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A Rare Case of Crowned Dens Syndrome Mimicking Aseptic Meningitis

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Key Words
Crowned dens syndrome · Calcium pyrophosphate dehydrate crystals · Odontoid process · Meningitis · Cervical computed tomography scan · Corticosteroids

Abstract
Background: Crowned dens syndrome (CDS), related to microcrystalline deposition in the periodontoid process, is the main cause of acute or chronic cervical pain. Microcrystalline deposition most often consists of calcium pyrophosphate dehydrate crystals and/or hydroxyapatite crystals. ***Case Presentation:*** This report describes the case of an 89-year-old woman who presented with sudden onset, high fever, severe occipital headache, and neck stiffness. A laboratory examination revealed a markedly elevated white blood cell count (11,100/μl) and C-reactive protein level (23.8 mg/dl). These clinical findings suggested severe infection such as meningitis with sepsis. However, the results of blood culture, serum endotoxin, and procalcitonin were all negative, and cerebrospinal fluid studies revealed only a slight abnormality. The patient was first diagnosed with meningitis and treated with antiviral and antibiotic agents as well as non-steroidal anti-inflammatory drugs, but they only had limited effects. A cervical plain computed tomography (CT) scan and its three-dimensional (3D) reconstruction detected a remarkable crown-like calcification surrounding the odontoid process. On the basis of the CT findings, the patient was diagnosed as a severe case of CDS and was immediately treated with corticosteroids. The patient's condition drastically improved within a week after one course of corticosteroid therapy. ***Conclusion:*** Some atypical symptoms of CDS are misleading and may be misdiagnosed as meningitis, as happened in our case. A CT scan, especially a 3D-CT scan, is necessary and useful for a

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definitive diagnosis of CDS. CDS should be considered as a differential diagnosis of a possible etiology for fever, headache, and cervical pain of unknown origin.

Background

Crowned dens syndrome (CDS) is a radioclinical entity defined by the association of a microcrystalline deposition in the cruciform ligament around the odontoid process and periodic acute cervico-occipital pain with fever, neck stiffness, and biological inflammatory syndrome [1, 2]. The microcrystalline deposition, most often calcium pyrophosphate dehydrate (CPPD) crystals and/or hydroxyapatite crystals, can remain asymptomatic or be responsible for chronic cervical pain or spinal cord compression [1–3]. In general, CPPD crystal deposition disease is clinically associated with acute episodic mono- 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 the knees, wrists, metacarpophalangeal joints, elbows, and shoulders [3, 4].

This report describes the case of an 89-year-old woman who presented with sudden onset, high fever, severe occipital headache, and neck stiffness. Meningitis was suspected, but she was subsequently diagnosed as having CDS based on a remarkable calcification surrounding the odontoid process detected by a computed tomography (CT) scan. The patient was first treated with antiviral and antibiotic agents as well as non-steroidal anti-inflammatory drugs (NSAIDs), but they only had limited effects. However, the patient's condition drastically improved with corticosteroid administration.

Case Presentation

An 89-year-old Japanese woman with a history of hypertension and gastric ulcer was admitted because of sudden onset, high fever, severe occipital headache, and neck stiffness. At admission on June 24, 2012, her body temperature was 38.5°C and her blood pressure 180/96 mm Hg. Upon neurological examination, she regained full consciousness and did not show any neurological defect, except for severe cervical rigidity together with Kernig's sign. Initial routine laboratory examinations (table 1) revealed a markedly elevated white blood cell count (11,100/μl) and C-reactive protein level (23.8 mg/dl). The level of serum uric acid (4.0 mg/dl) was not elevated. The blood examination results for connective tissue disease or vasculitis, such as rheumatoid factor, cytoplasmic anti-neutrophil cytoplasmic antibody (ANCA), perinuclear (P-) ANCA, anti-nuclear, anti-cardiolipin, anti-CL/β2GPI, anti-double-strand-DNA, and anti-cyclic citrullinated peptide antibodies, were all negative or unremarkable. These findings suggested severe infection such as sepsis. However, blood culture revealed a negative result, and no trace of endotoxin was detected. Additionally, the serum procalcitonin level (0.40 ng/ml) was not elevated. Routine cerebrospinal fluid studies revealed a slight abnormality (cell 5/μl and protein 109.2 mg/dl), whereas cerebrospinal fluid culture, anti-herpes simplex virus, and varicella-zoster virus antibodies were all negative (table 1). Brain magnetic resonance imaging (MRI) demonstrated almost normal findings, with no gadolinium enhancement. Based on the patient's clinical symptoms and data, she was first diagnosed with severe aseptic meningitis and treated with strong antiviral and antibiotic agents (acyclovir, 10 mg/kg intravenously three times daily; ampicillin hydrate, 6 g intravenously daily; ceftriaxone sodium hydrate, 4 g intravenously daily) as well as NSAIDs such as loxoprofen sodium hydrate and diclofenac sodium. However, these

