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CASE REPORT

Orthostatic hypotension as an unusual presentation of spinal calcium pyrophosphate deposition disease: case report and review of literature

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Abstract. Calcium pyrophosphate crystal deposition disease (CPPD), also known as pseudogout, with spinal involvement, is associated with clinical manifestations of acute nerve compression or chronic spinal stenosis. Precipitation of crystals of calcium pyrophosphate dihydrate in connective tissues can lead to acute inflammatory arthritis, degenerative chronic arthropathies, and radiographic evidence of cartilage calcification.

We present a case of an 87-year-old woman, with unstudied chronic polyarthralgia and symptomatic orthostatic hypotension. It were documented acute calcium pyrophosphate deposition wrist arthritis, and cervical CT and MRI was suggestive of spinal involvement of CPPD. Workup excluded other causes of OH. Surgical approach could be indicated to minimize the symptoms, but it was contra-indicated due to the patient's performance status, so histological diagnosis was not possible. Muscle atrophy played an important part in the rapid progression of this insidious chronic disease. Conservative and symptomatic treatment achieve scarce short-term clinical improvement.

Spinal involvement of CPPD was thought to be rare but recent studies show a higher prevalence than expected. We call for attention to the extent of structural changes that may occur when not early diagnosed nor treated. High clinical suspicion is required and this is, to our knowledge, the first report of orthostatic hypotension as a presentation of CPPD.

Keywords: chondrocalcinosis, calcium pyrophosphate deposition disease, calcium pyrophosphate dihydrate deposition, orthostatic hypotension, orthostatic intolerance, pseudogout.

What is new/important?

i) to highlight the first case report to our knowledge of orthostatic hypotension as a presentation of Calcium pyrophosphate crystal deposition disease (CPPD);
ii) to call for attention to the extent of structural changes that may occur when CPPD is not early diagnosed nor treated;
iii) the presence of neurogenic orthostatic hypotension should guide appropriate workup.

INTRODUCTION

The spectrum of calcium pyrophosphate crystal deposition disease (CPPD) includes several clinical syndromes [1]. Precipitation of crystals of calcium pyrophosphate dihydrate in connective tissues is associated with acute inflammatory arthritis, degenerative chronic arthropathies, and radiographic cartilage calcification [1, 2, 3, 4]. It has been estimated to affect up to 7 percent of the adult populations of Europe and the United States, especially persons of advanced age and women [1]. In this case, we describe an approach to orthostatic hypotension which is revealed as an unusual presentation of cervical spine compression related to spinal involvement of CPPD.

CASE REPORT

An obese 87 years-old woman was admitted to the emergency department due to an altered mental state. She had had previous episodes of dizziness with temporary loss of balance with standing. Her history included unstudied chronic polyarthralgia, occasional episodes of wrist arthritis treated with corticotherapy, being still independent

and able to walk with minimal aid. She was lethargic and hypotensive. An urinary sepsis motivated hospital admission. After resolution of the infection, we found persistent orthostatic hypotension, with a systolic blood pressure drop of 60 mmHg without reflex tachycardia, and syncope when standing. A review of prescriptions excluded hypotensive medications. The electrocardiogram and Holter monitoring revealed persistent atrial flutter with a controlled ventricular rate of unknown duration. As a result, the patient was anticoagulated and underwent successful cardioversion. An echocardiogram with contrast was performed, which ruled out any cardiac shunt and showed normal results. Cervical doppler excluded significant carotid stenosis. Anemia, hypoglycemia, and altered thyroid function were not present. Adrenal failure and pheochromocytoma were ruled out as cortisol levels, plasma catecholamines, and metanephrines were within normal range. Amyloidosis was considered, but serum amyloid A testing yielded negative results, and a tissue biopsy was not performed. Additionally, thoracic abdominopelvic CT, endoscopic studies, normal immunoglobulins levels and serum and urinary electrophoresis excluded malignancy and did not reveal findings suggestive of amyloidosis. Hospital stay was further complicated and prolonged by an uncomplicated nosocomial urinary tract infection. After resolution of the infection, the patient still was unable to maintain orthostatism without hypotension. Additionally, there was a flare-up of arthritis in the wrist, accompanied by elevated inflammatory markers, despite sterile urine and blood cultures. Arthrocenthesis revealed calcium pyrophosphate crystals. Rheumatoid factor, anti-CCP and ANAs were negative. Anti-ganglionic acetylcholine receptor antibodies were also negative. Considering the absence of reflexive tachycardia, clinically grade 4 neurogenic OH, spinal imaging was performed. CT and MRI showed significant high cervical spine changes, particularly in the atlantoaxial joint, with periodontoid ligaments calcification, crowned dens or retro-odontoid pseudotumor, osteophyte formation, narrowing of intervertebral discs, causing diminished endocanalar space and basilar impression.

