Progressive thoracic myelopathy caused by spinal calcium pyrophosphate crystal deposition because of proximal junctional vertebral compression fracture after lumbopelvic fusion

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Abstract

Purpose We describe cases presenting with progressive thoracic myelopathy after lumbopelvic fusion attributed to proximal junctional vertebral compression fracture (PJF) followed by spinal calcium pyrophosphate dehydrate (CPPD) crystal deposition.

Methods The study included six patients, ranging from 62 to 75 years. All patients had been treated previously with lumbopelvic fusion. The mean period from the detection of PJF to the onset of myelopathy was 4.8 months. Notably, five patients demonstrated upper-instrumented vertebra (UIV) collapse.

Results After revision surgery involving decompressive laminectomy and extension of the spinal fusion, all patients experienced significant improvement. Photomicrographs of the resected ligamentum flavum showed CPPD crystals and multinucleated giant cells.

Conclusions The combination of mechanical stress plus PJF and CPPD crystal deposition followed by a foreign body reaction to the deposited crystals caused myelopathy. Patients with radiographic evidence of PJF, especially UIV collapse, after lumbopelvic fusion should be followed carefully for the emergence of myelopathy.

Keywords Adjacent segment disease · Calcium pyrophosphate dehydrate · Proximal junctional vertebral compression fracture · Thoracic myelopathy · Lumbopelvic fusion

Introduction

Fixation of spinal segments following spinal instrumentation can increase the stresses on unfused adjacent segments and cause accelerated degeneration. Any abnormal process that develops in the mobile segment next to a spinal fusion is known as an adjacent segment disease (ASD) [1–3]. Proximal junctional vertebral compression fracture (PJF) is one type of ASD that can sometimes result in severe neurological deficits [4, 5].

Spinal deposition of calcium pyrophosphate dehydrate (CPPD) crystals occasionally leads to neurological deficits through compression of the neural elements. However, thoracic myelopathy caused by CPPD crystal deposition due to PJF as an ASD has never been reported.

The purpose of this article is to describe our experience with six patients presenting after lumbopelvic fusion with progressive thoracic myelopathy attributed to PJF, followed by spinal CPPD crystal deposition in the adjacent segment immediately above the instrumented segment.

Methods

Between June 2007 and December 2010, we treated six patients (four women and two men) with progressive thoracic myelopathy arising from CPPD crystal deposition presenting as an ASD after lumbopelvic fusion. Figure 1 shows typical findings of CPPD crystal deposition.

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Fig. 1 Case 3: typical findings of CPPD crystal deposition immediately above the UIV collapse. *Left* sagittal T2-weighted MR image. *Right* sagittal CT scan

Demographic information for the study group is shown in Table 1. The patients' age at the time of revision surgery ranged from 62 to 75 years. All patients presented with a progressive thoracic myelopathy and had previously undergone instrumented long fusion from the thoracolumbar junction to the pelvis for degenerative lumbar disease. All these patients developed neurological deficits because of PJFs followed by CPPD crystal deposition of the adjacent segment immediately above the instrumented segment. T10–T11 were involved in three patients and T9–T10, T11–T12 and T12–L1 each in one patient. Before the onset of myelopathy, the patients had back pain without any traumatic episode. The presence of PJF was determined by radiographic examination. However, because the

patients had no neurological symptoms or any evidence of calcification or spinal stenosis at the time, their clinician chose careful observation with a rigid brace.

Results

The mean period from the detection of a PJF to the appearance of thoracic myelopathy was 4.8 months, with a range of 2–11 months. When myelopathy developed, five of the six patients demonstrated upper-instrumented vertebra (UIV) collapse and disc injury causing anterior subluxation of the supra-adjacent vertebra. Magnetic resonance (MR) imaging revealed an oval-shaped excrescence, uniformly hypointense on T1- and T2-weighted images, situated posterior and/or anterior to the dural sac. A CT scan showed that the lesion included calcification. Three of the six patients exhibited not only a calcified ligamentum flavum (LF), but also a calcified herniated nucleus pulposus (HNP), causing spinal stenosis. Four patients underwent emergency surgery after they were unable to walk. The mean duration to the surgery was 9.5 h, with a range of 7–12 h. Two other patients underwent scheduled surgery with urgency. All patients underwent decompressive laminectomy and removal of the calcified LF and extension of the spinal fusion to the upper/middle thoracic spine. The new upper level was selected to cross over the apical vertebra of the thoracic kyphosis of each patient. Photomicrography of the resected LF showed CPPD crystal deposition, degenerated elastic fibers, extended fibrosis and multinucleated giant cells. None of

