ORTHOPAEDICS COURSE

A New Pathological Classification of Lumbar Disc Protrusion and Its Clinical Significance

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Lumbar disc protrusion is common. Its clinical manifestations and treatments are closely related to the pathological changes; however, the pathological classification of lumbar disc protrusion is controversial. This article introduces a new pathological classification comprising four types of lumbar disc protrusion according to intraoperative findings. The damage-herniation type is probably caused by injury and is characterized by soft herniation, the capsule can easily be cut and the broken disc tissue blocks overflow or is easily removed. The broken disc substances should be completely removed; satisfactory results can be achieved by minimally invasive endoscopic surgery. The degeneration-protrusion type is characterized by hard and tough protrusions and the pathological process by degeneration and proliferative reaction. The nerve should be decompressed and relaxed with minimally invasive removal of the posterior wall; the bulged or protruded disc often need not be excised. The posterior vertebral osteochondrosis with disc protrusion type is characterized by deformity of the posterior vertebral body, osteochondral nodules and intervertebral disc protrusion. The herniated and fragmented disc tissue should be removed with partially protruding osteochondral nodules. Intervertebral disc cyst is of uncertain pathogenesis and is characterized by a cyst that communicates with the disc. Resection of the cyst under microscopic or endoscopic control can achieve good results; and whether the affected disc needs to be simultaneously resected is controversial. The new pathological classification proposed here is will aid better understanding of pathological changes and pathogenesis of lumbar disc protrusion and provides a reference for diagnosis and treatment.

Key words: Clinical significance; Lumbar disc protrusion; Pathological classification

Introduction

Lumbar disc protrusion is common. Its pathogenesis is unclear but is known to include endogenous factors (hereditary, developmental and degenerative) and exogenous factors (stress, nutrition, strain, trauma and so on). The term "lumbar disc protrusion" describes the morphology and its classification is usually based on the position and morphology of protrusion on radiographic images. However, the morphology of the protrusion often does not correlate with clinical symptoms, which are more closely related to the various pathological changes. Therefore, the types of pathological change should be considered in the classification of lumbar disc protrusion.

Currently, the pathological classification of lumbar disc protrusion is extremely controversial. The classifications in common use include the MacNab, Spengler, American Academy of Orthopaedic Surgeons (AAOS) and International Society for the Study of Lumbar Spine (ISSLS) classifications and others. The MacNab classification has two categories: protrusion and herniation. The former includes localized and generalized subtypes, whereas and the latter includes extruded, ruptured prolapse and sequestered subtypes[1]. The Spengler classification has protruded, extruded and sequestered types[2]. The classification proposed by the AAOS and ISSLS has degenerated, bulged, protruded and extruded types. The latter is also divided into subligamentous, transligamentous and sequestered subtypes[3]; however, protrusion of the intervertebral disc is collectively referred to as disc herniation, which is inconsistent with the MacNab classification. The classification proposed by Zhou *et al.* has protruded, ruptured and sequestered

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TABLE 1 Pathological classifications of lumbar disc protrusion in common use

Classification	Categories
MacNab[1]	Protrusion (including localized and generalized types) Herniation (including extruded, ruptured prolapse and sequestered types)
Spengler[2]	Protruded Extruded Sequestered
AAOS&ISSLS[3]	Degeneration Bulge Protrusion Extrusion (including subligamentous, transligamentous and sequestered types)
Zhou[4]	Protruded Ruptured Sequestered

types[4]. In conclusion, the various classifications of lumbar disc herniation are confusing and inconvenient for clinical purposes (Table 1).

In clinical practice, lumbar disc protrusions differ considerably in their pathologic and immunologic characteristics and are associated with different pathological changes in the surrounding tissues. They also have various pathogeneses; thus treatments, including surgical procedures, should logically be chosen according to the pathological changes. We are therefore here proposing a new pathological classification, which includes damage-herniation, degenerative-protrusion, osteochondrosis with disc protrusion and intervertebral disc cyst types[5–10]. We further suggest that clinical evaluation, including the choice of surgical procedure, should be varied according to the pathological type.

Damage-herniation Type

Our damage-herniation type is equivalent to "herniation" in the MacNab classification, "extruded type" or "sequestered type" in the Spengler classification, "extrusion" in the AAOS&ISSLS classification and "extruded", "prolapsed", "soft herniation" and "true herniation" in other classifications. Intraoperatively, this type of protrusion is characterized by a thin, soft, flexible superficial annulus fibrosus and posterior longitudinal ligament, which would cause pain when touched or subjected to pressure. The capsule is often easy to open with an instrument, after which the disc fragments overflow or are easily removed with a clamp. The disc fragments are isolated and separated from, or weakly adherent to, the maternal disc (Fig. 1). The inflammation and edema associated with closed herniations of this type cause increased local pressure[11]. During intraoperative discography, the contrast agent can extend to the posterior longitudinal ligament or into the spinal canal, which indicates intervertebral disc ruptured[8]. Factors such as external force or injury can rupture these herniations, resulting in the disc tissue overflowing and breaking through the posterior longitudinal ligament into the spinal canal.

Pathological Changes

Optical microscopic examination of these herniations shows that the normal structure of the annulus fibrosus or nucleus pulposus has been disrupted; they contain loosely arranged fibers, damaged tissue, focal infiltration of inflammatory cell and neovascularization. Granulation tissue, neovascularization and local inflammatory reactions of this type are more obvious than with the degeneration-protruded type (Fig. 1) and are related to post-injury tissue repair[6,7,9,10].

The manifestations of intervertebral disc protrusion when examined by transmission electron microscopy fall into two main categories. One category is evidence of tissue destruction and cell apoptosis, including matrix necrosis (irregular or rat-bite-like, transparent, dissolved lesions of the matrix, edema or dissolution between collagenous fibers, and deposition of proteins), cell necrosis, apoptosis and dysfunction (condensation of nuclear chromatin, dark staining, karyopyknosis, mitochondrial dissolution, expansion of rough endoplasmic reticulum pool, and darkly stained or wrinkled cytoplasm). The other category is evidence of proliferation and active cell synthesis, including hyperplasia of stromal collagenous fibers, edema in the interstitial collagen, cell edema, mitochondrial swelling, expansion of the rough endoplasmic reticulum pool, hyperplasia of ribosomes, enlarged nuclei, disappearance of nuclear pores and hyperplasia of heterochromatin[7].