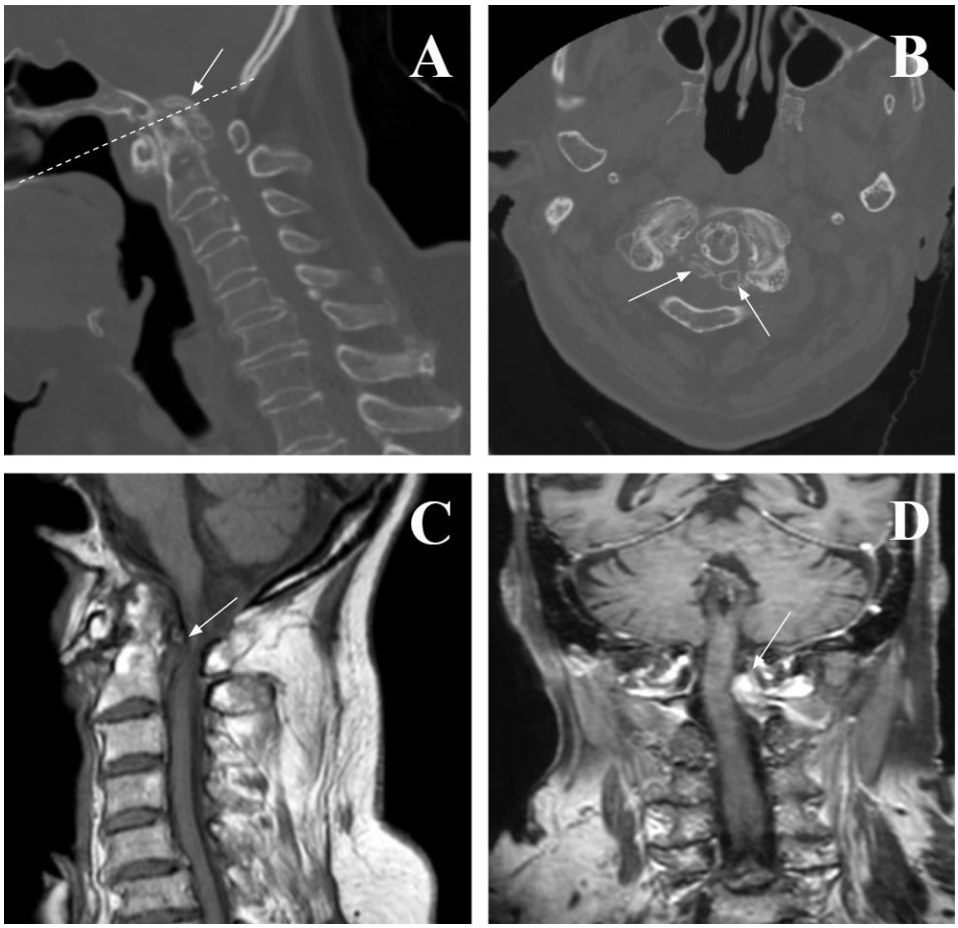


Figure 1. Cervical CT (A,B) and MRI (C,D) showed atlantoaxial joint changes, with periodointoid ligaments calcification, retro-odontoid pseudotumor (arrows) and basilar impression (dashed line), reducing endocanalar space.

Taking into account chronic joint complaints that responded to corticosteroid, acute wrist arthritis, raised inflammatory parameters without evidence of infection, we considered it as a probable spinal involvement of CPPD manifesting as neurogenic OH. Concerning both the extent of degenerative changes, the patient frailty and myopathy associated with the prolonged hospital stay, surgical treatment was set apart. Conservative treatment with colchicine and corticosteroids and symptomatic approach with midodrine, compression garments and the use of a cervical collar when standing, achieved scarce clinical improvement. Eventually evolved with progressive dysphonia, tetraparesis and constipation in one month, and increased dependence in daily life activities.

DISCUSSION

Calcium pyrophosphate crystal deposition in the *ligamentum flavum* and at the cervical spine level, or in the posterior longitudinal ligament, can manifest with symptoms of acute nerve compression or chronic spinal stenosis [1, 2, 4]. Literature review on this theme was not made easy by the lack of consistency in terminology for spinal involvement of CPPD [1, 2, 9, 10, 12]. Different designations are used for similar or related entities, such as crowned dens syndrome, ossification or calcification of the *ligamentum flavum*, or retro-odontoid pseudotumor [4, 11, 12]. Spinal involvement of CPPD disease was thought to be rare but recents study reported a higher than expected prevalence of atlantoaxial CPPD crystal deposition, including symptomatic involvement of the spine [2, 3, 4].

