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Research Article

GENERAL REVIEW OF OSSIFICATION OF POSTERIOR LONGITUDINAL LIGAMENT

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ABSTRACT

Ossification of posterior longitudinal ligament is a hyperostotic condition which results in ectopic ossification in the posterior Longitudinal Ligament in the Spine, which can lead to sever myelopathy and paralysis. Ossification of posterior longitudinal ligament was reported in 1838 in Japan for the first time and the first autopsy was reported in 1969. It mostly effects patients between age 50-70 and it is more common in Asian countries (Japan, Korea, and China) therefore, it known as Asian disorder. According to Japanese ministry of health Ossification of posterior longitudinal ligament is divided into four subtypes, including segmental, continues, mixed and circumscribed type. Diagnosis can be done with X-ray, Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) scan, pathology of this disorder is still not clear. To conclude, OPLL is a progressive disease, which thickens and ossifies ligamentous tissue in spine, it is the most common cause of myelopathy. Patients in early stages can be treated conservatively but for developed OPLL, patients may require surgical management. The purpose of this study was to offer a latest introduction of OPLL for readers, particularly for medical students.

Keywords: DISH (defused idiopathic skeletal hypertrophy), ACF (Anterior Cervical and Fusion), SDL (Single Door Laminoplasty), VBSO (Vertebral Body Sliding Osteotomy), T-OPLL (Thoracic Ossification of posterior longitudinal Ligament).

INTRODUCTION

OPLL (ossification of posterior longitudinal ligament) was reported in 1838 for the first time. Years later an OPLL autopsy was reported in 1969 in Japan. A 3mm ossified mass was found (C3-C4 region) in a 47 year old patient. [1] OPLL cases were mostly found in Asian countries so it was called the Asian disease. [2] On the contrary OPLL cases were rarely found in Europe and the USA, However Cases of DISH (diffuse idiopathic skeletal hyperostosis) were very well known in the USA and Europe. About half of the patients diagnosed with DISH had OPLL. In Europe and United States OPLL has come to be recognized as a subtype of DISH, [3] which increases the risk of spinal cord injury following a traumatic events. OPLL is a progressive disease, which thickens and ossifies posterior ligamentous tissue in the cervical spine and causes ectopic bone formation in posterior longitudinal ligaments. OPLL reduces range of motion in limbs and it occurs in most often in obese men, which is the main cause of myelopathy and spinal cord stenosis in the cervical spine. [5,6,7,8] It mostly effects people between the ages 50-70 years, in addition, it can occasionally occur in children (though in very rare cases). The most common location for OPLL is the C4-C6 vertebrae and is rarely found at the C1-C2 level. It effects 92% in the cervical spine, 15% in the thoracic spine and 4% in other spinal levels. [9,10,11] Dural ossification can be seen in almost 10% of cases with OPLL. It has been estimated that up to 25% of patients presenting with cervical myelopathy have features of OPLL. [12] Whereas 15% of OPLL occurs in the thoracic spine which may lead to severe myelopathy, dyskinesia, sensory disturbances, fecal & urinary incontinence and even paralysis, this is called T-OPLL. Thoracic ossification of posterior longitudinal Ligament is slowly progressed, therefore symptoms are typically seen in advanced stages. OPLL is well classified and diagnosed with 2-dementional and 3-dementional CT scan. According to the Japanese health ministry, OPLL has four types (segmental type, continuous type, mixed type and circumscribe type). T1 segment is most frequently affected in both men and women followed by T1-T2 and T3-T4, severe OPLL in thoracic spine occurs more in women in comparison to men (20% vs. 4.5%), however, Thoraco-Lumbar ossified lesions are most common in women compared to men. Ossified lesions were frequently seen at the intervertebral and vertebral levels around the cervical-thoracic and thoracolumbar junctions in men with severe OPLL, whereas OPLL was more diffusely distributed in the thoracic spine in women with severe OPLL. [13, 14] T-OPLL has a much higher disability rate, in comparison to C-OPLL (cervical ossification of posterior longitudinal ligament). Posterior surgical approach is chosen in above 80% of thoracic OPLL cases. A study has identified five new potential pathogenic loci for T-OPLL: rs201153092 and rs13051496 in the COL6A1 gene, rs199772854, rs76999397 and rs189013166 in the IL17RC gene which may help clarify molecular etiology of T-OPLL. [14] Symptoms of OPLL include sensory and motor dysfunction of both upper and lower extremities, abnormal reflexes, bladder dysfunction, cervical pain and discomfort, and numbness of the upper extremities. [15] However, 5% of patients were reported free of symptoms. [16, 17]

Classification:

Different studies have classified OPLL in different ways such as; Fujimori and Kawaguchi has classified OPLL into Bridging and non-bridging types.[18. 19] Kawagachi has classified OPLL in to three different types (flat, irregular and localized). [20] On the other hand, a study by Yang has categorized OPLL based on the association between dura and the posterior longitudinal ligament. [21] Jayakumar in 1996 classified OPLL by shape (hook, staple, bridge, bridge and total types). [22] In 2011a research by Chen classified OPLL as a free type, continues type and broken type. [23] Fujimori and Yukawa have classified OPLL as hill, plateau, square, and mushroom, irregular or round shape. [24-25] In 2013 Hossam's research classified OPLL in triangular, teardrop and boomerang types.[26] Back in 1993 Epstein classified OPLL as rectangular, oval, triangular, and pedunculated types. [27] Onishi in 2012 classified OPLL as centralized and laterally deviated types. [28] Terada classified OPLL in three different types (plank, sprinkle and rod shaped). [29] Finally, OPLL was also categorized based on location. [30] Other common classification methods include K line (-/+), sign of Dural ossification and pattern of distribution. [31]

In the latest report the Committee for Ossification of Spinal Ligaments established a commonly known classification system for OPLL [Figure:1], that system categorized OPLL in to the following four types: [32-34]

- Segmental type: one or more separated ossified lesions behind the vertebral bodies.
- Continuous type: a long lesion extending over several vertebral bodies.
- Mixed type: a combination of continues and mixed type.
- Localized type: this type of OPLL is mainly

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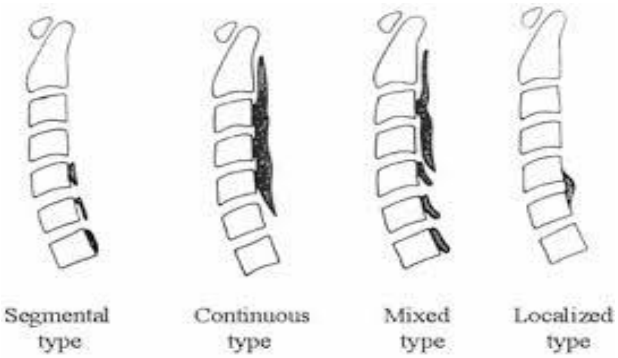

Figure 1: This Diagram illustrates classification of OPLL according to the Japanese Ministry of Health, Labor and Welfare.

Epidemiology & Pathogenesis:

OPLL prevalence was reported 3.4%-5.7% in Korea, 1.5% to 3.7% in japan, and 1.0% to 1.7% in Europe and the US. OPLL cases were found 2.2% among Asian Americans which is more often than White Americans. [34] Children with IDC (inter-vertebral Disc calcification is recommended for conservative treatment with

affirmative short term and long term clinical effects (long term observation may require). An epidemiologic study of OPLL in China involving 2029 Chinese and 500 Mongolian patients. According to this study, the prevalence of OPLL was 1.6% in Chinese and 1.8% in Mongolians. [35]

The pathogenesis of OPLL is poorly understood. Studies have detected the following metabolites are significant larger in OPLL groups, such as; Thiapoline, thyroxin, fatty acid, palmitoylcarnitine and acyl carnitine. In addition, BMPR-IA gene equally plays an important role in formation of OPLL. Other researches have proven investigations that leptin can stimulate the osteogenic differentiation and proliferation of embryonic cell, bone marrow stromal cells and osteoblastic cells. The Osteogenic effect of leptin were found higher, bone mineral density was also reported in patients with OPLL which might play a role in pathogenesis of OPLL.

Clinical finding/Diagnosis:

Radiographs are very helpful in diagnosis of OPLL, especially when located in the Cervical Spine. Diagnosis can be done with X-ray, MRI and CT scan, where thickened ossified borders can be seen in endochondral zone. CT scan sagittal sequences can help classify the type of OPLL and has higher reliability. [36] Three-dimensional CT can be used both to quantify the volume of OPLL and classification purpose. [37] MRI (magnetic resonance imaging) is used for detecting myelomalacia as a result of OPLL compressing the spinal cord. It is also useful to assess for foraminal stenosis that could be the cause of radiculopathy.