On examination by transmission electron microscopy, evidence of destruction is more obvious in damage-herniation than in other types. This evidence includes extensive matrix necrosis or dissolution, swelling, rupture or disintegration of collagenous fibers, clasmatosis or necrosis of nucleus pulposus cells, and deposition of materials of high electron density in surrounding tissues. The pathological mechanism of this damage is thought to be inflammatory. Activated lysosomal enzymes, degrading enzymes and cytotoxic responses represent intense responses to damage. The resultant necrotic tissue absorbs water strongly, liquefying the fragmented disc tissue and increasing the pressure, thus further accelerating the process of break-down[7].

Immunohistochemistry shows infiltration of the herniation by T lymphocytes and macrophages. Cluster of differentiation $(CD)_{68}$-positive and $CD_{45}RO$-positive cells, which play important roles in the immune response, can be seen on the boundaries of the area of inflammatory cell infiltration and distributed along blood vessels. Compared with the degenerative-protrusion type, more CD_4-positive T cells (delayed type hypersensitivity T lymphocytes) and CD_8-positive T cells (cytotoxic T lymphocytes) are visible (Fig. 1). After immunofluorescence labeling with IgG and IgM, large amount of yellow-green granular or banded fluorescence reaction zones are found in the areas of inflammatory cell infiltration. Peripheral blood concentrations of IgG and IgM are higher than with the degenerative-protrusion type; however, concentrations of IgA, complement C3 and circulating immune complex do not differ significantly between these two types[6,9]. In addition, the number of interleukin (IL)-17-positive cells and

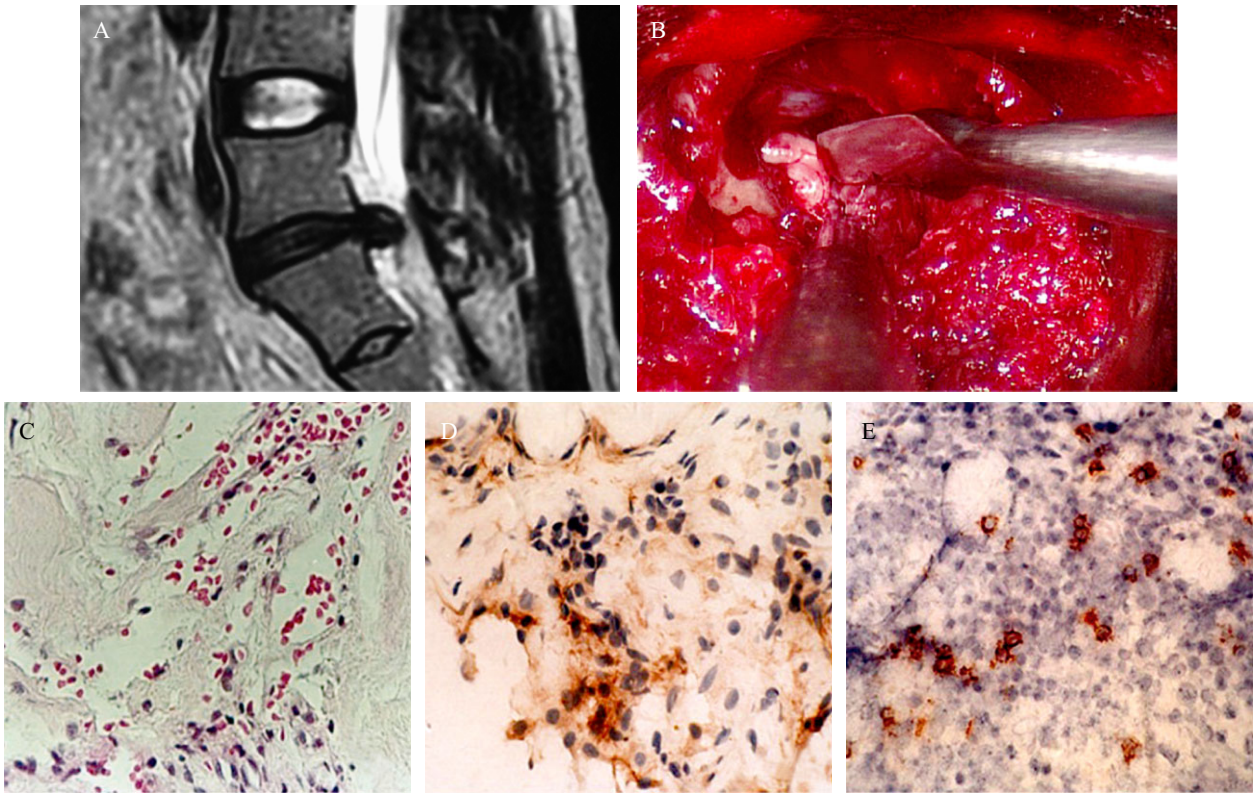

Fig. 1 Images obtained from a 20-year-old man with damage-herniation of the intervertebral disc. (A) T2 weighted sagittal MRI showing intervertebral disc protrusion of L_5S_1 segment. (B) Posterior spine endoscopy view showing that the protrusion is enclosed by a thin capsule and the disc fragments have overflowed after the capsule was cut open. (C) Optical microscopy image showing the herniated disc tissue is infiltrated by inflammatory cells with neovascularization and obvious inflammatory reaction. HE staining, ×200 (D, E) Immunohistochemical staining showing the herniated disc tissue is infiltrated with (D) CD_4-positive and (E) CD_8-positive T cells. 3,3'-Diaminobenzidine staining, ×400.

the strength of mRNA expression of IL-7 are significantly greater than in the degenerative-protrusion type[10].

Therefore, disc degeneration, damage-herniation and inflammatory repair are the essential pathological characteristics of damage-herniation. Infiltration with T lymphocytes and deposition of immunoglobulin IgG or IgM, which are autoimmune reactions to the damage, further aggravate the tissue damage and the resultant increased pressure causes fragmentation and dissolution of the nucleus pulposus tissue. Ultimately, fragments separate from the maternal disc and herniate into the spinal canal[6,7,9].

Pathogenesis

In the damage-herniation type, the disc tissue is ruptured and separated, indicating that the pathogenesis is likely related to damage. Studies have shown that patients with this type of disc protrusion usually have a traceable history of trauma (such as lumbar sprain, fall injury and so on) that has likely caused or aggravated tearing or slight damage to the annulus fibrosus[12]. So-called acute traumatic protrusion of the intervertebral disc may represent acute rupture of the herniated disc substances[12]. The herniated substances may be enclosed and contained by the annulus fibrosus and posterior longitudinal ligament, forming high-pressure lesions; this is known as the contained type. However, the herniated substances can also break through the superficial annulus fibrous and posterior longitudinal ligament or be sequestered in the canal; this is known as the uncontained type.

