Pathology of Spinal Cord Lesions Caused by Ossification of the Posterior Longitudinal Ligament

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Introduction

Ossification of the posterior longitudinal ligament (OPLL) causing spinal cord compression was first reported in 1838 by Key [1]; this was followed by only two reports [2,3] in the first part of this century. Ossification of the posterior longitudinal ligament was not recognized as a definite clinical entity until 1960. In Japan, Tsukimoto [4] first described this pathological condition following autopsy findings in 1960. Since then, a number of reports have appeared [5–8]. Increased recognition of OPLL led the Ministry of Public Health and Welfare of Japan to appoint a special study group, the Investigation Committee on OPLL, in 1974, and extensive studies ranging from basic research to clinical investigations have been conducted.

Although OPLL is rare among Caucasians, it is a significant cause of myelopathy in middle-aged and older Japanese adults. The patients initially suffer from numbness and pain in the upper extremities and the neck. The disease progresses gradually and results in gait disturbance, spastic paralysis, and bladder disturbance. OPLL-induced myelopathy can be said to be characterized by a chronic, gradually enhanced, persistent compression of the spinal cord. Detailed pathological investigations of the spinal cord in OPLL are limited [4,9–13]. This chapter is concerned with the pathological changes of the spinal cord as observed in autopsied cases.

Pathological Characteristics of Spinal Cord Damage Caused by OPLL

The spinal cord was markedly flattened by compression caused by the ossified mass, and the compression was most severe at the level of the intervertebral disk. The diameter of the spinal cord in transverse section was about 2 mm (Fig. 1). The posterior protrusion of the intervertebral cartilage played an important role in damage to the spinal cord; damage by OPLL was correlated to spinal canal stenosis. At the upper cervical level, the spinal canal is wider, so marked cord compression did not develop despite a large ossified mass (Fig. 2). On the other hand, in the lower cervical level, severe spinal cord damage was brought about by ossification because the spinal canal is narrow (Fig. 3).

Pathological Changes of Gray Matter

The anterior horns were moderately flattened (Fig. 4) and showed loss of nerve cells (Fig. 5) and proliferation of glial cells. Fibrous gliosis of the anterior horns was found even at the level where no marked deformity of the spinal cord was found. The spinal cord damage was pathologically classified into four categories on the basis of the degree of destruction (stage 0–3) [14] (Table 1). In stage 0 and stage 1, major pathological changes in the gray matter and the degree of compression of the spinal cord were well correlated to deformity of the anterior horn. In stage 2 and stage 3, neurons were almost completely obliterated and necrosis with cavitation was frequently observed. Destruction of the spinal cord in stage 2 and stage 3 is considered to be irreversible; therefore, surgical treatment is recommended at stage 1.

Pathological Changes of White Matter

In the white matter, myelin destruction and loss of axons were seen, with status spongiosus. The anterior...
column was damaged by the direct compression caused by the ossified mass, but damage in the anterior column was slighter than that in the lateral and posterior column. The main pathological changes in the spinal cord caused by OPLL were found in the gray matter rather than the white matter. The most intensively damaged part of the spinal cord extended from the middle part of the gray matter to the ventral part of the posterior column with cavity formation. This distribu-

<table>
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<th>Stage</th>
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<tr>
<td>0</td>
<td>Normal or mild compression of anterior horn without neuronal loss</td>
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<tr>
<td>1</td>
<td>Mild compression of anterior horn with partial neuronal loss</td>
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<tr>
<td>2</td>
<td>Marked deformity of anterior horn with severe neuronal loss</td>
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<tr>
<td>3</td>
<td>Severe spinal cord damage with cystic cavity</td>
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tion of spinal cord lesions caused by OPLL has been reported by Inoue [9], Murakami et al. [11], and Yamamura et al. [15].

Nerve Root Damage by OPLL

In addition to myelopathy, radiculopathy also presents important clinical neurological signs and symptoms in this disorder. The anterior nerve roots are injured by direct compression caused by the ossification where the roots emerge from the spinal cord. The nerve roots are also injured at the place where the roots penetrate the dura mater by being displaced and stretched posteriorly by the ossified mass. Histological examination showed marked loss of nerve fibers in both anterior and posterior roots at the levels of the severely compressed cord.

The Relationship Between Morphology and Pathology of the Spinal Cord in OPLL

The cross-sectional shape of the spinal cord at the most severely affected segment was classified into two categories: boomerang (convex lateral surfaces and concave anterior surface) and triangular (angular lateral surfaces and flat anterior surface) [16]. In cases with a boomerang shape, even when the compression was severe major pathological changes were restricted to the gray matter, and the white matter was relatively well preserved (Fig. 6). In cases with a triangular shape, pathological changes were more severe: both white matter and gray matter were involved, and only the anterior column was free of pathological changes (Fig. 7). There were severe pathological changes over more than one segment, and both descending and ascending degeneration were observed. The transverse area of the spinal cord was greater than 60% of normal in most of the cases in which the cord had a boomerang shape, but it was reduced to less than 60% of normal in more than one segment in the cases with a triangular cord shape. In conclusion, a triangular-shaped spinal cord with a transverse area less than 60% of normal in more than one segment appeared to be associated with severe and irreversible pathological changes in cases of OPLL.