primary treatments were not effective, and the patient's condition, particularly the high fever and severe occipital headache with neck stiffness, gradually deteriorated. On June 28, a cervical plain CT scan detected a remarkable crown-like calcification surrounding the odontoid process (fig. 1a–c). A three-dimensional (3D) reconstruction obtained from data of the cervical plain CT confirmed this remarkable crown-like calcification on the posterior side of the dens (fig. 1d). A cervical MRI scan did not demonstrate any direct compression of the cervical cord (data not shown). Based on these radiographical findings, the patient was diagnosed as a severe case of CDS. Immediately, corticosteroid administration (prednisolone, 30 mg orally daily, tapering it off by 5 mg a week) was started. The patient's symptoms and laboratory data drastically improved within a week after one course of corticosteroid therapy.

Discussion

CDS is defined as a combination of acute feverish cervical pain and calcification surrounding the odontoid process [4, 5]. CDS was first described and presented by Bouvet et al. [6] in 1985. They described 4 female cases who experienced severe cervical pain and underwent tomographic examination revealing radiopaque densities surrounding the top and sides of the odontoid process in a crown- or halo-like distribution [3, 6]. The diagnosis of CDS is based on the combination of clinical, biological, radiological, and therapeutic findings: acute periodic attacks of feverish cervico-occipital pain and stiffness with biological inflammatory syndrome, radiological identification of a crown-like calcification surrounding the odontoid process due to microcrystalline deposits, and a drastic improvement of symptoms under the treatment with NSAIDs or colchicine [1–6]. In most of the previously described cases, NSAIDs led to complete recovery within a few days along with normalization of inflammatory markers [1–6]. However, Sato et al. [4] reported a case of CDS who did not recover by NSAIDs but whose condition drastically improved with corticosteroid therapy. This patient presented with polyarticular pain in addition to acute feverish cervical pain, stiffness, and consciousness disturbance, and typical CPPD crystals in the synovial fluid were proven by biopsy in the right knee joint [4]. Sato et al. [4] finally diagnosed this patient with CDS coincident with the exacerbation of pseudogout. Similarly, in the present case, NSAIDs administration (loxoprofen sodium hydrate and diclofenac sodium) was insufficient to improve the patient's condition and serum inflammatory markers. Of course, there are clinical differences in disease severity between the present case and the previous one reported by Sato et al. [4]. However, in both cases, a moderate dosage of corticosteroids (prednisolone, 30 mg orally daily) led to a drastic improvement in the pathological conditions. Therefore, we recommend that corticosteroid therapy should be used primarily and more actively in the early phase of CDS cases.

The triad of fever, headache, and neck stiffness is often suggestive of infectious meningitis and can easily lead to a lumbar puncture [1, 4, 7]. As illustrated by the present case, some atypical symptoms of CDS, including this triad, may mimic meningitis and lead to misdiagnosis. Patients with symptoms suggestive of meningitis are not rare in clinical practice, and therefore CDS should be considered as a differential diagnosis of a possible etiology for fever, headache, and neck pain of unknown origin [1, 4]. In the present case, the serum procalcitonin level was very useful to rule out an infectious disease in the inflammatory syndrome. Moreover, when occipito-temporal, mandible, and shoulder girdle pain is associated with inflammatory syndrome, CDS may also mimic polymyalgia rheumatica (PMR) and/or giant cell arteritis (GCA) and lead to an unnecessary temporal artery biopsy