Table 1 Patient demographics

Case	1	2	3	4	5	6
Sex	Female	Female	Female	Female	Male	Male
Age (years)	62	75	74	72	71	72
Body mass index (kg/m ²)	28.2	26.8	25.5	28.8	21.0	25.5
Bone mineral density (g/cm ²)	0.390	0.439	0.538	0.562	–	0.600
Principal diagnosis for initial surgery	Canal stenosis	Degenerative kyphosis	Canal stenosis	Degenerative scoliosis	Canal stenosis	Degenerative kyphoscoliosis
Pre-/postoperative ASIA Impairment Scale score	C/E	C/D	B/D	B/D	D/E	D/E
Previously fused segment	T10–S	T11–S	T11–S	T11–S	L2–iliac	L1–iliac
Vertebral compression fracture	T10	T11	T11	T11	L1	L1
Time to revision after last operation (months)	8	3	36	30	9	5
Time to onset of myelopathy after detection of proximal junctional fracture (months)	4	2	3	11	5	4
Time to revision surgery after patient was unable to walk (h)	7	10	9	12	–	–
Affected spinal level	T9–T10	T10–T11	T10–T11	T10–T11	T11–T12	T12–L1
Calcification	LF/HNP	LF/HNP	LF/HNP	LF	LF	LF
Fused segment of revision surgery	T5–S	T7–S	T7–S	T6–S	T8–iliac	T8–iliac

the six patients exhibited any systemic features of CPPD disease or other metabolic condition that might have caused CPPD crystal deposition. All patients experienced significant improvements in their myelopathy after surgery, but three had a persistent sensory deficit. The pre- and postoperative American Spinal Injury Association (ASIA) Impairment Scale scores were B, C or D and D or E, respectively.

Illustrative cases

Case 1

A 62-year-old woman underwent MR imaging to discern the source of her progressive myelopathy of approximately 2 days duration. She had previously undergone a T10–sacrum fusion for degenerative lumbar canal stenosis. A UIV (T10) collapse had been detected 4 months before the appearance of myelopathy. At that time, she was equipped with a rigid brace. There was no evidence of pathological changes to the LF at that time (Fig. 2). On admission, she was unable to walk. A neurologic examination revealed muscle weakness with 2/5 grade for the manual muscle test in the bilateral lower extremities. A nodular lesion, hypointense on T1- and T2-weighted MR images, had effaced the spinal canal at the T9–T10 segment (Fig. 3 left). A CT scan showed that the lesion contained calcified material (Fig. 3 right). The patient

Fig. 2 Case 1 before the onset of myelopathy. *Left* lateral roentgenograph showing a T10 vertebral compression fracture. *Right* sagittal T2-weighted MR image demonstrating a T10 vertebral compression fracture. There was no evidence of spinal cord compression at that time

Fig. 3 Case 1 after the onset of myelopathy. *Left* sagittal T2-weighted MR image revealing a hypointense lesion within the T9–T10 segment (white arrows). *Right* sagittal and axial CT scan revealing the lesion's high density, which confirmed the presence of CPPD in the LF and HNP within the T9–T10 segment (black arrows). High-density areas also appeared to be present on the two inferior segments, T10–T11 and T11–T12 (asterisks). We confirmed on CT scans that they were present before the development of the vertebral compression fracture in T10 and that they remained unchanged after the onset of myelopathy. By contrast, pathological CPPD crystal deposition (black arrows) at the T9–T10 level appeared only after the collapse of T10. Therefore, the findings have no clear clinical association with the pathological CPPD crystal deposition at the T9–T10 segment

underwent T9 laminectomy and extension of the initial spinal fusion up to T5 (Fig. 4). When the spinal canal was unroofed, we observed a bulging calcified LF, which compressed the dural sac from the posterior side (Fig. 5). Histologically, the lesion showed disseminated CPPD crystal deposition surrounded by multinucleated giant cells (Fig. 6). At the 3-year follow-up examination, the patient was doing well.

