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Myelopathy Due to Ossification or Calcification of the Ligamentum Flavum: Radiologic and Histologic Evaluations

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The clinical, radiologic, and histologic features of ossification and calcification of the ligamentum flavum were studied in 18 patients. Ossification (15 patients) usually occurred in the lower thoracic spine in men of various ages, while calcification (three patients) was found exclusively in the cervical region of older women. Histologic examinations of ossification showed mature lamellar bone associated with proliferated cartilage replacing the ligamentum flavum (endochondral ossification). This corresponded well with radiographic and computed tomographic (CT) appearances. In the cases with calcification of the ligamentum flavum, calcification within the degenerated ligamentous fibers was observed on histologic examination, and correlated well with an oval nodular density on radiographs and CT. The two conditions differ in clinical, radiologic, and histologic considerations. Pathomechanisms in the development of these lesions and clinical significance are also discussed.

Ossification or calcification of the ligamentum flavum causes pressure against the spinal cord and nerve roots in the thoracic [1–5] and cervical regions [6–8]. With the advent of computed tomography (CT) and safe contrast material (metrizamide), those lesions causing myelopathy have been well observed [4, 5]. However, it has not been systematically studied as to how or whether ossification differs from calcification of the ligamentum flavum in etiologic, radiologic, and histologic characteristics. This paper attempts to correlate radiologic and histologic features of the two conditions.

Materials and Methods

Our series included 18 patients with ossification or calcification of the ligamentum flavum who had undergone laminectomy because of progressive myelopathy or radiculomyelopathy. Ossification was found in 15 (13 men and two women, age range 28–67 years, mean, 49 years). Three patients had calcification. All these were women, aged 62, 64, and 70 years.

Ossification occurred not only in older patients (12 cases aged 40–67 years), but also in relatively young people. We had one patient in his 20s and two in their 30s. All the patients with ossification had sensory disturbance of the lower extremities. Gait disturbance and muscle weakness in both legs were found in 13 patients and disturbed voiding in five. The average duration from onset of symptoms to final diagnosis was 16 months (range, 1 month to 7 years).

All three patients with calcification had numbness in all limbs or both legs, and gait disturbance was seen in two. One patient had a history of fever and arthritis of the knee 1 month before admission. In all three cases of calcification, duration from onset of symptoms to hospital admission was less than a month, in marked contrast to the pattern found with ossification patients.

Radiologic examinations included plain lateral radiography and tomography in 18 patients, myelography using iophendylate or metrizamide in 18 patients, and CT in 16 patients. CT was obtained on either a Siemens Somatom 2 (256 × 256 matrix with 4 mm slice thickness), a Pfizer AS & E (512 × 640 matrix with 5 mm slice thickness), or an EMI 5005 (320 × 320 matrix with 13 mm slice thickness).

Surgical specimens in some patients were radiologically examined by soft x-ray. After fixation and decalcification, the specimens were sectioned sagittally and horizontally, and were stained either by hematoxylin-eosin or Masson stain.

Results

Ossification of the Ligamentum Flavum (15 Patients)

Ossification usually involved two or more spinal levels in one subject. It was found most often in the lower third of the thoracic spine, particularly at the T9–T10 and T10–T11 levels. The upper and middle thirds were involved in five patients, all of whom had ossification of the posterior longitudinal ligament at the thoracic spine.

On lateral plain radiographs or tomograms, ossification appeared as a beaklike or moundlike bony excrescence arising from the laminae (fig. 1A). Definition of those lesions in the upper thoracic spine was difficult in five patients because of the overlapping thoracic cage and shoulder girdle.