The abnormal pressure within the disc, swelling and inflammatory chemicals can stimulate the nerve ending and nociceptors in the outer layer of the ruptured annulus fibrosus and cause lumbago; the mechanical compression and inflammatory chemical mediators can cause nerve root injury and pain. Severe mechanical compression can also cause denaturation and demyelination of nerve fibers, resulting in disturbances in the influence of the nerves on the nutrition and maintenance of body tissue and thus secondary damage. The herniated disc substances can release phospholipase A_2, which damages the epineurium of nerve roots; the resultant inflammatory reaction involves fat tissue and ligaments within the spinal canal and releases various inflammatory mediators, stimulates the nerve root, causes inflammatory edema and pain and heightens pain sensitivity. Slowing of nerve conduction velocity and electromyographic

abnormalities can be detected by electrophysiological examination.

In the damage-herniation type, the disc tissue is infiltrated by mononuclear macrophages and T lymphocytes and immune complex is deposited, demonstrating the presence of an autoimmune reaction. After embryogenesis, the nucleus pulposus, which is derived from the chorda dorsalis of the mesoderm, is closely enveloped by the annulus fibrosus and cartilage endplate; they separate it from the circulatory and immune systems and allow it to harbor hidden autoantigens. Lymphocyte transformation tests have confirmed that type I and II collagen, glycoprotein and cartilage endplate matrix of normal intervertebral disc are auto-antigenic and can cause delayed type hypersensitivity[13]. T lymphocytes are more easily induced to differentiate into CD_4-positive or CD_8-positive cells for glycoprotein in the nucleus pulposus than for collagen in the annulus fibrosus; the nucleus pulposus is therefore more intensely auto-immunogenic than the annulus fibrosus[14]. The neovascularization associated with damage-herniation can facilitate exposure of the hidden autoantigens in the nucleus pulposus to the immune system, activating T or B lymphocytes via the recognition, processing and presentation of macrophages or other antigen presenting cells. The activated T cells produce immune regulating cells and effector cells, which damage disc tissue by delayed type hypersensitivity or cytotoxic reactions. The activated B cells differentiate into plasma cells and secrete antibodies, which damage disc tissue with these autoantigens via the macrophage and complement systems; additionally, the cytotoxic effect of the activated B cells is synergistic with cellular immunity. However, systemic humoral immune responses usually only increase slightly[6,9]. A study has shown that contact between nerves and the nucleus pulposus induces inflammatory reactions and damage; infiltration of inflammatory cells was detected when the whole of the lumbar annulus fibrosus was manually damaged in experimental animals[15]. In addition to degeneration, damage and repair, there is an autoimmune reaction in protrusion of the damage-herniation type that exacerbates inflammatory responses, vascular ingrowth, cell infiltration, tissue destruction or dissolution, and increases internal pressure. Minor stress can then result in extrusion or sequestration of disc fragments which, in combination with the cytokines and inflammatory mediators simultaneously produced by the immune cells, leads to inflammatory edema of nerve roots and lumbocrural pain. More research is needed to clarify the immunogenic aspects and specific pathogenesis.

Clinical Manifestations and Treatment

The mean age of onset of this type is younger than that of the degenerative-protrusion type; however, it does occur in older persons. The usual symptoms are lumbago and radicular pain, the specific symptoms and signs being determined by the position of the protrusion and the involved neural structures. Protective postures, such as spine tilting, are relatively common in these patients and the straight leg raising test is often positive. Actions such as coughing or sneezing increase the pressure within the spinal canal and aggravate lumbocrural pain. Patients often keep their hip and knee flexed to relax the sciatic nerve and relieve pain. Central herniation causes cauda equina damage, and herniated fragments occasionally get into the subarachnoid space, resulting in severe sphincter dysfunction and leg symptoms.

The soft damage-herniation type causes mechanical, chemical and inflammatory stimulation of peripheral tissues or nerves as well as immune reactions; treatment is mainly symptomatic or surgery. Bed rest or traction can reduce the local pressure and drugs or physical therapy can relieve the symptoms[16]. Studies of autoimmune factors have confirmed that inhibition of local inflammatory and immune responses is effective. Non-steroidal anti-inflammatory drugs and epidural steroid injection have achieved good clinical results. The herniated nucleus pulposus can cause infiltration of macrophages or other inflammatory cells and neovascularization. Although the herniated nucleus pulposus, especially if sequestered, can shrink or be absorbed spontaneously, aggravation of nerve injury accompanies this process. Therefore, comprehensive evaluation of the clinical manifestations and other findings is important. Although imaging, especially determination of the shape of the protrusion and signal changes on MRI, can contribute to assessment of pathological changes, appropriate treatment cannot be accurately determined by the shape of the protrusion on imaging alone[17,18].

Disc fragments must be completely removed surgically, especially sequestered fragments (including those rare ones that have got into the subarachnoid space); their locations can be traced ascertained according to the clinical manifestations and MRI findings. To reduce the possibility of recurrence, fragments inside the disc should be removed through the break in the annulus fibrosus after the herniated nucleus pulposus has been removed. However, the non-fragmented normal disc tissue should not be resected because excessive resection of normal disc tissue aggravates the damage, jeopardizes stability and increases the incidence of endplate arthritis or even discitis. In a few cases, the break in the maternal annulus fibrosus has closed and an "intact" surface has formed by self-repair after the separation of a sequestered nucleus pulposus from its maternal disc. In such cases, the "split" sequestered nucleus pulposus should be removed, leaving the "intact" maternal intervertebral disc *in situ*. In the damage-herniation type, good results can be achieved by completely removing fragments or sequestered substances by minimally invasive endoscopic surgery.

