Calcium pyrophosphate dihydrate deposition disease of the filum terminale

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Abstract

Introduction Calcium pyrophosphate dihydrate crystal deposition disease (CPPDD) is a rare benign inflammatory joint disorder characterized by the presence of calcium pyrophosphate dihydrate crystal in the interarticular and periarticular tissue. It has been rarely described with spinal localization.

Methods A 50-year-old woman, affected by CPPDD, presented a progressive weakness of both lower limbs associated with neurogenic claudication. Neuroradiological examinations revealed the presence of two intradural calcified lesions at level L3–L4, with no post-contrast enhancement.

Results Surgery was performed and the histopathological exams documented the presence of rod-shaped crystals embedded in a fibrocartilaginous stroma. The postoperative course was uneventful and the patient experienced complete symptoms relief with a 5-year follow-up.

Conclusion Intradural CPPD localization at the filum terminale is an extremely rare occurrence. Total removal should be preferably attempted with a long-term focal control of the disease as we observed in our case.

Keywords Calcium pyrophosphate dihydrate deposition disease · Filum terminale · Spine · Neurogenic claudication

Introduction

Calcium pyrophosphate dihydrate crystal deposition disease (CPPDD) is a rare benign inflammatory joint disorder characterized by the presence of calcium pyrophosphate dihydrate crystal in the interarticular and periarticular tissue [1, 2]. Patients affected by CPPDD often present a mono or oligoarthropathy, generally involving knees, wrists, metacarpophalangeal joints, pubic symphysis and hip; tophaceous pseudogout (tumoral or massive CPPDD) is one of its rarest clinical forms characterized by focal deposition of CPPD [1, 3–5]. It has been rarely described with spinal localization, where it affects prevalently the fibrous and cartilaginous structures such as intervertebral disc and annulus fibrosus, ligamentum flavum, posterior longitudinal ligaments and transverse ligaments [5].

We report the first case of a 50-year-old woman affected by CPPDD, who developed a progressive neurogenic claudication due to intradural tumoral CPPD localization.

Case report

A 50-year-old woman, affected by CPPDD, was referred to our Department for the treatment of lumbar intradural focal CPPD localization.

The diagnosis of chondrocalcinosis had been made at the age of 36 for the occurrence of fever, arthralgia which prevalently involved the metacarpophalangeal joints and the wrists and less significantly the knees, resembling mainly a pseudo-osteoarthritis form, according to Mc Carty's classification [6] and high erythrocyte sedimentation rate and the evidence of radiodense deposits of CPPD at the level of articular cartilage on radiological examination. Since then,

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Fig. 1 **a** Sagittal T2-weighted MR image showing two intradural hypo-intense *round-shaped* lesions at L3–L4 level. The CT scan showed a prevalently calcified component of the masses, respectively at L3 (**b**) and L4 (**c**)

she had been started on colchicine therapy with progressive relief of articular pain symptoms.

After 14 years of disease, the patient presented a progressive weakness of both lower limbs associated with neurogenic claudication after 50 m of walking. She exhibited lumbar extension limitation. At the neurological examination mild sensory loss to pinprick and moderate hyposthenia of both lower limbs were detected. Decreased patellar and ankle jerks were observed bilaterally.

Computed tomography and magnetic resonance images of the lumbar column revealed the presence of two intradural calcified lesions (8 and 11 mm in diameter, respectively) at level L3–L4, with no post-contrast enhancement (Fig. 1). No significant hypertrophy of the ligamentum flavum was observed; however, at L3–L4 levels, signs of calcifications of the posterior elements, in particular the ligaments, could be observed. The other segments of the spine did not show significant alterations, with the exception of initial signs of degenerative changes in the intervertebral discs.

The patient underwent a L3–L4 laminectomy; during surgery the laminae were found to be thicker than normal and the ligamentum flavum appeared stiff and strongly adherent to the laminae. Once the dura mater had been exposed, there were no signs of dural ossification; after opening the dura mater three calcified spot were observed over the arachnoid membrane. The arachnoid membrane was then opened, revealing two calcified, oval nodules. They were attached to the filum terminale by a vascular pedicle, which was coagulated and cut; intraoperative neurophysiologic exam excluded any motor activity in the attaching fibres. There were no stiff adhesions to nerve roots (Fig. 2).

The histopathological exams documented the presence of irregular massive deposits of prevalently rod-shaped calcium pyrophosphate dihydrate crystals of various size,

embedded in a fibrocartilaginous stroma and resembling a multinodular pattern; the polarized light microscopy showed positively birefringent signal.

The postoperative course was uneventful and the patient experienced an immediate symptoms relief. After 5 years, the patient has no symptom relapse and the radiological imaging confirms the complete removal of the calcified lesions, with no evidence of recurrence.

Discussion

Calcium pyrophosphate dihydrate crystal deposition disease (CPPDD) is also known as “pseudogout”, for the first description of gout-like symptoms without sodium urate crystals and as “chondrocalcinosis” for the characteristic multiple foci of calcification in hyaline and fibrocartilage of the joints and intervertebral discs [2].

Although diffuse or non-tumoral deposition of CPPD involving large articular joints and para-articular tissues represents the most frequent clinical form, focal, massive and tumoral CPPDD have been also described in these tissues [2, 4, 7, 8].

Tumoral CPPDD involves prevalently the temporomandibular joint, followed by the cervical spine and hand. Clinically, it has a wide range of manifestations, from asymptomatic to severely destructive arthropathy or conditions simulating a neoplasm depending on the site of the focal localization. Tumoral CPPDD occurs in patients with a mean age of 60 years and mostly in females [2].