On myelography, a complete block was encountered in six patients, and the posterior subarachnoid space was partly excavated

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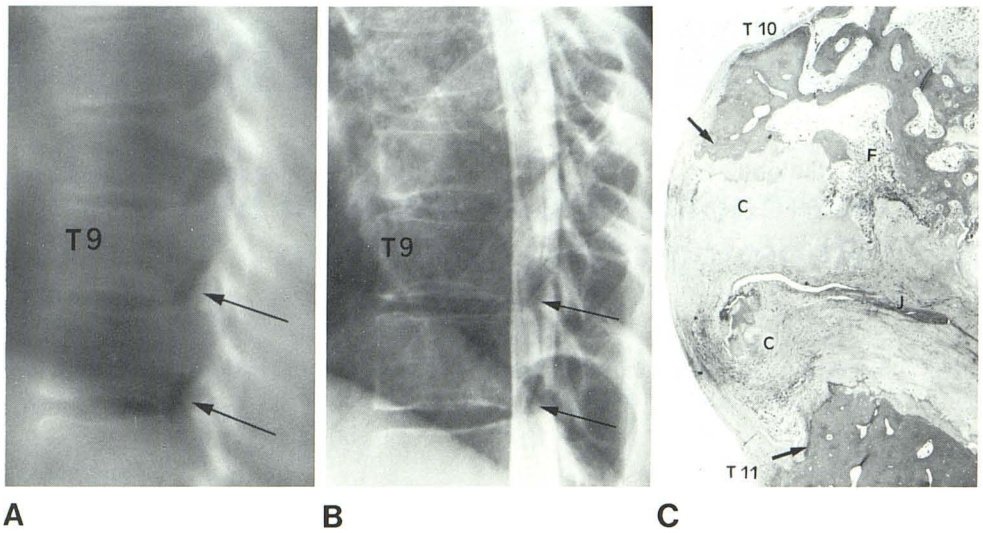

Fig. 1.—Ossification of ligamentum flavum at levels of T9–T10 and T10–T11. **A**, Pluridirectional tomogram in sagittal plane shows beaklike excrescences arising from lamina (*arrows*). **B**, Metrizamide myelography in lateral view shows dorsal aspect of spinal cord indented by ossification (*arrows*). **C**, Photomicrograph of ossification corresponding to T10–T11 level of **A**. Ossified masses of mature lamellar bone and haversian canal extend from laminae above and below (*arrows*). Proliferation of cartilaginous (C) and fibrous (F) tissues in and around bone tissue. J = intervertebral joint. (Masson stain ×2.5.)

by lesions in eight patients (fig. 1B). In the other patient the myelographic result was equivocal. CT after myelography showed the lesion impinging on the posterolateral aspect of the spinal cord (fig. 2A).

CT was optimal for delineation of ossification. Of 13 patients with CT examination, ossifications were found at 40 spinal levels; all were confirmed at surgery. At seven spinal levels the ligamentum flavum ossified only in its lateral part adjacent to the intervertebral joint (the capsular portion), forming an excrescence arising from the joint. At the other 33 levels the ligament was involved in both the capsular and the interlaminar parts, resulting in an extensive mass along the anterior margin of the lamina (fig. 2A). In 38 of 40 spinal levels the ligament was ossified bilaterally ventral to the laminae.

Certain histopathologic features were found in almost all the ossification cases. The ligamentum flavum was replaced by mature bone (fig. 1C). Lamellar bone structure which reached to the edges of two laminae extended in places over the proliferated cartilage and fibrous tissue adjacent to the intervertebral joint. Bone tissue was definitely differentiated from cartilage in some parts but mingled with it in others (fig. 2B). Islands of fibrous tissue of undetermined origin were seen in and around bone tissue, but there were no inflammatory cells. Calcification was seen less prominently. Thus ossification of the ligamentum flavum was considered to be endochondral in nature.

Calcification of the Ligamentum Flavum (Three Patients)

Calcification was found at a total of five spinal levels in three patients. Unlike ossification, calcification of the ligamentum flavum was found predominantly in the cervical spine at the C5–C7 levels. Radiologic and histologic features of calcification also differed from those in ossification. On lateral plain films or tomograms an oval nodular density was observed in the posterior cervical canal (fig. 3A). On CT, this calcification presented in a unique fashion, as an oval calcified mass ventral to the lamina (fig. 3B). The dense mass was seen in the interlaminar part of the ligament but not in the capsular part, and the unossified part of the ligament was thickened. All the levels were involved bilaterally.

On histologic examination, the ligamentum flavum was thickened and degenerated. Calcified granules (which conglomerated in some areas) were deposited within the degenerated ligamentous fibers (fig. 3C). The superficial layer was pushed toward the canal by the calcification and the degenerated fibers of the ligament. No mature bone was formed within the ligament. Similar histologic features were common to all three patients. The patient who had a history of fever and arthritis of the knee joint also had a proliferation of inflammatory cells in the degenerated ligament.