Degenerative-protrusion Type

The degenerative-protrusion type is diffuse or focal protrusion caused by degeneration of the intervertebral disc; it is equivalent to "protrusion" in the MacNab, Spengler and Zhou classifications, "degeneration", "bulge" and "protrusion" in the AAOS&ISSLS classification, and "bulge", "displacement" or "hard herniation" in the other classifications. This type of protrusion is characterized by tough, hard, relatively inflexible, protruded lesions and pain is not induced by touching or

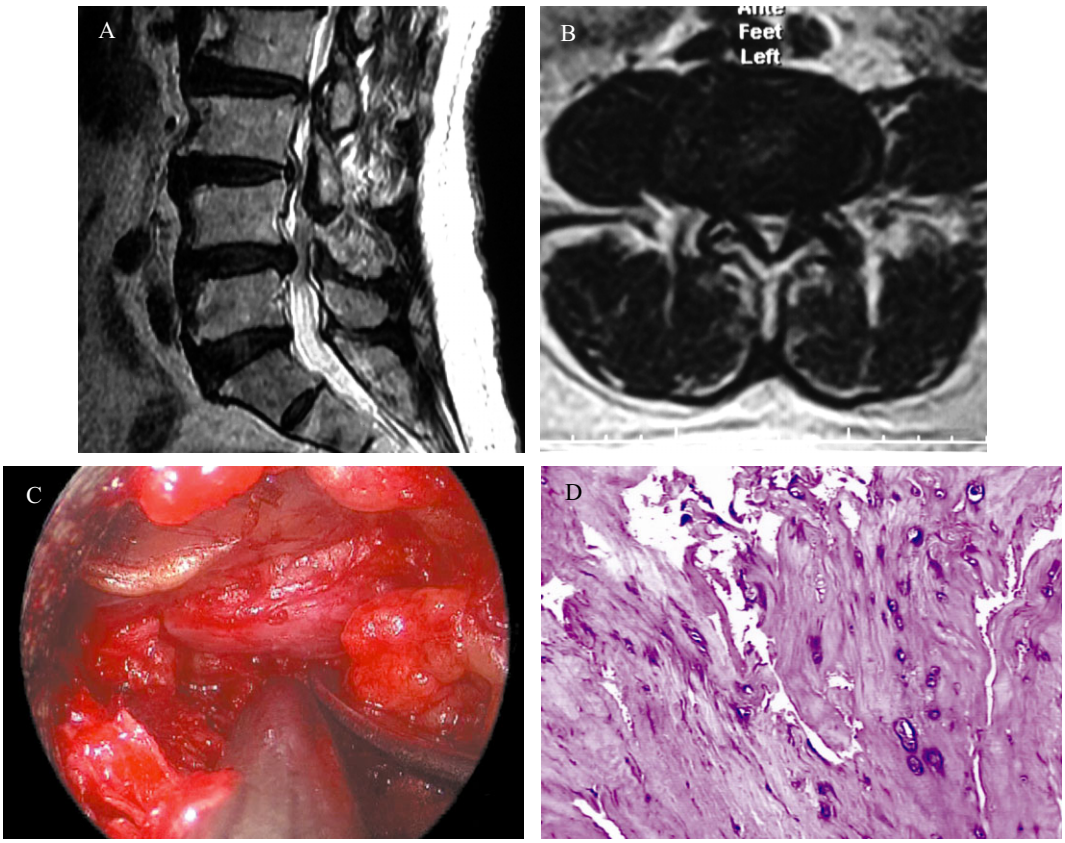

Fig. 2 Images obtained from a 71-year-old man with degenerative protrusion of intervertebral disc. (A) T2 weighted sagittal MRI showing intervertebral disc protrusion of L_{4-5} segment. (B) T2 weighted cross-sectional MRI showing hypertrophy of the facet joint and ligamentum flavum and stenosis of the lateral spinal canal. (C) Posterior spine endoscopy view showing that the protrusion is hard and there are no disc fragments that could be removed after the surface of the protrusion has been cut open. (D) Optical microscopy image showing degeneration of fibrocartilage matrix in protruded disc tissue without neovascularization. HE staining, ×200.

applying pressure. The protruded lesions are contiguous with the maternal disc. After the surface of the protrusion has been cut open, there are no disc fragments that can be removed and resection of the protrusion is difficult (Fig. 2)[7]. The pressure of protruded lesions is usually normal, not differing significantly from that of the nucleus pulposus[10]. During intraoperative discography, the disc either fills diffusely with the contrast medium and expands outward, or exhibits a dispersed, multi branched shape without central filling, which indicates a tear of the annulus fibrosus[8].

Pathological Changes

On microscopic examination, the structure of the nucleus pulposus and annulus fibrosus is relatively intact, with a small, dense nucleus pulposus, thickened annulus fibrosus, dense and disordered tissues, and proliferation of cartilage matrix, cartilage-like lacunae cells and collagenous fibers (Fig. 2)[7].

On transmission electron microscopic examination, evidence of proliferation is more obvious than with the degenerative-protrusion type; this evidence includes extensive proliferation of collagenous fibers in a dense and disordered arrangement, and active cell synthesis. The hyperplasia of the collagen fibers, which is related to the age of the patient and degeneration and instability of the spine, is an adaptive change that minimizes spinal instability[7].

Degeneration of the nucleus pulposus, proliferation of the cartilage matrix and annulus fibrosus, and positive type I collagen staining of chondrocytes can be seen by immunohistochemistry staining. There is infiltration of a few macrophages (CD_{68}-postive or $CD_{45}RO$-positive cells), but no T lymphocytes, CD_4-positive or CD_8-positive cells. Immunofluorescent staining for IgG and IgM is negative, and peripheral blood concentrations of IgM and IgG are lower than in the damage-herniation type[6,9]. Degeneration of the intervertebral disc may be the result of the synergistic effect of many factors that influence gene expression through the cytomembrane and intracellular signal transduction pathway and cause dynamic imbalance of synthesis and degradation of proteoglycan and collagen, cell apoptosis and tissue degeneration[19].

Therefore, a pathological process characterized by degeneration and proliferative reactions is the essential pathological characteristic of degenerative-protrusion.

Pathogenesis

The intervertebral disc is the "hinge" of vertebral activity. This type is associated with degeneration, accumulation of chronic damage, stimulation by stress and proliferative responses. Because the degenerated cells of the disc are similar to the degenerated cells found deep in the cartilage in osteoarthritis, it is speculated that adverse mechanical environmental and structural factors play an important role in the pathogenesis. The combination of proliferation of fibrocartilage matrix and proteoglycans and the abnormal composition and distribution of collagen fibers in the disc result in proliferation and posterior protrusion of the intervertebral disc, which is hard and pushes the nerve root backward. With increasing degeneration and proliferation in the ligamentum flavum, facet joint and anterior joint capsule, symptoms of compression develop. Because the degeneration gradually aggravates and causes symptoms, stenosis of the nerve channels is often more severe than in the damage-herniation type.