Mechanism of Spinal Cord Damage by OPLL

Not only direct compression that is mechanically induced by ossification but also the secondary circulatory disturbance should be taken into consideration as important factors in the damage to the spinal cord. Mair and Druckman [17] considered, from pathological examination of cervical spondylosis, that the lesions had resulted from compression of the anterior spinal artery and its branches by the protruded disk. Yamazaki et al. [18] reported an autopsy case of OPLL showing occlusion of the anterior spinal artery. Braig et al. [19] reported, from a microangiographic study, that narrowing of extraspinal arteries by contact with spondylotic ridges contributed to the reduction of blood supply to the cervical cord in cervical spondylosis. However, we considered that circulatory disturbance of the venous system was a more important factor than that of the arterial system.

Kameyama et al. [20] showed that the location of cysts on a transverse plane commonly extended from the intermediate zone and the posterior horn to the lateral aspects of the posterior column bilaterally in the cervical cord of OPLL (Fig. 8) and cervical spondylosis. There were prominent thick-walled vessels, predominantly venules, within and around the cysts accompanied by dilated perivascular spaces (Fig. 9). Kameyama
et al. considered that venous congestion and subsequent necrosis play a significant role in the pathogenesis of spinal cord cysts secondary to chronic compression. Coalescence of dilated perivascular spaces seemed to also contribute to formation of the cysts.

Other Pathological Findings in OPLL

Hypertrophy of the Posterior Longitudinal Ligament and Ossification of the Dura Mater

As a cause of compression myelopathy, hypertrophy of the posterior longitudinal ligament (PLL) is also important. Hypertrophy of the PLL is more rare than OPLL, and there is a controversy about its nature and pathology as to whether this is the early stage of OPLL. Hypertrophy of the PLL was mainly composed of chondroid tissue without formation of a remarkable ossified mass as in OPLL [21] (Fig. 10).

In OPLL, ossification takes place not only in the ligament but also in the dura mater. Considering that the dura mater plays an important role in protecting the spinal cord against damage, ossification of the dura mater may be an important factor in damage to the spinal cord.

Aberrant Peripheral Nerve Bundles and Remyelination of Peripheral-Type Myelin

Aberrant peripheral nerve bundles (APNB) are defined as masses or bundles of nerve fibers without perineural sheath cells ranging from 30 to 200µm in diameter [22]. They are found exclusively in the intraspinal perivascular space and in the spinal subarachnoid space. Bodian and Luxol Fast Blue (LFB) stains showed that most of...
the constituent nerve fibers in APNB were myelinated. APNB have been found in syringomyelia, spinal cord injury, prolapsed intervertebral disk disease, neurofibromatosis, and familial amyloidotic polyneuropathy. In our examined cases of OPLL, many APNB were distributed throughout the posterior and lateral column, and the posterior subarachnoid space was filled with APNB (Fig. 11). They are considered to be reactive and regenerative in the damaged spinal cord.

In the severely damaged cord, peripheral-type myelin, which was stained dark blue by LFB plus periodic acid-Schiff (LFB + PAS) stain, was observed at the posterior and lateral column near the entrance zone of the posterior roots. Remyelination by peripheral-type myelin has been described also in cases of multiple sclerosis, spinal trauma, and vascular disorder, and is considered to consist of remyelination around the preserved axons by Schwann cells originating from the posterior roots.

Waller Degeneration of the Spinal Cord in OPLL

When recording histological findings of spinal cord damage caused by OPLL, we have to distinguish primary spinal cord lesions from secondary changes of Wallerian degeneration. We could observe descending degeneration of the pyramidal tract and comma tract in the caudal segments below the most seriously damaged part (Fig. 12) and the posterior column and spinocerebellar tract in the oral segments by means of a detailed histological examination of preparations of transverse sections of each segmental level of the spinal cord.

Summary

Compression of the spinal cord was marked at the level of the intervertebral disk, and the spinal cord was strikingly flattened anteroposteriorly. Intensive damage was seen in the gray matter as compared to the white matter. The white matter showed demyelination and axon loss with status spongiosus, which was more marked in the posterolateral than in the anterior column. The cross-sectional shape of the spinal cord at the most severely affected segment was classified into two categories: boomerang and triangular. A triangular-shaped spinal cord with a transverse area less than 60% of normal in more than one segment appeared to be associated with severe and irreversible pathological changes in cases of OPLL.

The most seriously damaged parts of the spinal cord showed tissue necrosis and cavity formation that extended from the central parts of the gray matter to the ventral parts of the posterior column. Venous congestion and subsequent necrosis seemed to play a significant role in the pathogenesis of spinal cord cysts secondary to chronic compression. Spinal cord damage was pathologically classified in four categories as to the degree of destruction (stage 0–stage 3). Destruction of the spinal cord in stage 2 and stage 3 is considered to be irreversible; therefore, surgical treatment is recommended at stage 1. The spinal nerve roots that showed marked demyelination and axon loss were damaged by ossification where the anterior nerve roots emerge from the spinal cord and where the roots penetrate the dura. As causes of compression myelopathy, hypertrophy of the PLL and ossification of the dura mater were also important. Aberrant peripheral nerve bundles and peripheral-type remyelination were observed in severely damaged parts of the spinal cord.
References