:
CPPD = calcium pyrophosphate dihydrate

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Guarantor of integrity of entire study, E.Y.C.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, E.Y.C., W.Y.L., W.C.B.; clinical studies, E.Y.C., W.Y.L.; statistical analysis, E.Y.C., T.W., A.G., W.C.B.; and manuscript editing, E.Y.C., W.Y.L., T.W., A.G., C.B.C., D.L.R.

Conflicts of interest are listed at the end of this article.

Figure 1

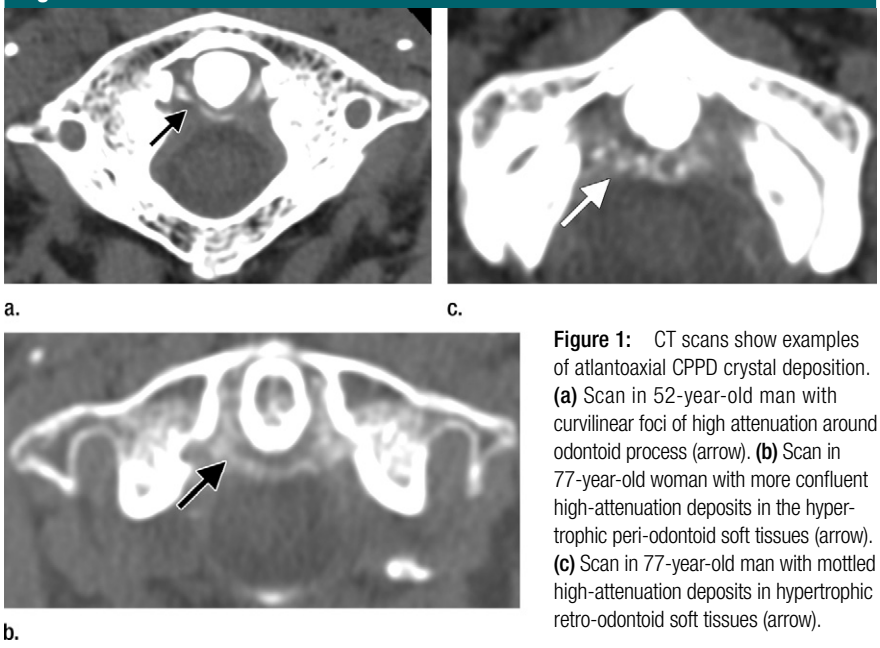


Figure 1: CT scans show examples of atlantoaxial CPPD crystal deposition. **(a)** Scan in 52-year-old man with curvilinear foci of high attenuation around odontoid process (arrow). **(b)** Scan in 77-year-old woman with more confluent high-attenuation deposits in the hypertrophic peri-odontoid soft tissues (arrow). **(c)** Scan in 77-year-old man with mottled high-attenuation deposits in hypertrophic retro-odontoid soft tissues (arrow).

Figure 2

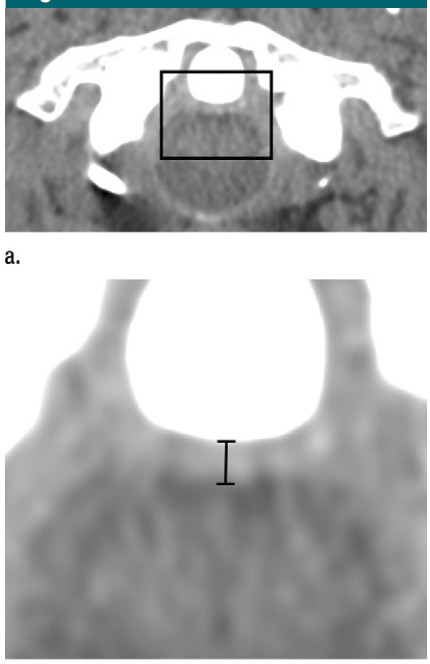


Figure 2: Method of measurement of retro-odontoid soft tissue. **(a)** Axial section corresponding to level of expected center of transverse ligament was selected and magnified. **(b)** Square region in **a** corresponds to magnified field of view in **b**, where electronic calipers were used to measure distance between posterior osseous margin of odontoid process and posterior edge of retro-odontoid soft tissue, which, in this case, is 1.8 mm.