The disc protrusion and stenosis of nerve channels compress and stimulate the nerve and hinder the blood supply and venous return. The main physiopathologic mechanism of the nerve compression syndrome is a capillary countercurrent caused by obstruction of venous return and venous congestion associated with compression of nerve roots. Nerve roots are more sensitive to compression than peripheral nerves; a pressure of 410 kPa can cause a change in axial flow and obstruct the transport of protein from nerve cells to the distal axon. When the pressure reaches the mean arterial pressure, arterial blood no longer enters the nerve roots, resulting in changes in neural structure and function. In addition to ischemic damage to the nerve root, compression can cause changes in capillary permeability in nerves. A persistent pressure of 617 kPa for more than 2 min can cause nerve edema, and subsequently disturb capillary blood flow and thus nerve function. Severe long-standing edema induces chronic nerve injury and secondary intraneural fibrosis; recovery is very slow after nerve compression has been relieved.

Clinical Manifestations and Treatment

Patients with this type of disc protrusion are often relatively elderly and describe a gradual onset and a long history of recurrent attacks. Lumbocrural pain can gradually intensify; however, this is not typical. Low back pain is not severe and the straight leg raising test is often slightly positive or negative. Symptoms of spinal stenosis, such as intermittent claudication, are obvious. Imaging shows obvious evidence of degeneration and proliferation with stenosis of the spinal and nerve root canals.

Treatment includes rest, physiotherapy, weight loss, drugs and surgery, the appropriate treatment(s) being selected according to the findings of comprehensive evaluation of clinical symptoms and the degree of protrusion and stenosis.

Because patients with this type usually have degeneration, protrusion, hyperplasia and stenosis in multiple segments, the segment and position of the disc responsible for the clinical symptoms should be determined preoperatively. During surgery, limited decompression at the responsible level can relieve the symptoms; thus, extensive resection aimed at preventing the lamina from compressing the spinal canal should be avoided, only the protrusion demonstrated by imaging should be resected. Because the protrusion is hard in this type, severe stenosis of the nerve root canal and nerve compression result from lack of cushioning. Thus, the tissue that is inducing the compression must be carefully removed. Surgical instruments such as lamina clamps or neural stripping irons would aggravate nerve injury if they were forced into the area of stenosis. To avoid aggravation of nerve injury, minimally invasive decompression of nerve structures is advisable; for example, the posterior wall of the canal can be removed with a high-speed burr. With removal of the posterior wall, the nerve can be decompressed and given enough space to move; thus, bulged or protruded discs often need not be excised.

Osteochondrosis with Disc Protrusion Type

Posterior vertebral body osteochondrosis is osteochondrosis in the secondary ossification center in the vertebral epiphyseal plate. This type is characterized by deformity of the posterior vertebral body, cartilage nodules and protrusion of the adjacent intervertebral disc. It has previously been called posterior vertebral separation, posterior vertebral fracture, posterior vertebral cartilaginous node and intervertebral disc ossification[5]. During surgery, the posterior vertebral body and the intervertebral disc are both found to have protruded. Osteocartilaginous protrusion, as a component of lumbar disc protrusion, is hard, extensive and difficult to resect (Fig. 3). The internal pressure of the protrusion is usually normal[10]. Intraoperative discography shows that the nucleus pulposus has almost normal morphology, being round, oval or horseshoe shaped in the lateral view. The disc is engorged and is posterior to its normal position disc. Additionally, a multi branch dispersion shape or an annulus fibrosus crack may be observed depending on the degree of protrusion of the intervertebral disc[8].

Pathological Changes

The protrusion of posterior vertebral osteochondrosis consists of the nucleus pulposus, annulus fibrosus and mature lamellar bone formed by the cartilage endplate and epiphyseal ring, and is hard. This condition may be associated with atypical Scheuermann disease of the posterior lumbar vertebral body[5]. Scheuermann disease is a vegetative disorder characterized by wedging caused by ischemic necrosis of the vertebral epiphyseal ring; diagnostic criteria include wedging for more than three adjacent vertebral bodies, kyphosis of more than 5°, and exclusion of a trauma history and other pathological changes. Some researchers define atypical Scheuermann disease as a combination of cartilaginous nodes, irregular changes in endplates and vertebral deformation, but without wedging for