Discussion

This report has shown that ossification and calcification of the ligamentum flavum have different clinical, radiologic, and histologic presentations. There seems to be no difficulty in the diagnosis of calcification because of its characteristic plain radiographic and CT findings. Also, this condition characteristically occurs in the cervical region of older women.

Although ossification of the ligamentum flavum has become an important disease (as a cause of thoracic radiculomyelopathy), patients with the condition are sometimes still not correctly diagnosed for months and years. This is probably due to two reasons. First, bony spicules or ossification at the capsular insertion of the ligamentum flavum is frequently observed in the lower thoracic spine in both cadaver specimens [9–12] and plain radiographs [13–15]. Paradoxically, such frequency of the lesions may lead to a diagnostic pitfall in myelopathic patients with excessive ossification of the ligament. Second, since myelography is usually performed with the patient in prone position, defects in the posterolateral subarachnoid space may be missed. Those diagnostic difficulties are overcome by CT as well as by metrizamide myelography in lateral and oblique views, particularly with the patient in supine position [4, 5].

Radiologic features of both ossification and calcification of the ligamentum flavum are well correlated to pathologic findings. In ossification the ligament is replaced by mature lamellar bone and cartilage forms an ossified bridge extending from the upper and lower edges of the adjacent two laminae. This histologic evidence corresponds well to lateral plain radiographs and tomograms, which show a beaklike or moundlike bony excrescence arising from the laminae. A lucent area seen between the upper and lower edges of a beaklike excrescence on both lateral plain films and tomograms represents unossified fibrous tissue and cartilage (figs. 1A and 1C). Proliferated cartilage and bone formation adjacent to the intervertebral joint support CT findings, where the capsular part of the

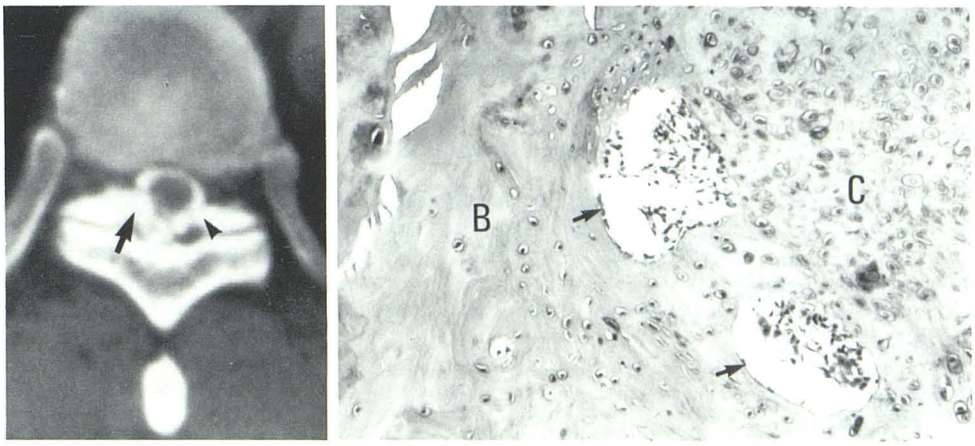

Fig. 2.—Ossification of ligamentum flavum at T9–T10 level. **A**, CT with intrathecal metrizamide shows ossified mass (*arrow*) impinging on right posterolateral aspect of spinal cord. Less prominent ossification along lamina on left side (*arrowhead*). **B**, Photomicrograph of ossification shows two main parts, consisting of lamellar bone (B) and hyaline cartilage (C). Bone marrow with osteoblasts (*arrows*). Osteocytes are seen between main bulks of bone and cartilage. (H and E ×100.)