CPPD crystal deposition, age, and sex was analyzed with the t test and χ^2 test, respectively. Logistic regression was used to model the presence of CPPD deposition as a function of age and sex combined. Retro-odontoid soft-tissue thickness was correlated with age by using Spearman rank correlation. The relationship between retro-odontoid soft-tissue thickness, sex, and the presence of CPPD deposition was assessed by using t tests. Finally, linear regression analysis was used to model the square root of the retro-odontoid soft-tissue thickness as a function of age, sex, and CPPD crystal deposition. The square root transformation was used to to stabilize the variance and meet the linear regression assumptions.

Results

Study Population

A total of 513 patients (354 male, aged 6–99 years [mean age, 48 years]; 159 female, aged 18–98 years [mean age, 62 years]) met our inclusion criteria. Age and sex distributions are shown in Figure 3 and the Table. Of note, the mean age of female patients (62 years) was significantly greater than that of male patients (48 years) ($P < .0001$, t test). In addition, there were significantly more male patients than female patients ($P < .0001$, χ^2 test).

Atlantoaxial CPPD Crystal Deposition

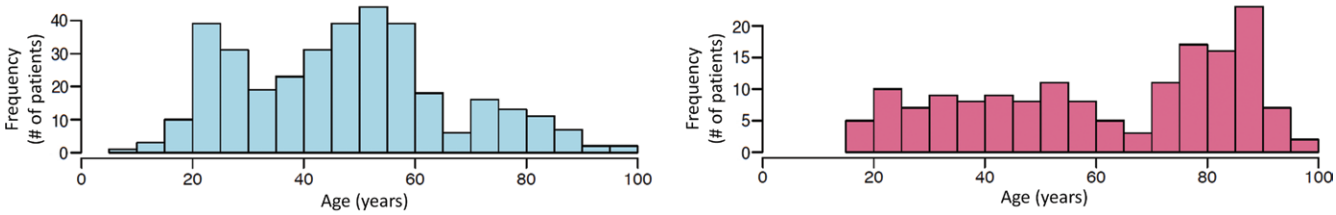
The overall prevalence of atlantoaxial CPPD crystal deposition was 12.5% (64 of 513 patients). The mean age of the patients with CPPD crystal deposition was 80 years (standard deviation, 19 years), whereas the mean age of patients without CPPD crystal deposition was 48 years (standard deviation, 13 years; $P < .0001$, t test). The prevalence of CPPD crystal deposition increased with age, as shown in Figure 4 ($P < .0001$, logistic regression coefficient). In patients aged 60 years and older, the prevalence of CPPD crystal deposition was 34% (58 of 170 patients). In patients aged 80 years and older, the prevalence of CPPD crystal deposition was 49% (37 of 75 patients).

The prevalence of CPPD crystal deposition was higher in female patients than in male patients (22% [35 of 159 patients] vs 8.2% [29 of 354 patients], respectively; $P < .0001$, χ^2 test); however, after adjusting for age, there was no additional effect of sex on calcification (logistic regression coefficient for sex = 0.162, $P = .645$; logistic regression coefficient for age = 0.010, $P < .0001$; likelihood ratio $R^2 = 0.36$).

Retro-Odontoid Soft-Tissue Thickness

The average retro-odontoid soft-tissue thickness was 2.4 mm (range, 1–8 mm). There was a positive correlation between advancing age and retro-odontoid soft-tissue thickness (Fig 5a; Spearman $\rho = 0.48$, $P < .0001$). This relationship existed after adjusting for sex and the presence of CPPD crystal deposition in a multiple linear regression analysis (linear regression coefficient for age = 0.006, $P < .0001$). The combination of advancing age and presence of CPPD crystal deposition was associated with greater retro-odontoid soft-tissue thickness (linear regression coefficient for the interaction of age and

Figure 3



a. b.

Figure 3: Bar charts show age distribution of **(a)** male and **(b)** female patients. There were 354 male patients and 159 female patients ($P < .0001$, χ^2 test). Of note, female patients were disproportionately older than male patients (mean age, 62 years vs 48 years, respectively; $P < .0001$, *t* test).