[1, 8]. Several previous reports describe chondrocalcinosis among a wide spectrum of rheumatic diseases that can mimic PMR and/or GCA because of constitutional symptoms, but not especially in the form of CDS [1, 8–10]. In GCA cases, in particular biopsy-negative GCA cases, Gonzales-Gay et al. [10] observed that PMR and headaches were the most frequent manifestations. These findings raise an important question: are some biopsy-negative GCA cases really GCA or do they include PMR and underrecognized CDS? In clinical practice, some atypical cases of CDS can be difficult to distinguish from PMR and/or GCA. In previous reports [1, 8–10], we did not find any clinical symptom allowing us to distinguish between CDS and PMR and/or GCA. Therefore, the most effective and practical approach we can propose is to perform a CT scan of the cervical spine.

CT scanning focusing on C1 and C2 is the gold standard of CDS diagnosis [1–7, 11]. The findings of CT scans make it possible to identify the anatomical substratum of CDS [1–7, 11]. The typical, tiny, half-ringed, crown-like form of calcification behind the dens is described as the most important and definitive feature of CDS [1–7, 11]. The CPPD and/or hydroxyapatite microcrystalline depositions in periarticular structures, such as the cruciform ligament, around the top and sides of the odontoid process are considered responsible for the various clinical manifestations of CDS [1–4]. In the present case, a cervical CT scan, especially the 3D-CT, was much more useful in assessing calcifications of the dens area than the MRI scan. Additionally, the findings of the CT scan could lead to the definite diagnosis of CDS, even in cases in which it is difficult to identify CPPD microcrystalline deposits directly. Another useful aspect of CT scans is their ability to rule out differential diagnoses of CDS, such as unrecognized odontoid fractures or cervical cord compression, but it is important to keep in mind that CT scans may fail to detect true CDS [1].

Conclusion

Some atypical symptoms of CDS are misleading and may be misdiagnosed as meningitis, as happened in the present case. CDS should be considered as a differential diagnosis of a possible etiology for fever, headache, and cervical pain of unknown origin. CT scanning, especially 3D-CT scanning, is useful and necessary for a definitive diagnosis of CDS. Conventionally, NSAIDs have been regarded as the first-line drugs for CDS. However, in cases that do not improve upon NSAIDs administration alone, treatment with a moderate dosage of corticosteroids is recommended. At present, CDS is a rare neurological condition, and there are only a few case reports about the disease. Therefore, further research and an accumulation of cases are necessary to obtain a good understanding of the pathological conditions of CDS.

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Disclosure Statement

The authors declare that they have no competing interests. There are no financial conflicts of interest in this study.

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Table 1. The initial routine laboratory examination results

	Value (unit)		Value (unit)	Normal range
Blood cell count		Serological study		
WBC	11,100 (/μl)*	RF	4.0 (IU/ml)	<15
RBC	384 (10 × 4/μl)	C-ANCA	<10 (EU)	<10
Hb	11.2 (g/dl)	P-ANCA	<10 (EU)	<10
Ht	32.6 (%)	ANA	<40 (fold)	<40
MCV	84.9 (fl)	anti-ds-DNA-Ab	5.0 (U/ml)	<10
MCH	29.2 (pg)	anti-cardiolipin-Ab	8.0 (U/ml)	<10
MCHC	34.4 (g/dl)	anti-CL-β2GPI-Ab	2.4 (U/ml)	<3.5
Plt	26.1 (10 × 4/μl)	anti CCP Ab	1.5 (U/ml)	<4.5
Blood biochemistry		SS-A	<1.0 (fold)	<1.0
T-Bil	0.4 (mg/dl)	SS-B	<1.0(fold)	<1.0
GOT	17 (IU/l)	CEA	0.9 (ng/ml)	<5.0
GPT	12 (IU/l)	CA19-9	15.0 (U/ml)	<37.0
γ-GTP	19 (IU/l)	CA125	26.3 (U/ml)	<35.0
ALP	237 (IU/l)	sIL-2R	325 (U/ml)	190–650
TP	6.0 (g/dl)	Cerebrospinal fluid		
Alb	3.0 (g/dl)	Cell	5 (/μl)*	0–3
BUN	16.1 (mg/dl)	Mono:Poly	3:2	
Cre	0.39 (mg/dl)	Protein	109.2 (mg/dl)*	3–40
UA	4.0 (mg/dl)	Glucose	71 (mg/dl)	50–75
Na	136 (mEq/l)	Bacterial culture	negative	
K	3.4 (mEq/l)	anti-HSV-IgM-Ab	0.24 (EIA-value)	<0.8
Cl	100 (mEq/l)	anti-HSV-IgG-Ab	<0.20 (EIA-value)	<0.2
CRP	23.8 (mg/dl)*	anti-VZV-IgM-Ab	0.37 (EIA-value)	<0.8
PCT	0.40 (ng/ml)	anti-VZV-IgG-Ab	<0.20 (EIA-value)	<0.2
FBS	138 (mg/dl)			
HbA1c	5.1 (%)			

