Cervical radiculomyelopathy caused by deposition of calcium pyrophosphate dihydrate crystals in the ligamenta flava

Case report

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A case of cervical radiculomyelopathy caused by multiple calcified nodules in the ligamenta flava is presented. Roentgenological examination of the cervical spine showed radiopaque nodular lesions, 7 × 7 × 5 mm in size, located in the paramedian portion of the posterior spinal canal. The nodules were removed surgically and they were confirmed to be calcifications of ligamenta flava. Microscopic examination of the nodules with the polarized light revealed extensive deposition of crystals. By x-ray diffraction study, the crystal was determined as calcium pyrophosphate dihydrate (CPPD: \( Ca\_{2+}P_2O_7 \cdot 2H_2O \)). Although CPPD deposition in the cartilage has been known as pseudo-gout syndrome, deposition in the ligament has been reported only in a few cases. This is the first case with radiopaque calcified nodules in the ligamenta flava causing spinal cord compression, the composition of which proved to be CPPD.

KEY WORDS • cervical radiculomyelopathy • ligamentum flavum • chondrocalcinosis • calcium pyrophosphate dihydrate crystal deposition • pseudo-gout syndrome

Since the detailed descriptions by Žižtian and Sit’aj,10 and by McCarty, et al.,5,6 the clinical syndrome associated with calcification of the articular cartilage has received increased attention in the past several years. Žižtian and Sit’aj10 described the entity as “articular chondrocalcinosis” from their roentgenological observations. At about the same time, McCarty, et al.,5,6 analyzed deposited crystals from the inflamed joint and confirmed them to be calcium pyrophosphate dihydrate (CPPD). They preferred the term “pseudo-gout syndrome” because of its clinical resemblance to classical gout. Recently, McCarty7 proposed the designation of “CPPD crystal deposition disease” for the syndrome.

Although many cases have been reported with CPPD deposition in the intervertebral disc, causing prominent osteophytosis and destruction of the apophyseal joint, only four cases of CPPD deposition in the ligamentum flavum have appeared in the world literature.1,2 We report a unique case of CPPD crystal deposition in the ligamenta flava, producing spinal cord compression.

Case Report

This 63-year-old woman was admitted to Kitasato University Hospital in October, 1977, complaining of gait disturbance. She had been in good health until November, 1976, when she first noticed a tingling sensation in the fingertips of both hands. Four months after the initial symptoms, she first noticed difficulty in walking and clumsiness of the fingers of both hands. These symptoms progressed gradually until the time of admission. She had no history of spinal injury or joint pain. Family history was noncontributory.

Examination. On admission, general physical examination showed no abnormalities. Blood pressure
was 130/80 mm Hg, and pulse rate was 60/min. Neurologically, her motor system was disturbed; her gait was severely spastic, there was marked muscle weakness in both hands, and deep tendon reflexes were exaggerated in all four extremities except for biceps reflexes, which were hypoactive. A Babinski sign was not elicited. Slight hyperalgesia and hypesthesia were noticed in the area between the C-6 and T-1 dermatomes. Vibration sense was impaired moderately in both lower extremities, but position sense was not affected.

Complete blood count and urinalysis on admission were within normal limits. Erythrocyte sedimentation rate was moderately elevated, at 26 mm/hr. Blood chemistry showed: Ca 9.3 mg, inorganic P 3.9 mg, Mg 2.0 mg, Cu 124 µg, uric acid 6.1 mg, Fe 101 µg, and a total iron binding capacity of 274 µg/100 ml. Alkaline phosphatase was 7 K-A units. All of these findings were within the normal range of our laboratory. C-reactive protein and rheumatoid factor were negative. Glucose tolerance test was nondiabetic. The level of parathyroid hormone in the blood was normal, at 0.14 ng/ml. Testing for HL-A B27 antigen was reported to be negative.

Cerebrospinal fluid (CSF) obtained by lumbar puncture contained 1 cell/cu mm; total protein was 86 mg/dl; and sugar was 73 mg/dl. Queckenstedt's test revealed moderate subarachnoid block in the neutral and anterior flexed neck positions, and complete block in neck extension.