CPPD crystal deposition = 0.0067, P = .004, multiple R^2 = 0.35). There was no significant difference between the retro-odontoid soft-tissue thickness in men versus that in women (mean, 2.4 mm vs 2.3 mm, respectively; P = .2574, *t* test). The mean retro-odontoid soft-tissue thickness in patients with CPPD crystal deposition was greater than that in patients without CPPD crystal deposition (3.4 mm vs 2.2 mm, respectively; $P < .0001$; Fig 5b).

Summary of Demographic Characteristics

Age (y)	No. of Male Patients	No. of Female Patients	No. of Patients with Calcification*
<20 (*n* = 14)	10	4	0 (0)
20–29 (*n* = 85)	68	17	0 (0)
30–39 (*n* = 62)	45	17	0 (0)
40–49 (*n* = 83)	65	18	2 (2.4)
50–59 (*n* = 99)	83	16	4 (4.0)
60–69 (*n* = 42)	31	11	4 (9.5)
70–79 (*n* = 53)	28	25	17 (32)
80–89 (*n* = 54)	19	35	21 (39)
90–99 (*n* = 21)	5	16	16 (76)

* Numbers in parentheses are percentages.

Discussion

In this study, we demonstrated that atlantoaxial CPPD crystal deposition is more common than previously recognized. In fact, nearly half of our patients aged 80 years and older had atlantoaxial CPPD crystal deposition at CT. We have confirmed that there is an increasing prevalence of such deposition with advancing age (4–7,24,25). In addition, the presence of CPPD crystal deposition was associated with thicker retro-odontoid soft tissues.

The true prevalence of CPPD crystal deposition is unknown. Previous studies have primarily used conventional radiography as a diagnostic tool and have found CPPD crystal deposition to be highest in the peripheral articulations, particularly the knee, with rates reported to be as high as 8.1% in those older than 63 years (1425 patients) (7), 17.5% in those aged 80–84 years (1727 patients) (4), and 44% in those older than 84 years (100 patients) (24).

To date, there have been relatively few reports of CPPD crystal deposition in the cervical spine, in part because clinical radiography is much less sensitive to soft-tissue calcifications related to the superimposition of adjacent structures (17). To our knowledge, the only study to date in which CT was used to determine the prevalence of CPPD crystal deposition in the cervical spine was performed in 1995 by Zapletal et al (25), who evaluated 700 consecutive patients undergoing CT of the brain or paranasal sinuses and found a prevalence of 8.8% in those aged 60 years and older and an overall prevalence of 5.7%. The prevalence data in our study were much higher than those obtained by Zapletal et al (25): We found a prevalence of 34% in patients aged 60 years and older and an overall prevalence of 12.5%. This is likely related to the increased sensitivity of current-generation CT scanners, which use thinner collimation than the scanners used by Zapletal et al (5.0-mm collimation).

The importance of noting the high prevalence of incidental atlantoaxial CPPD crystal deposition is demonstrated in the diagnosis of crowned dens syndrome, which is seen in patients who present with severe neck pain due to calcium deposits about the odontoid process (22). As expected, a major diagnostic criterion is the finding of periodontoid calcific deposits. Our study demonstrated that this finding is very common and often incidental, highlighting the importance of using other criteria such as fever or positive biologic inflammatory markers to make the diagnosis (10), particularly in the elderly.

We have demonstrated that atlantoaxial CPPD crystal deposition is associated with greater retro-odontoid soft-tissue thickness in older subjects, even after separately adjusting for age. This finding supports the few case reports in the literature of CPPD crystal deposits causing enlarged retro-odontoid masses (15,16), although other causes have also been demonstrated, including osteoarthrosis and rheumatoid arthritis (25–27). The presence of atlantoaxial