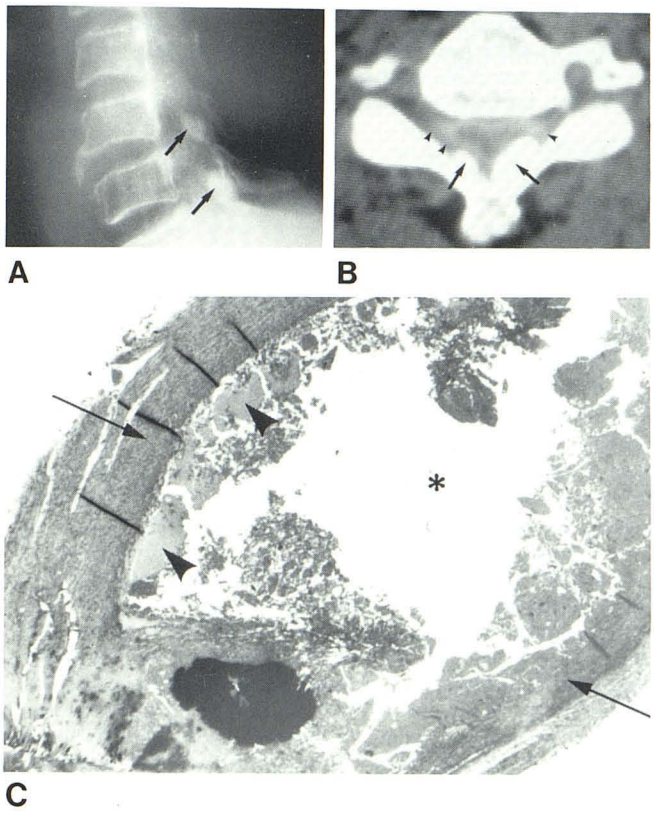

Fig. 3.—Calcification of ligamentum flavum. **A**, Tomogram in sagittal plane shows two nodular densities in posterior half of spinal canal at C5 and C6 levels (*arrows*). **B**, CT at C5 level with intrathecal metrizamide shows oval masses ventral to both halves of lamina (*arrows*). Thick, unossified area of ligamentum flavum is seen as soft-tissue density (*arrowheads*). Note deformity of spinal cord. **C**, Photomicrograph of calcification. Calcification (*arrowhead*) occurs within degenerated fibrous tissue. Superficial and deep layers of ligament are relatively preserved (*arrows*). Large calcified mass (*asterisk*) in central part of ligament was missed at section of specimen. (H and E ×2.)

ligament is always involved (although in many of our cases both the capsular and interlaminar portions were involved). Thus it is assumed that ossification begins at the edges of the laminae near the capsular insertion of the ligament and extends medially, upward, and downward as it involves the ligament. General ossifying diathesis in individuals and chronic mechanical stress on the site of ligamentous insertion might cause this ossification.

Unlike ossification, calcification of the ligamentum flavum tends to occur within the degenerated and thickened ligament in the cervical spine. The calcified mass has no continuity with the lamina, and the superficial and deep layers of the ligament are relatively preserved. Such histologic evidence again explains the findings on plain lateral film and CT where an oval mass appears isolated from the lamina or only partly contacting it. The nodular shape of such lesions seems to be specific to the ligamentum flavum [8], since calcification associated with chondrocalcinosis in other parts is usually linear [16, 17].

The etiology and mechanism of calcification remain unclear, but probably are distinct from those of ossification. McCarty et al. [16] found calcium pyrophosphate dihydrate in the inflamed joint and preferred the term "pseudogout syndrome" for it. Chondrocalcinosis also seems to arise in various conditions such as hereditary hemochromatosis, hyperparathyroidism, diabetes mellitus, and classical gout [8, 17]. As described previously [8], some of the calcified deposits are scattered throughout the degenerated ligament and are associated with inflammatory reaction. Inflammatory cells had also proliferated within the degenerated ligamentous fibers in one of our patients in this series. Thus we speculate that ossification of the ligamentum flavum develops when the ligament is thickened secondary to inflammation or metabolic disorders, and calcified granules are deposited in it.

In addition to etiologic considerations of these conditions, the radiologic differentiation of ossification from calcification provides significant information for their clinical management. Ossification of the ligamentum flavum is often associated with ossification of the posterior longitudinal ligament and thickening of the laminae [2, 3], and it usually extends along the joint and pedicle laterally. Wide laminectomy and removal of the lesion are therefore necessitated in this condition. CT is useful for localization of the ossification, even in cases with upper thoracic involvement.

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