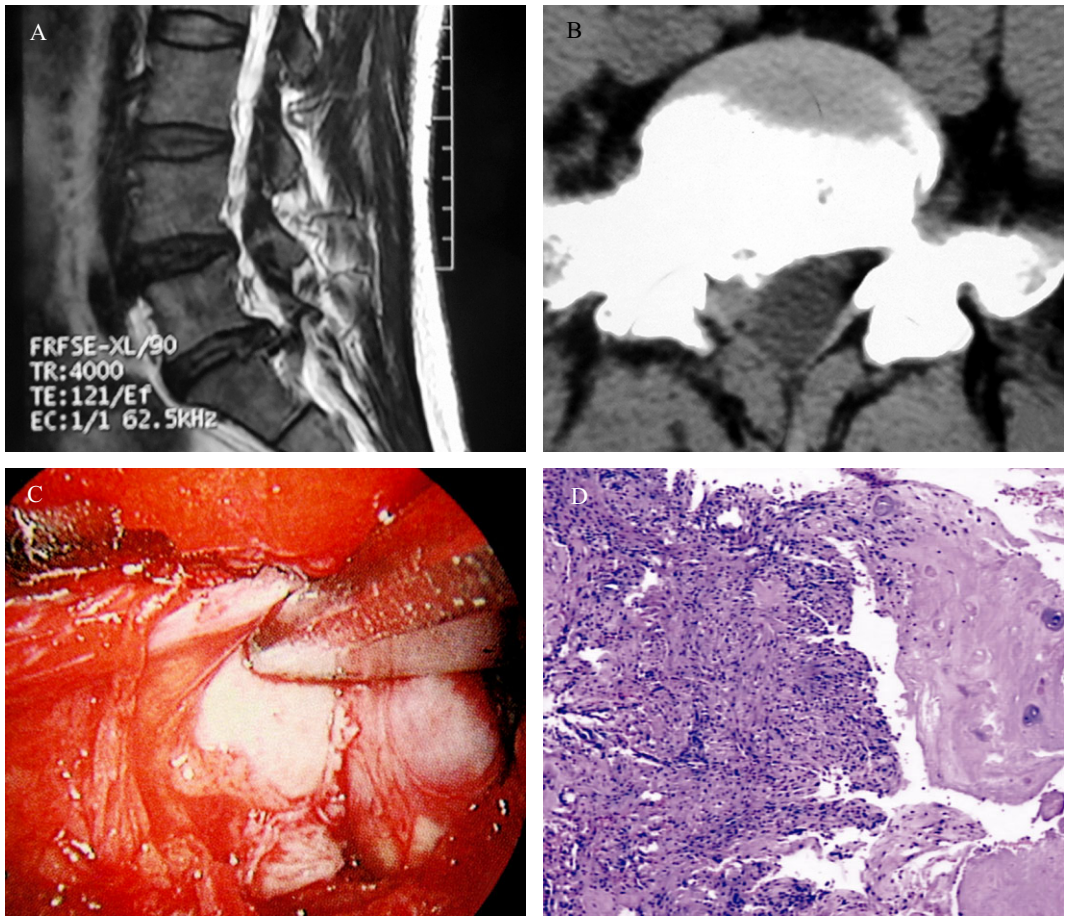

Fig. 3 Images obtained from a 42-year-old man with posterior vertebral osteochondrosis combined with damage-herniation of the intervertebral disc. (A) T2 weighted sagittal MRI showing posterior partial defect of the superior endplate of S_1 vertebra combined with disc herniation of L_5S_1. (B) Cross-sectional CT image showing disc herniation located posterior to the vertebral ossification. (C) Posterior spine endoscopy view showing that the protrusion is hard and the nucleus pulposus has broken through the weak area into the spinal canal. (D) Optical microscopy image showing degeneration of fibrocartilage matrix in the herniated disc tissue with surrounding formation of neovascularization and granulation tissue. HE staining, ×200.

more than three adjacent vertebral bodies. The basic pathology of atypical Scheuermann disease is osteochondrosis in the vertebral secondary ossification center characterized by Schmörl nodules, which have a high detection rate of 25.6% by MR examination in these patients[5].

Posterior vertebral osteochondrosis with disc protrusion is a common vertebral abnormality in adolescents before maturation of the epiphysis or when the vertebral epiphyseal cartilage ring has not yet united with the vertebral body. The nucleus pulposus breaks through developmental defects and cracks in the cartilage plate into the space between the vertebrae and the epiphyseal ring, making the epiphyseal ring move backward after repeated trauma or stress. The broken cartilage plate and epiphyseal ring separate from the posterior edge of the vertebral body and ossify gradually, forming a ridge-like kyphosis at the posterosuperior or posteroinferior vertebral body and bony posterior wall. The nucleus pulposus, cartilage plate and annulus fibrous move backward, forming an osteocartilaginous protrusion, and extend into the spinal canal. Slightly retro-displaced protrusions with mature ossification can fuse with vertebral body. The abnormalities in the cartilage endplate decrease the infiltration and dispersion, and cause nutritional disorders, accelerated degeneration, decreased elasticity and increased hardness of the intervertebral disc. The increased pressure in the annulus fibrosus and vertebral body combined with resultant cracks in the posterolateral annulus fibrosus lead to further protrusion of the intervertebral disc. Protrusion of the disc and dysplasia of the posterior vertebral body are the essential pathological characteristics of this type, in which the vertebral bone defect fills with disc tissue.

Pathogenesis

Posterior vertebral osteochondrosis with disc protrusion gradually and progressively compresses the cauda equina and

nerve roots and pushes them backward. Its pathogenesis involves many factors, including severity of compression and stenosis, herniation of the nucleus pulposus, dynamic stimulation and protrusion position. In juvenile patients, the degeneration and hyperplasia are slight and there is space for compensation. With increasing age, degeneration and hyperplasia of the posterior ligamentum flavum and facet joint intensify. Combined with the anterior protrusion, the compression causes symptoms such as intermittent lumbocrural pain that are often progressive. This type can be combined with disc herniation in which the nucleus pulposus herniates into the spinal canal via a damaged weak area of the annulus fibrosus. This type has a similar pathogenic mechanism to the damage-herniation type (mechanical compression, inflammatory mediators and immune factors leading to nerve root pain) and can be seen as a particular variation on the damage-herniation type (Fig. 3). Posterior vertebral osteochondrosis is a common vertebral abnormality that is usually combined with disc protrusion; care should therefore be taken to ascertain whether patients with disc herniation also have posterior vertebral osteochondrosis.

Clinical Manifestations and Treatment

Posterior vertebral osteochondrosis with disc protrusion characteristically has an insidious onset and no history of trauma and is more common in juvenile and male patients, which may be related to their vigorous activity. The main symptoms of this type are pain and limitation of activity that is relieved by rest and aggravated by activity. Pain and numbness of one or both legs develops gradually, usually combined with symptoms of lumbar disc protrusion and spinal stenosis; however, nerve root symptoms are not as frequent as in the damage-herniation type. The straight leg raising test is positive without radiating pain and signs, such as sensory dysfunction, muscle atrophy and abnormalities of tendon reflex, are usually absent. Patients with lumbar spinal stenosis characteristically have intermittent claudication and radiating pain, numbness and weakness of legs. Those who also have the damage-herniation type usually have a history of trauma or acute attacks and obvious symptoms of nerve root damage.

X-ray films show arc sag or photic zones at the superior or inferior edges of the posterior vertebral bodies with surrounding bone sclerosis, irregularity of endplates and vertebral deformation. CT scans show posterior vertebral osteochondral protrusion together with disc protrusion, surrounding bone sclerosis and low density areas between the protrusion and vertebral bodies; these appear as partial posterior wall or separated posterior bone on cross-sectional scanning. Sagittal scanning may show the posterior vertebral wall to be strip-like cocked backwards and the corresponding vertebral bone defects to be filled with intervertebral disc tissue. MRI shows Schmörl nodules (low signals are related to sclerosis of bone trabecula and high signals to surrounding inflammatory reactions and bone marrow edema), irregularity of endplates, narrowed intervertebral spaces, degeneration and protrusion of intervertebral discs and so on. The protrusion is located in a central or paracentral position with the nucleus pulposus herniated into the spinal canal in patients who also have damage-herniation type protrusion[5].

In patients with mild symptoms and protrusion, treatments such as bed rest, back muscle exercises, drugs and other conservative treatments are advocated. In patients with severe symptoms, especially those with cauda equina syndrome, weakness or large protrusions combined with herniation of the nucleus pulposus, surgery is recommended to prevent irreversible nerve damage.