Figure 5

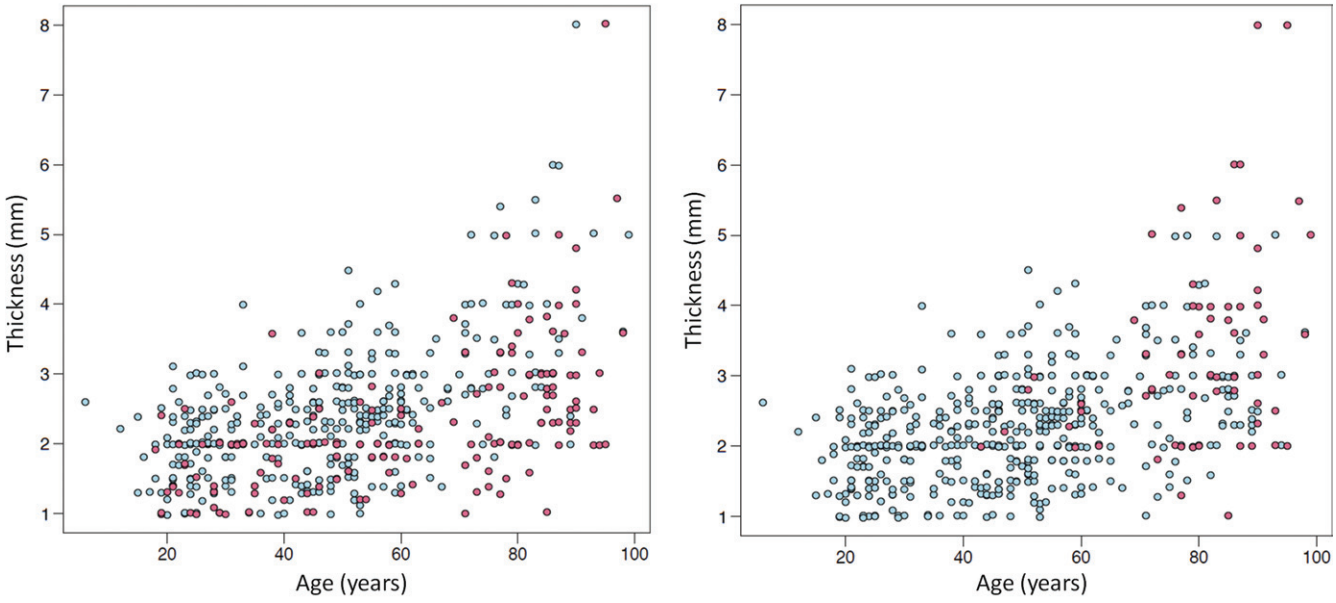


Figure 5: Scatter plot of age versus retro-odontoid soft-tissue thickness in **(a)** male (blue) and female (red) patients and **(b)** patients without CPPD crystal deposition (blue) and those with CPPD crystal deposition (red). There is significant positive correlation ($\rho = 0.48$, $P < .0001$) between age and retro-odontoid soft-tissue thickness in entire population.

Figure 4

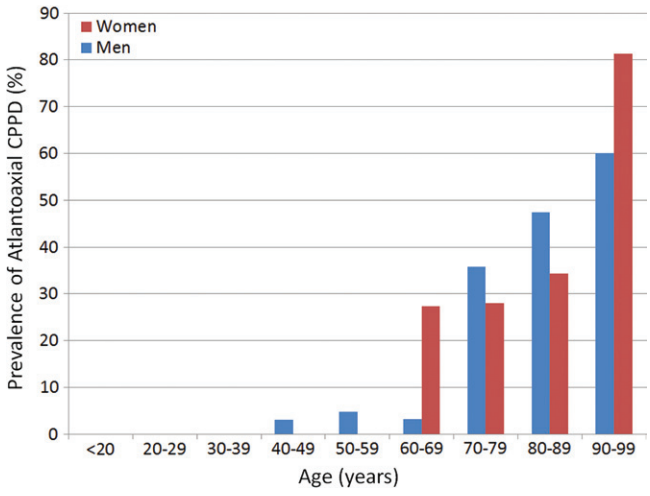


Figure 4: Bar chart shows prevalence of atlantoaxial CPPD deposition according to age group. Prevalence increases with advancing age for both male (blue) and female (red) patients ($P < .0001$, logistic regression coefficient).

CPPD crystal deposition should alert the interpreting radiologist to pay particular attention to the retro-odontoid soft-tissue thickness.