Spine involvement has been increasingly reported during the last decade [3]. The more commonly affected region is the cervical tract, followed by the lumbar and thoracic types. In particular at the cervical level, the CPPD deposition may appear as a periodontoid mass (not

Fig. 2 Intra-operative findings. **a** The dura was opened; three calcified spot were observed over the arachnoid membrane. **b** The arachnoid was then opened, revealing the presence of the first calcified mass. **c, d** The two calcified lesions appeared deeply hidden

among the nerve roots of the cauda equine and attached to the filum terminale by a vascular pedicle (arrow), which was coagulated and cut (**e**)

distinguishable by rheumatoid disease) or as focal ossification of the ligamentum flavum in the subaxial cervical spine [3]. The thoracic and lumbar localization may involve the nucleus pulposus of the intervertebral disc, the annulus fibrosus, the yellow ligaments and the posterior longitudinal ligaments with secondary myelopathy for spinal cord compression and vertebral stenosis [5, 9].

Markiewicz et al. [10] measured the incidence of CPPDD in specimens of ligamenta flava in a series of consecutive patients undergoing spinal decompression for vertebral stenosis. They observed that patients with the symptoms of spinal stenosis, who were also CPPD positive, presented with more acute onset than in the CPPD-negative patients; except for this aspect, both the groups of patients shared the same clinical manifestations of lumbar stenosis. Overall, the failure rate after the surgical decompression was about 20 %, with no mention on a different incidence in CPPD positive patients and they stated that some patients may benefit from medical management delaying or avoiding at all the need of surgery.

More recently, Yayama et al. [11] analysed a series of consecutive patients undergoing decompressive laminectomy spinal stenosis with no history and/or evidence of genetically bound bone, joint, or musculo-ligamentous tissue abnormalities and who had not taken specific therapeutic agents such as corticosteroids or immunosuppressants and reported CPPDD in the ligamentum flavum in 36 % of patients. This study does not report any consideration on the surgical success rate (this was not the purpose of the study).

Muthukumar et al. [3] reported on a series of six patients with CPPDD involving the ligamentum flavum of the cervical and thoracic spine; all but one did not experience local recurrence during a follow-up which ranged from 7 months to 3 years. One patient had a recurrence of CPPDD at a new level after 2 years.

Anyway, most of the authors who dealt with this pathology with spinal localization agree on the indication of surgical removal for decompression, reporting not currently known local recurrences; on the other hand, these patients must be followed longer because the surgical procedure aims to obtain symptoms relief, not to cure the systemic disease [3].

We performed a total removal of the intradural lesions and after 5 years there are no recurrences; we are still following the patient in our clinic with periodical clinical and radiological evaluations.

To our knowledge, we report on the first case of intradural CPPDD of the filum terminale. In the literature, masses of calcifications of the filum terminale requiring surgical removal have been described in a case of tumoral calcinosis [12] and in a case of gouty tophi in the filum terminale in a patient without systemic gout [13].

Nevertheless, tumoral CP-PDD must be differentiated from tophaceous gout, tumoral calcinosis, and malignant or benign tumours. In gout, urate crystals are water soluble and are not preserved in conventionally fixed histological sections and they appear as needle-shaped crystals easily distinguished from rhomboid crystals of CPPD. Tumoral calcinosis is another entity characterized by massive calcified deposits in soft tissues composed mainly by

hydroxyapatite [2]. The crystals of CPPD are 2–40 µm with rhomboid shape, but small-long rods and even squares may be seen; they appear birefringent with polarized light. They may present chondroid metaplasia and atypical chondrocytes, which could raise the suspicion of chondroma or chondrosarcoma, but calcified chondroma contains calcium phosphonate deposits [4].

At present, the specific mechanism underlying the formation of CPPD deposits remains unknown [3, 11]. Matrix mineralization, changes in the constitution of proteoglycans, secretion of amorphous materials and proteoglycans by hypertrophic chondrocytes are some of the more frequent hypotheses described in the literature [11]. The focal occurrence of CPPD on the filum terminale may hardly be explained by one of those theories, even if we consider the fibrous component of the filum.

Indeed, the filum terminale is a thin fibrous band constituted by two parts: the filum externa (from the dural sac to the coccyx) and the filum interna (from the conus to the dural sac). Various studies have demonstrated abundance of collagen and elastic fibres, as well as undifferentiated, progenitor cells or multipotent precursors, explaining, according to some authors, the occurrence of ependymal tumours or teratoma at that level [14–16]. In particular Tubbs et al. [17] described the presence of smooth muscle, nerve, bone, cartilage and adipose tissue in samples from cadaveric filum externa.

We do not believe that the involvement of the filum terminale may be explained considering possible mechanisms of contiguity, because the dura was macroscopically intact. In the literature, a dural involvement has been reported only in a single case of tumoral calcinosis [18]. On the other hand, we think that the presence of a vascular pedicle should not be underestimated: the distribution of the vascularization of the filum terminale appears constant in normal conditions, with a single artery, the artery of the filum (preferably described as the inferior termination of the artery of the lumbar enlargement), arising from the termination of the anterior spinal axis and a vein localized behind the artery, as in the spinal cord [19]. It has been demonstrated that tumoral or vascular lesions of the filum terminale may be vascularized by the artery of the lumbar enlargement descending to an abnormally low level, rising, in this specific setting, the suspicion that crystal deposits may have been transported in the filum through haematogenous dissemination mechanism.

Nevertheless, no conclusive data may be address to explain the focal occurrence of CPPD on the filum terminale.

Conclusion

Intradural CPPD localization at the filum terminale is an extremely rare occurrence. Total removal should be

preferably attempted with the aid of intraoperative neurophysiologic examination, with a long-term focal control of the disease as reported in our experience and according to the literature.

Conflict of interest The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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