On x-ray study, spondylotic change of the cervical spine was minimal. Oval, calcified nodules, measuring 7 × 7 × 5 mm, were found in the posterior part of the spinal canal (Fig. 1). These were observed more clearly by tomogram (Fig. 2). The nodules were shown on the axial tomogram to be situated symmetrically in the paramedian portion of the posterior spinal canal (Fig. 2 right). There was a total of five nodules, one at C3–4, two at C4–5, and two at C6–7. Complete skeletal survey revealed no abnormal findings except for a linear calcification of the lateral meniscus of the left knee joint. Preoperative myelography showed extradural compression corresponding to the nodules (Fig. 3).
Calcified crystals in ligamentum flavum

Operation. Laminectomy was performed from C-2 through T-1. Calcified nodules, as shown on the x-ray studies, were found in the ligamenta flava. They were fairly well demarcated from the normal ligament. The nodules were composed of fine granules, and were chalky white in color. They had the consistency of pumice, less hard than bone. Although the nodules adhered to the dura mater tightly, it was possible to remove them completely.

Postoperatively, the patient showed remarkable improvement of neurological signs and symptoms and was discharged in January, 1978.

Histological Study. Microscopically, the nodules contained two types of materials, both positive for calcium by Kossa’s stain. One contained many fragments of coarse, angulated materials, and the other was composed of a finely granulated or amorphous substance. A transitional pattern between them was also observed (Fig. 4 left). The finely granulated substance tended to be deposited at the border of the nodules. The deposits were scattered throughout the degenerated ligament. Some of them were associated with inflammatory reactions. Frequently clustered around the deposition were chondrocytes, considered to be chondrocytic metaplasia of

FIG. 3. Myelogram showing the spinal cord compressed by the extradural lesions corresponding to the calcified nodules.

FIG. 4. Microphotograph of the calcified nodules in the ligamenta flava. Left: Two types of materials are observed in the ligamentum flavum. They are composed of finely granulated or amorphous substance and of coarse, angulated fragments. The former has a strong tendency to lie at the border of the nodules. H & E, × 35. Right: Section taken far from the spinal lamina. The chondrocytes are considered to be chondrocytic metaplasia of fibroblasts, a result of the degeneration of the ligamentum flavum. H & E, × 75. Insert: Higher magnification of metaplastic chondrocytes. H & E, × 189.
fibroblasts, a result of the degenerative process of the ligament (Fig. 4 right). With the polarized light microscope, the finely granulated substance was revealed to be positively birefractive crystals. Scanning electron microscopy demonstrated rod- or pillar-shaped crystals with a length of 80 μm to 3 μ (Fig. 5).

The crystals deposited in the tissue were examined by x-ray microdificrometer. The x-ray diffraction pattern of the crystal coincided well to that of CPPD \( \text{Ca}_2\text{P}_2\text{O}_7 \cdot 2\text{H}_2\text{O} \), reported in ASTM card No. 27-1062 (Fig. 6), and was distinctively different from that of dicalcium orthophosphate, hydroxyapatite, or sodium urate.

**Discussion**

The entity of chondrocalcinosis has not yet been fully established. It seems to arise in various conditions such as hereditary hemochromatosis, hyperparathyroidism, diabetes mellitus, and classical gout, or it may arise independently.\(^5\) Investigation of the present case failed to determine its predisposing factors.

A unique finding in the present case is the nodular opacifications in the ligamenta flava seen on x-ray study. The x-ray findings of CPPD deposition disease have been studied extensively by Resnick, et al.,\(^6\) and by Žitňan and Sitja.\(^7\) They reported that the morphology of the calcification was either linear or diffuse. Nodular calcification was not described in their reports.

We could find only two previous cases in which nodular calcification was observed in the ligamenta flava.\(^1,8\) The nodules in both cases compressed the cervical spinal cord. One of these cases, reported by Nanko, et al.,\(^8\) (first case of Kamakura, et al.) was similar to the present case roentgenologically, histologically, and in the operative findings. Although they suspected pseudo-gout syndrome because of the presence of calcification of multiple joint cartilages, crystal deposition was not observed in their case. The other case was reported recently by Ellman, et al.\(^1\) In their report, spinal cord was found at the operation to be compressed by the tophaceous material in the ligamentum flavum. The material was confirmed to be CPPD by its x-ray diffraction pattern. In the absence of roentgenological description and clinical details in that report, it is difficult to discuss their case in relation to ours.

Three cases with hemochromatosis and deposits of CPPD in the ligamentum flavum have been reported by Bywaters, et al.\(^4\) The CPPD was slight in the lumbar region, and was seen as linear deposits on x-ray examination. These three patients were reported to have no neurological manifestations.

Ours is the first case with spinal cord compression by radiopaque calcified nodules in the ligamenta flava, of which the composition was proved to be CPPD. It is our opinion that, as a result of the disturbance of calcium metabolism, CPPD may have become deposited in the metaplastic chondrocytes in the ligamenta flava in this case.
Calcified crystals in ligamentum flavum

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References


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