There are several limitations to our study. Our sample included patients with acute trauma and is not necessarily representative of the general population. This is highlighted by the fact that we had many more men (354 patients) than women (159 patients) and that there were disproportionately higher numbers of men aged 20–30 years and elderly women. However, ethical concerns with the delivery of ionizing radiation preclude the evaluation of consecutive patients in the general population. In addition, although CT is generally regarded as sensitive for the detection of small calcifications, it is certainly less sensitive than histologic examination (17), which may result in underestimation of the true prevalence. Furthermore, not all CT-evident calcifications relate to CPPD crystal deposition at histologic examination, although histologic analysis is generally not performed in the clinical setting and characteristic calcifications are generally assumed to be due to CPPD crystal deposition (22,28). With regard to retro-odontoid soft-tissue thickness, we did not evaluate any potential causes other than CPPD crystal deposition that could be diagnosed at imaging, such as osteoarthrosis or an inflammatory arthropathy. Another limitation of this

study is that measurements of thickness of retro-odontoid soft tissue were made from axial images, in part because many reconstructions provided were actually sagittal oblique owing to differences in patient head position (ie, head turning). Finally, consensus interpretation was used in this study and intra- and interobserver reliability could not be assessed.

In conclusion, CPPD crystal deposition in the cervical spine is underrecognized, with a higher prevalence than previously reported. CPPD deposition shows a positive correlation with age and retro-odontoid soft-tissue thickening.

Disclosures of Conflicts of Interest: **E.Y.C.** No relevant conflicts of interest to disclose. **W.Y.L.** No relevant conflicts of interest to disclose. **T.W.** No relevant conflicts of interest to disclose. **A.G.** No relevant conflicts of interest to disclose. **C.B.C.** No relevant conflicts of interest to disclose. **W.C.B.** No relevant conflicts of interest to disclose. **D.L.R.** No relevant conflicts of interest to disclose.