In patients with posterior vertebral osteochondrosis with disc protrusion, the protrusion is hard. To achieve complete decompression, the posterior bone wall and disc protrusion, which generates the compression, need to be resected. It is difficult to completely remove the compression without removing its hard trailing edge. At levels above the conus medullaris, an anterolateral approach is usually selected for completely removing the hard or central protrusion anterior to the spinal cord because of the spinal cord's poor tolerance of manipulation. For lesions of the lower lumbar spine, the surgical procedure can be decided according to the lesions and their pathogenic mechanisms. The symptoms of spinal stenosis can be relieved by decompressing the nerve and achieving a buffer space. Decompression of the stenosis responsible for the symptoms can be satisfactorily achieved by removing the posterior wall and protrusion compressing the nerve. Aggravation of nerve compression must be avoided; therefore excessive traction on the nerve to achieve complete removal of ossification or radical resection is not advocated. For patients who also have herniation of the nucleus pulposus, satisfactory results can be achieved by removing herniated and fragments of the nucleus pulposus. Although internal fixation and bone graft fusion can eliminate dynamic stimulation, there is no evidence that fixation and fusion is needed in patients without preoperative spinal instability[20].

Intervertebral Disc Cysts

Intervertebral disc cysts are cysts that communicate with the disc and are very rare. They must be distinguished from other intraspinal cysts, such as juxta-articular synovial cysts of facet joints, cysts around the nerve, ganglion cysts, arachnoid cysts and cysts of the posterior longitudinal ligament[21,22]. Intervertebral disc cysts and cysts of the posterior longitudinal ligament are both located on the ventral side of the dural sac and are closely connected with the intervertebral disc or posterior longitudinal ligament through the pedicle. The inner wall of both consists of fibrous connective tissue with a synovial lining, and the clinical manifestations and treatments are similar. Intervertebral disc cyst may be interlinked with the intervertebral disc; thus, defects of the annulus fibrosus may occur after excision of such cysts[23].

Pathological Changes and Pathogenesis

Histological examination shows that the walls of intervertebral disc cysts consist of dense fibrous connective tissue, with hemosiderin deposition and mucinous degeneration, but no

cell lining, intervertebral disc tissue, nervous tissue, tumor cells, neovascularization or cell infiltration. The cysts contain bloody or serum-like clear fluid and their walls connect with the adjacent disc. There is a pipeline between the cyst and the disc, with a slight tear on the annulus fibrosus. During surgery, adhesions are found to be minimal. The walls of intervertebral disc cysts reportedly contain intervertebral disc tissue such as cartilage[24,25].

The cause and pathogenesis of intervertebral disc cysts is still unclear. Chiba *et al*. postulated that the bloody fluid and hemosiderin deposition in disc cysts originated from hematomas caused by intervertebral disc damage, tears of the posterior annulus fibrosus and hemorrhage from the posterior vertebral epidural venous plexus[21]. Kobayashi *et al*. suggested that the degeneration and damage in intervertebral discs results in intervertebral disc protrusion and overflow of liquid from within the disc, causing inflammatory reactions and a reactive pseudomembrane, thus forming a cyst[26]. The patients are young and therefore their discs have a high water content; this liquid infiltrates the cyst to form cystic fluid. These cysts can cause bone erosion, which indicates they exert pressure and that there may be a check valve mechanism; therefore the pressure and volume can increase quickly and need to be closely observed. Tokunaga *et al*. reported transformation of intervertebral disc protrusion into intervertebral disc cysts in two cases, cartilage tissue being found in the cyst walls by MRI[25]. They speculated that the fibrous tissue capsule and neovascularization are generated during absorption of an intervertebral disc protrusion and the protruded nucleus pulposus is engulfed by mononuclear macrophages, hemorrhage in the cyst then increases; increasing the intracapsular pressure and the hematoma is absorbed.

Clinical Manifestations and Treatment

Intervertebral disc cysts are rarely encountered clinically. One hundred intervertebral disc cyst have been reported with a mean age of onset of about 33 years and a male predominance. Chiba *et al*. reported eight cases of intervertebral disc cyst and summarized their characteristics, which include younger age of onset than intervertebral disc protrusion but similar clinical manifestations to typical lumbar disc protrusion, usually with involvement of a unilateral nerve root[21]. Intervertebral disc cysts show as round or oval liquid cystic masses with low signals on T1 weighted images and high signals on T2 weighted images. Slight degeneration of the affected intervertebral disc is evident on MRI images. During discography, the cyst and affected intervertebral disc may be found to be communicating and severe radiating leg pain may occur during the injection. The symptoms are greatly relieved by excision of these cysts. Pathologic examination shows the cyst walls consist of dense fibrous connective tissue. They contain bloody or clear serum and have no intervertebral disc tissue or specific lining cell layer (Fig. 4).

Symptomatic intervertebral disc cysts often require surgery or other interventions; only three cases in which symptoms improved and the cyst gradually vanished with conservative treatment have been reported. Resection of these cysts under microscopic or endoscopic guidance can achieve good results. Whether the affected intervertebral disc needs to be resected simultaneously is controversial; most researchers believe that intervertebral discs with no obvious degeneration and protrusion can be left *in situ*. Kang *et al*. reported achieving satisfactory results in five cases by percutaneous aspiration of fluid guided by CT; however, whether simultaneous injection of steroids is indicated is still controversial[27].

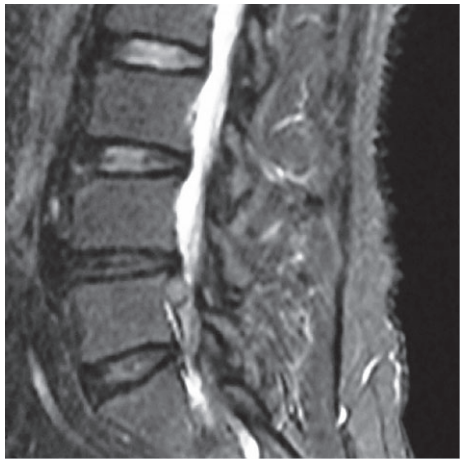

Fig. 4 Images obtained in patients with intervertebral disc cysts. Image obtained in a 51-year-old patient with radiating pain in the left leg. T2 weighted sagittal MRI showing intervertebral disc cyst of L_{4-5}. Posterior spine endoscopy showed that the cyst communicated with the disc; there were liquid and nucleus pulposus fragments inside the cyst.