Case 2

A 75-year-old woman had previously undergone a T11–sacrum fusion concurrently with L3 pedicle subtraction osteotomy for degenerative lumbar kyphosis. Two months before the onset of myelopathy, a UIV (T11) collapse had been detected. However, there were no neurological symptoms or radiographic evidence of any calcification or spinal stenosis at that time (Fig. 7a–c). The patient's clinician chose careful observation with a rigid brace. The patient then presented with a 1-week history of motor weakness and hypesthesia of her lower extremities. On admission, she was unable to walk and a neurological examination showed paraplegia. The MR image demonstrated an HNP at T10–T11 and hypertrophy of the LF, causing spinal stenosis (Fig. 8 left). A CT scan revealed calcification of the HNP and LF (Fig. 8 right), so the

Fig. 4 Case 1: lateral roentgenograph after revision surgery showing extension of the initial spinal fusion up to T5

Fig. 5 Case 1: intraoperative photograph immediately after laminectomy, showing that the calcified LF had compressed the dural sac

patient underwent emergency surgery. The lesion was exposed after T10 laminectomy and chalky white material was found deposited in the LF (Fig. 9a). Histopathology showed nodular calcification containing CPPD crystals

Fig. 6 Case 1: photomicrograph of histopathology showing disseminated calcification (*white arrows*) with multinucleated giant cells (*black arrows*). This suggests a foreign body reaction against the CPPD crystals. Hematoxylin and eosin staining; original magnification $\times 200$

(Fig. 9b, c). After revision surgery, the patient's symptoms improved dramatically and she was able to walk 1 week later, although she exhibited mild spasticity associated with sensory deficit in the lower limbs at the most recent follow-up period.

Discussion

This scenario of CPPD crystals being detected at the level of PJFs is unique and rarely known to occur following UIV collapse. All six patients had common features: they had previously undergone a long spinal fusion from the thoracolumbar junction to the pelvis, PJF was detected before the appearance of myelopathy, the location of the lesion was at the thoracolumbar junction and all were elderly patients with osteoporosis.

Many authors have reported patients who developed spinal stenosis, HNP, instability or PJF at a segment adjacent to a previously fixed segment [1–3]. The reported incidence of subsequent PJF after long instrumented fusion is 4–15 % [6–9].

O'Leary et al. [4] investigated the risk factors and outcomes for PJF of adult patients who had undergone spinal fusion from the thoracic spine to the sacrum. They reported that the incidence of PJF after surgery was 4.9 % (13 of 264) over an 8-year period at a single institution. In 10 of the 13 cases, the UIV was in the distal thoracic spine (T8–T12). In two of the ten cases, acute neurological deficits developed. They considered obese female patients older than 60 years of age with osteopenia to be the “at-risk” population.

Fig. 7 Case 2 before the onset of myelopathy. **a** Lateral roentgenograph showing a T11 vertebral compression fracture. **b** Sagittal T2-weighted MR image demonstrating a T11 vertebral compression

fracture. **c** Sagittal CT scan. White arrows indicate the T10–T11 disc level. No hypertrophy of the LF or calcification was detected at that time

Fig. 8 Case 2 after the onset of myelopathy. *Left* sagittal T2-weighted MR image revealing T10–T11 HNP and hypertrophy of the LF, which compressed the spinal cord. *Right* sagittal CT scan demonstrating the high density of the lesion (white arrows)

Watanabe et al. [5] retrospectively analyzed ten adult patients, who demonstrated PJF after surgery, among 428 patients, who underwent segmental spinal instrumented fusion. The location of the fractures was frequently in the thoracolumbar junction. Five patients developed UIV collapse plus an adjacent vertebral subluxation. Notably, two demonstrated severe neurological deficits after the fractures. The authors considered that UIV collapse followed by adjacent vertebral subluxation had the potential to cause a severe neurological deficit.

Similarly, in our series of six patients, the UIV was in the thoracolumbar junction and five patients presented with UIV collapse plus adjacent vertebral subluxation. The thoracolumbar junction connects the relatively rigid kyphotic thoracic spine, stabilized by the rib cage, to the lordotic lumbar spine. This transitional zone can experience substantial biomechanical stresses after lumbopelvic fusion, which will make it more susceptible to fractures. Moreover, it is known that the thoracolumbar junction is more prone to present with myelopathy. Cornips et al. [10]

hypothesized that this might be related to a greater mobility of the spine, a more delicate vascularization of the cord and/or lack of a protective layer of peripheral white matter surrounding the fragile gray matter of the conus.

Clinical evaluation of the present series suggests that there must be local factors promoting spinal CPPD crystal deposition. CPPD crystal deposition is occasionally observed in the cervical [11, 12] or lumbar spine [13, 14], but rarely in the thoracic spine [15, 16]. Generally, CPPD crystal deposition in the LF has been observed in normal asymptomatic elderly individuals as one of the physiological aging processes [17, 18]. However, the mechanism of CPPD crystal deposition in the present series cannot be explained simply as a physiological aging process, because the calcification was not detected on the CT scan at the time of occurrence of PJF. We are convinced that CPPD crystal must have been rapidly deposited after the occurrence of PJF until myelopathy developed. In three of our six treated patients, not only a calcified LF but also a calcified HNP was observed by radiographic examination. Symptomatic as well as incidental CPPD crystal deposition in the nucleus pulposus is well established [19].