References

1. Resnick D, Pineda C. Vertebral involvement in calcium pyrophosphate dihydrate crystal deposition disease: radiographic-pathological correlation. Radiology 1984;153(1):55–60.
2. Jones AC, Chuck AJ, Arie EA, Green DJ, Doherty M. Diseases associated with calcium pyrophosphate deposition disease. Semin Arthritis Rheum 1992;22(3):188–202.
3. Richette P, Bardin T, Doherty M. An update on the epidemiology of calcium pyrophosphate dihydrate crystal deposition disease. Rheumatology (Oxford) 2009;48(7):711–715.
4. Neame RL, Carr AJ, Muir K, Doherty M. UK community prevalence of knee chondrocalcinosis: evidence that correlation with osteoarthritis is through a shared association with osteophyte. Ann Rheum Dis 2003;62(6):513–518.
5. Zhang W, Doherty M, Bardin T, et al. European League Against Rheumatism recommendations for calcium pyrophosphate deposition. I. Terminology and diagnosis. Ann Rheum Dis 2011;70(4):563–570.
6. Doherty M, Dieppe P. Crystal deposition disease in the elderly. Clin Rheum Dis 1986;12(1):97–116.
7. Felson DT, Anderson JJ, Naimark A, Kannel W, Meenan RF. The prevalence of chondrocalcinosis in the elderly and its association with knee osteoarthritis: the Framingham Study. J Rheumatol 1989;16(9):1241–1245.
8. Sanmartí R, Pañella D, Brancós MA, Canela J, Collado A, Brugués J. Prevalence of articular chondrocalcinosis in elderly subjects in a rural area of Catalonia. Ann Rheum Dis 1993;52(6):418–422.
9. Bouvet JP, le Parc JM, Michalski B, Benlahrache C, Auquier L. Acute neck pain due to calcifications surrounding the odontoid process: the crowned dens syndrome. Arthritis Rheum 1985;28(12):1417–1420.
10. Aouba A, Vuillemin-Bodaghi V, Mutschler C, De Bandt M. Crowned dens syndrome misdiagnosed as polymyalgia rheumatica, giant cell arteritis, meningitis or spondylitis: an analysis of eight cases. Rheumatology (Oxford) 2004;43(12):1508–1512.
11. Wu DW, Reginato AJ, Torriani M, Robinson DR, Reginato AM. The crowned dens syndrome as a cause of neck pain: report of two new cases and review of the literature. Arthritis Rheum 2005;53(1):133–137.
12. Baysal T, Baysal O, Kutlu R, Karaman I, Mizrak B. The crowned dens syndrome: a rare form of calcium pyrophosphate deposition disease. Eur Radiol 2000;10(6):1003–1005.
13. Scutellari PN, Galeotti R, Leprotti S, Ridolfi M, Franciosi R, Antinolfi G. The crowned dens syndrome: evaluation with CT imaging. Radiol Med (Torino) 2007;112(2):195–207.
14. Salaffi F, Carotti M, Guglielmi G, Passarini G, Grassi W. The crowned dens syndrome as a cause of neck pain: clinical and computed tomography study in patients with calcium pyrophosphate dihydrate deposition disease. Clin Exp Rheumatol 2008;26(6):1040–1046.
15. Doita M, Shimomura T, Maeno K, Nishida K, Fujioka H, Kurosaka M. Calcium pyrophosphate dihydrate deposition in the transverse ligament of the atlas: an unusual cause of cervical myelopathy. Skeletal Radiol 2007;36(7):699–702.
16. Assaker R, Louis E, Boutry N, Bera-Louville A, Paul Lejeune J. Foramen magnum syndrome secondary to calcium pyrophosphate crystal deposition in the transverse ligament of the atlas. Spine 2001;26(12):1396–1400.
17. Kakitsubata Y, Boutin RD, Theodorou DJ, et al. Calcium pyrophosphate dihydrate crystal deposition in and around the atlantoaxial joint: association with type 2 odontoid fractures in nine patients. Radiology 2000;216(1):213–219.
18. Dirheimer Y, Bensimon C, Christmann D, Wackenheim C. Syndesmo-odontoid joint and calcium pyrophosphate dihydrate deposition disease (CPPD). Neuroradiology 1983;25(5):319–321.
19. Constantin A, Marin F, Bon E, Fedele M, Lagarrigue B, Bouteiller G. Calcification of the transverse ligament of the atlas in chondrocalcinosis: computed tomography study. Ann Rheum Dis 1996;55(2):137–139.
20. Fenoy AJ, Menezes AH, Donovan KA, Kralik SF. Calcium pyrophosphate dihydrate crystal deposition in the craniovertebral junction. J Neurosurg Spine 2008;8(1):22–29.
21. Lahmer T, Ingerl D, Heemann U, Thürmel K. If the knee hurts, don't forget the spine! J Clin Neurosci 2011;18(3):424–425.
22. Goto S, Umehara J, Aizawa T, Kokubun S. Crowned dens syndrome. J Bone Joint Surg Am 2007;89(12):2732–2736.
23. Roverano S, Ortiz AC, Ceccato F, Paira SO. Calcification of the transverse ligament of the atlas in chondrocalcinosis. J Clin Rheumatol 2010;16(1):7–9.
24. Wilkins E, Dieppe P, Maddison P, Evison G. Osteoarthritis and articular chondrocalcinosis in the elderly. Ann Rheum Dis 1983;42(3):280–284.
25. Zapletal J, Hekster RE, Straver JS, Wilmink JT, Hermans J. Association of transverse ligament calcification with anterior atlantoodontoid osteoarthritis: CT findings. Neuroradiology 1995;37(8):667–669.
26. Larsson EM, Holtås S, Zygmunt S. Pre- and postoperative MR imaging of the craniocervical junction in rheumatoid arthritis. AJR Am J Roentgenol 1989;152(3):561–566.
27. Toolanen G, Larsson SE, Fagerlund M. Medullary compression in rheumatoid atlanto-axial subluxation evaluated by computerized tomography. Spine 1986;11(3):191–194.
28. Sekijima Y, Yoshida T, Ikeda S. CPPD crystal deposition disease of the cervical spine: a common cause of acute neck pain encountered in the neurology department. J Neurol Sci 2010;296(1-2):79–82.