The key manifestation in this case was the presence of orthostatic hypotension. OH consists in a sustained decrease in blood pressure of more than 20 mmHg for systolic pressure or more than 10 mmHg for diastolic pressure three minutes after standing upright or during a head-up tilt at 60 degrees. Orthostatic hypotension in the absence of adequate compensatory heart rate increase, is typically neurogenic, caused by central or peripheral nervous system diseases that result in autonomic failure [5, 7, 8]. OH is common, often multifactorial, and has a great impact on the elderly population, but the presence of a neurogenic orthostatic hypotension, should prompt the realization of spinal imaging after appropriate workup [6, 7]. Articular complaints are prevalent, usually degenerative, but they must not be dismissed in the absence of adequate workup excluding etiologies with available treatments with impact in the natural history of disease [1, 9].

Our patient had known major risk factors for CPPD, i.e., old age, previous history of polyarthralgias and wrist arthritis [1, 4]. CPPD disease can be idiopathic, hereditary or related to metabolic diseases [1]. We did not perform genetic testing and we did not find family history of CPPD. We did not encounter concurrent metabolic disturbances nor disorders that justified neurogenic OH. Autoimmunity panel was negative, but co-occurrence of rheumatoid arthritis is frequent [4, 9]. To establish definitive CPPD it requires synovial fluid examination and identification of CPP crystals, and identification of CPP crystals on the synovial fluid of the acute wrist arthritis established CPPD in this case [1]. Although there were no unequivocal signs of myelopathy on MRI, the diminished endocanalar space and basilar impression seemed to cause cervicomedullary compression in orthostatism and elevation of the headland above 30º, supporting our hypothesis of neurogenic OH secondary to bulbar and cervical spinal medulla compression from extensive spinal CPPD, along with contribution of degenerative changes and acquired muscle atrophy. The described cervical imaging findings were previously reported as imaging manifestations of spinal CPPD [1, 2, 10, 11]. Computerized tomography (CT) is alternatively used to identify CPPD with high sensitivity and specificity [2, 10]. A surgical approach could also be adopted to minimize the symptoms and set the definitive histological diagnosis, which was not possible [7, 11, 12]. The favorable response to early treatment with anti-inflammatory drugs highlights the importance of the timely diagnosis [1, 2, 4].

CONCLUSIONS

To the best of our knowledge, this case is the first report of orthostatic hypotension as a presentation of CPPD. It highlights the importance of maintaining a high clinical suspicion, especially when evaluating elderly women with articular symptoms that initiate around the age of 50 and exhibit some inflammatory characteristics. We emphasize the significance of early diagnosis and treatment of CPPD to prevent the progression of structural changes. In this regard, neurogenic orthostatic hypotension should serve as a guide for conducting a thorough diagnostic workup, including prompt spinal imaging.

Boala depunerii depozitelor de cristale de calciu pirofosfat (CPPD), pseudogută cu afectare vertebrală este asociată cu fenomene de compresie acută a nervilor sau cu stenoza cronică spinală. Precipitarea cristalelor în țesutul conjunctiv se asociază cu artrită, artropatie cronică degenerativă și evidențierea calcificărilor la nivel cartilaginos.

Prezentăm cazul unei paciente de 87 de ani cu poliartralgie cronică și hipotensiune ortostatică simptomatică. Pacienta avea depuneri la nivelul pumnului iar RMN-ul și CT-ul cervical au indicat afectare vertebrală. S-au exclus alte cauze. Teoretic, cazul ar fi necesitat intervenție chirurgicală, care însă nu a fost realizată având în vedere statusul pacientei și astfel nu am putut avea o confirmare histologică. Atrofia musculară a avut un rol important în progresia rapidă a bolii cronice.Tratamentul simptomatic a dus la o îmbunătățire pe termen scurt.

Afectarea vertebrală în CPPD este rară dar studii recente au arătat o prevalență mai mare decât cea așteptată. Pentru diagnostic este necesar un index de suspiciune mare și acesta este primul caz de CPPD cu prezentare ca hipotensiune ortostatică.

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Ethical disclosure: The conditions of the Helsinki Declaration were satisfied. Written informed consent was obtained.

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