Secondary pseudo intervertebral disc cysts reportedly occur occasionally after lumbar intervertebral discectomy. The symptoms are similar to those of intervertebral disc cysts, but they not identical. MRI images show the cysts are located on the ventral side of the dural sac and are attached to the disc; show low signals on T1 weighted images and high signals on T2 weighted images. These cysts usually contain serous, rarely bloody, fluid and have no hemosiderin deposition, which assists in distinguishing them from postoperative relapses of protrusion and hematomas. Some researchers believe that the protruded nucleus pulposus generates a pseudomembrane and that the residual pseudomembrane communicates with the disc after removal of nucleus pulposus fragments. Subsequently, the liquid of the nucleus pulposus flows into the pseudomembrane, accumulates and forms a cyst because of intervertebral activity[28]. Because their walls are fragile and there is weak postoperative inflammation, such cysts are usually absorbed and conservative treatment can be satisfactory. In patients with severe symptoms, surgical resection or aspiration can achieve good results and is suggested (Table 2).

In addition, in patients with lumbar disc protrusion there are usually abnormal signals from the intervertebral disc

TABLE 2 New pathological classification of lumbar disc protrusion

Classification	Intraoperative findings	Synonyms	Related type	Pathological characteristics	Pathogenesis	Clinical characteristics	Suggested surgical procedure
Damage-herniation type	Soft protrusion with thin superficial annulus fibrosis and disc fragments that can easily be removed	Extruded; prolapse; soft herniation	Herniation in MacNab classification; extruded or sequestered type in Spengler classification; extrusion in AAOS&ISSLS classification; ruptured and sequestered types in Zhou classification	Tissue destruction, neovascularization, infiltration of T lymphocytes and macrophages, deposition of IgG or IgM and expression of IL-7, ultrastructure characterized by evidence of destruction	Mechanical compression, inflammatory and autoimmune reactions	Frequent history of slight trauma, radiating nerve root pain, straight leg raising test positive	Complete removal of herniated or nucleus pulposus fragments
Degenerative-protrusion type	Hard, relatively inflexible protrusion and no disc fragments; difficult to remove	Bulge; displacement; hard herniation	Protrusion in MacNab; Spengler or Zhou classifications; degeneration, bulge and protrusion in AAOS&ISSLS classification	Proliferation of cartilage matrix and collagenous fibers with a dense and disordered arrangement, ultrastructure characterized by evidence of proliferation and active cell synthesis	Mechanical compression, stenosis of spinal and nerve canals	Patients are elderly, gradually intensifying pain, numbness, and weakness of legs and intermittent claudication	Minimally invasive decompression of nerve, usually with no need to resect the intervertebral disc
Osteochondrosis with disc protrusion type	Hard osteocartilaginous protrusion, extensive and difficult to resect	Hard herniation		Protrusion consists of nucleus pulposus and annulus fibrosus combined with mature bone tissue derived from cartilage endplate and epiphyseal ring	Mechanical compression, stenosis and dynamic stimulation	Patients are young with progressively intensifying radicular symptoms. CT shows posterior vertebral protrusion and defect	Minimally invasive decompression of nerve, with removal of herniation
Intervertebral disc cyst type	Located on the ventral side of the dural sac, cyst wall closely connected with intervertebral disc. A defect of the annulus fibrosus occurs after excision of the cyst	Discal cyst		Cyst wall consists of dense fibrous connective tissue with possible intervertebral disc tissue, such as cartilage, and no cell lining. The cysts contain fluid	Mechanical compression	Patients young, condition rare and accompanied by radicular symptoms. MRI shows liquid in cysts and radiography shows cysts communicate with the intervertebral disc	Excision of cyst or aspiration of cyst guided by imaging

and vertebral endplate on MRI. There is reportedly a high incidence (25%–50%) of high intensity zones in the posterior annulus fibrosus in those with low back pain and about 24% in a symptomatic subjects[28]. High intensity zones are associated with the granulation tissue and neovascularization that forms after the annulus fibrosus has torn and correlate with presence of low back pain. However, the significance of high intensity zones in subjects with low back pain and lumbar disc protrusion is controversial. In 1988, Modic *et al.* classified the abnormal signals of endplate bone on MRI as type 1 (low signals on T1 and high signals on T2), type 2 (high signals on T1 and high or equal signals on T2) and type 3 (decreased T1 and T2 signals); these signals are known as Modic change. On pathological examination, fibrovascularization is found in type 1, fat substitution in type 2 and bone sclerosis in type 3. Modic change has an incidence of 7.4%–12.0% in normal people and 17.6%–58.0% in patients with low back pain; female or obese subjects have a higher incidence[29]. Some scholars believe that type 1 Modic change reflects the repair process of the endplate and vertebrae after micro fractures[30]. We have found that the number of IL-17-positive cells and mRNA expression of IL-17 in protruded disc tissue are significantly greater in subjects with Modic changes than in those with protruded disc tissue but without Modic changes. Given that the nucleus pulposus is immunogenic, it has been speculated that the nucleus pulposus can penetrate the endplate bone through endplate cracks after the cartilage endplate has been damaged, inducing an immune response and local inflammation and causing pain. Autoimmune reactions may play an important role in the pathophysiological mechanism of Modic changes[31]. Modic changes are dynamic and there is not enough evidence to confirm that type 1 is more likely to be associated with low back pain than type 2. Thus, Modic changes cannot be used to evaluate surgery and its outcomes.

Conclusions

In conclusion, we believe that our pathological classification contributes to the understanding of the different pathological changes and pathogenesis of lumbar disc herniation and provides a guide to clinical diagnosis and treatment. The pathological classification should be comprehensively assessed together with the position, morphology and anatomical characteristics of the protrusion. For example, cross-sectional CT or MRI can display stenosis of the intervertebral foramen at the level of a disc protrusion, whereas sagittal MRI can better show the morphology and involvement of intervertebral foramina. Exiting nerve roots are compressed only when the damage-herniation displaces cephalad to the upper half of the intervertebral foramen. However, when extreme lateral disc herniation occurs through the intervertebral foramen, conservative treatment can often relieve the symptoms because the exiting nerve root is not located in the fibro-osseous channel and there is some room for movement. The pathogenesis of the degenerative-protrusion type is often related to stenosis of the nerve canal, which mainly results from hyperplasia of "hinge" tissue and causes intervertebral disc protrusion at the level of the intervertebral disc–ligamentum flavum and intervertebral joint capsule. Sufficient but limited decompression should be performed with the aim of relieving stenosis. To preserve stability, hard protruded or bulged discs should not be resected; relief of compression generally achieves a satisfactory curative effect.

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