* Abnormal value.

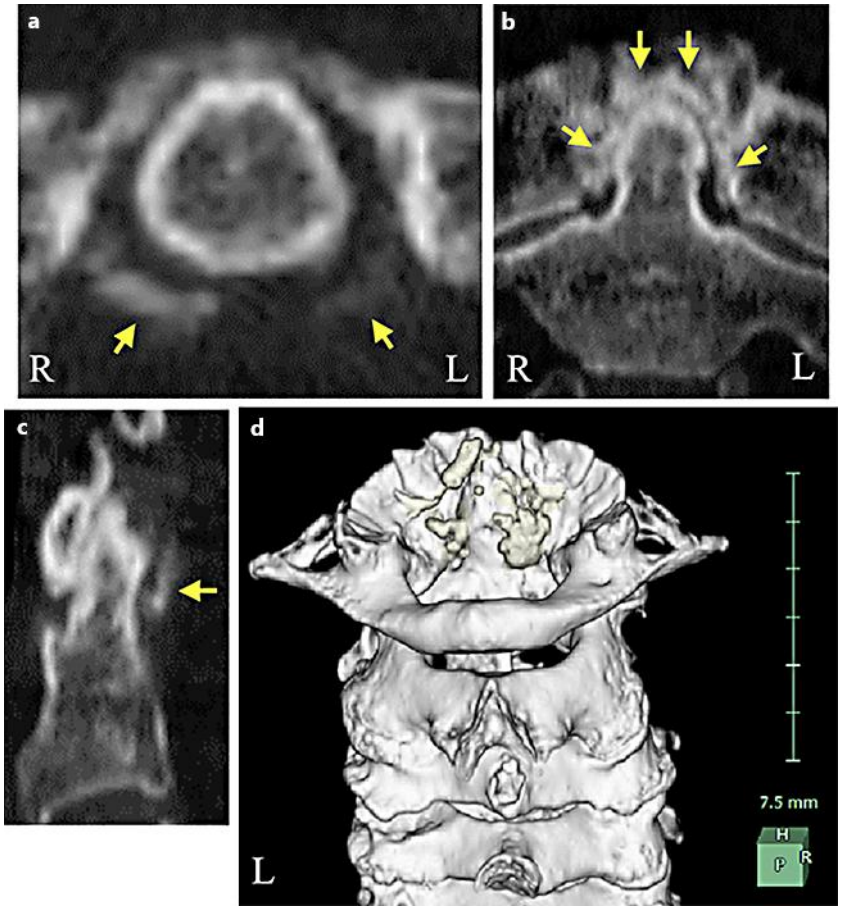

Fig. 1. Cervical CT scans around the odontoid process (dens). **a** The axial image demonstrates the right, dominant, half-ringed form of calcification at the posterolateral side of the dens. **b** The coronal image demonstrates the remarkable crown-like calcifications around the dens. **c** The sagittal image demonstrates the linear calcification at the posterior side of the dens. **d** A 3D reconstruction obtained from data of a plain cervical CT demonstrates the marked crown-like calcification at the posterior side of the dens. The diagnosis of CDS was confirmed by these cervical CT findings.