Although the exact mechanism underlying the formation of CPPD deposits is not clear, several etiologies have been postulated. Yayama et al. [20] investigated the histological and immunohistochemical features of degenerative changes in the LF with CPPD crystal deposition. Based on the histopathologic analysis, they postulated that rupture of elastic fiber bundles was the first change to occur in degeneration of the LF. Crystal deposition was seen within these fibrous and chondrometaplastic areas. Hypertrophic chondrocytes regulate CPPD crystal formation and tissue reconstruction by secreting cytokines. In our series, photomicrography of the resected LF showed degenerated elastic fibers and CPPD crystal deposition, findings that are consistent with previous reports.

Fig. 9 Case 2. **a** Tissue specimen of the removed LF containing white chalky material (*black arrow*). **b** Photomicrographs showing nodular calcification (*white arrow*) and degenerated elastic fibers in

the LF. Hematoxylin and eosin staining; original magnification $\times 200$. **c** These nodules (*white arrow*) were positive for von Kossa's stain; original magnification $\times 200$

Iwasaki et al. [12] reported four cases of calcification of the cervical LF, all in women over 60 years of age. They concluded that this calcification might have been induced by the degeneration or abnormal nutritional state of the LF. Similarly, in our series, four of the six patients were women and all were over 60 years of age. Endocrinologic changes may be involved, as indicated by the preponderance of the condition in older females. Using immunohistochemistry, some authors reported the presence of sex hormone receptors on hypertrophic chondrocytes. CPPD crystal formation in chondrocytes is regulated by sex hormones and transforming growth factor [21]. A combination of multiple factors, namely mechanical stress caused by lumbopelvic fusion, subsequent PJF and hormonal imbalance, could lead to rapid degeneration of the LF and/or nucleus pulposus followed by CPPD crystal deposition.

CPPD crystal deposition alone is not a sufficient cause of myelopathy in our series because the symptom progressed rapidly; other factors, such as inflammation, must be involved. CPPD crystal sometimes induces an acute inflammatory reaction. McCarty et al. [22] identified the crystals seen in the synovial fluid of such patients as CPPD and termed the syndrome associated with CPPD crystal deposition as “pseudogout”. Acute attacks of pseudogout have been described in the periodontoid, cervical, thoracic and lumbar regions [23, 24]. Imai et al. [25] reported that the inflammatory nature of CPPD crystal induced a neurological syndrome. Histopathologically, inflammatory granulation tissue adjacent to the LF was also observed in their series. Similarly, in our series, photomicrography of the resected LF showed granulation tissue comprising mainly lymphocytes and histiocytes, and many multinucleated giant cells were scattered within the tissue. The findings indicate a foreign body reaction to the deposited crystals. We are convinced that compression of the spinal cord by the hypertrophied LF and the inflammatory

granulation tissue induced by CPPD crystals caused the progressive myelopathy.

It is controversial whether the lumbosacral level needs to be fused. In fact, long fusions including the pelvis can result in cranial ASD. However, this does not necessarily mean that complications can be avoided by always stopping the fusion at L5. We sometimes find it necessary to perform long fusion including the pelvis to maintain both sagittal and spinopelvic balance and to improve the outcome. At present, we always inform the patients before the initial surgery (lumbopelvic fusion) that if serious cranial ASD develops, reoperation with decompression and extension of the fusion will be needed.

The limitations of our study are that we could not provide data on how many other patients developed PJF without neurological symptoms in the investigative period of the present study. Future research should focus on these aspects to investigate and understand what promotes rapid CPPD crystal deposition adjacent to lumbopelvic fusion.

Conclusions

The combination of chronic mechanical stress plus PJF and CPPD crystal deposition, followed by a foreign body reaction to the deposited crystals, caused thoracic myelopathy in the present series. To prevent such a catastrophic failure, lumbopelvic fusion in the osteoporotic elderly patient should not terminate in the middle of the thoracolumbar junction, but rather extend to T9 or T8. Asymptomatic patients with radiographic evidence of PJF, especially UIV collapse, after a spinal fusion from the thoracolumbar junction to the pelvis should be followed carefully for the emergence of progressive myelopathy. If possible, surgery should have preceded the development of myelopathy after occurrence of UIV collapse. Even if

appropriate surgery is performed early after the onset of myelopathy, the symptoms should improve.

Conflict of interest None.

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