All types of OPLL were better classified using 2- dimensional CT (continuous: 62%, segmental: 87%, mixed: 83%, localized: 92%) and 3-dimensional reconstructed CT images (continuous: 73%, segmental: 89%, mixed: 86%, localized: 92%). Rather than using lateral radiographs in combination with axial CT images (continuous: 17%, segmental 77%, mixed: 74%, localized: 88%). Diagnostic accuracy of lateral Radiographs and MRI was further explored by Kang et al. [38] Plain X-rays were able to better classify continuous (85.7%) and mixed (91.7%) OPLL compared to segmental (27.3%) and localized (20.0%) types, which has had slightly different accuracy (100% in continuous, 31.8% in segmental, 83.3% in mixed, and 60.0% in localized OPLL). [39]

Management of OPLL:

Myelopathy caused by OPLL can be treated in an early stage conservatively.[40] Conservative treatment involves observation, physical therapy, oral analgesic, regular clinical follow-up, application of a neck brace for cervical immobilization, decreased activity levels and physical therapy. [41, 42, 43] Some patients might require bed rest and a period of cervical traction. In comparison, patients with segmental and circumscribe OPLL subtypes had more common radicular pain.

However, Surgical intervention is required for chronic stage of OPLL (causes narrowing the spinal canal and cord compression), resulting in the compressing of the spinal cord and the nerve root which may lead to serious neurological deficit, even paralysis. Laminectomy with fusion and Laminoplasty are two favorite surgical options for OPLL Cases. Surgical pathway includes anterior, posterior and combined approach, however, radiological findings are important along with clinical findings to decide the appropriate surgical

intervention path. Studies have proven that the annual growth of OPLL was 7 times faster in Laminoplasty group compared to laminectomy and fusion group. Posterior instrumented fusion has a better effect on reduction of OPLL growth rate rather than motion preserving Laminoplasty. Additionally, the anterior enlargement of the spinal canal may provide safe and effective option for treatment for OPLL patients with myelopathy by anterior corpectomy and fusion and it may achieve better neurological recovery rate for OPLL. Anterior approach is the most common surgical choice 55.78% followed by posterior approach 43% and 1.2% for combine approach.

K-line is also important in choosing the right surgical approach in OPLL patients. It is a straight line drawn from the posterior-inferior aspect of C2 vertebral body to C7, which is used to assess effective lordosis. If hypertrophic calcification and osteophytes are seen behind the line or K-line negative cases than anterior approach is necessary. [44, 45, 46] The occupancy ratio is also important in deciding between an anterior versus Posterior approach. In patients with occupancy ratio 60% who underwent laminoplasty, there was significantly less ($p < 0.03$) improvement in neurologic recovery rate. [47] Posterior approach is considered for more than 3 vertebras involved and anterior approach for less than 3 vertebras involved.

Additionally, VBSO (vertebral body sliding osteotomy) is also considered in OPLL treatment due to higher surgical complications, this procedure does not manipulate OPLL mass directly which can significantly decrease surgical complications, has an excellent neurological outcome and is more helpful in restoring physiological lordosis. [48,49,50,51]

There are three ways to approach OPLL for surgical intervention: [Figure: 2, 3]

- Anterior approach
- Posterior Approach
- Combined Anterior-Posterior Approach

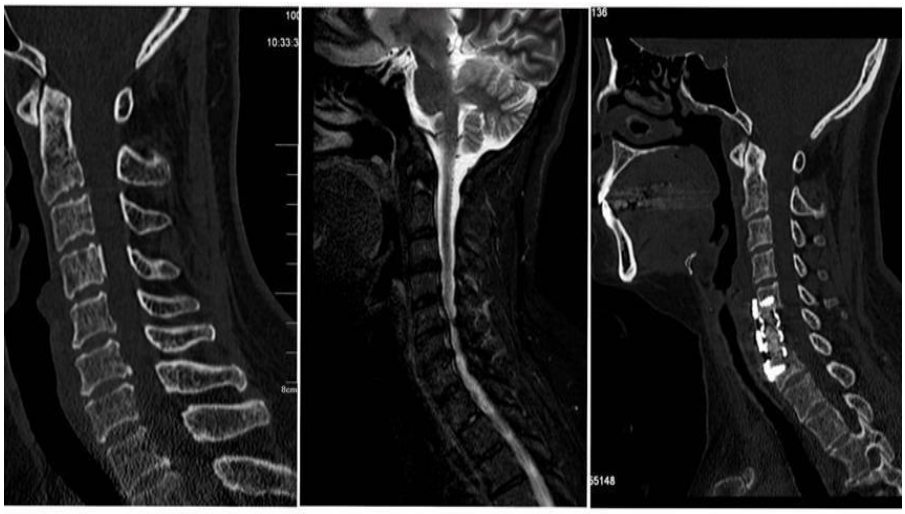

Figure 2: Shows examples of anterior approach, images from left to right, 1: preoperative CT scan, 2: preoperative MRI, 3: post-operative CT scan.

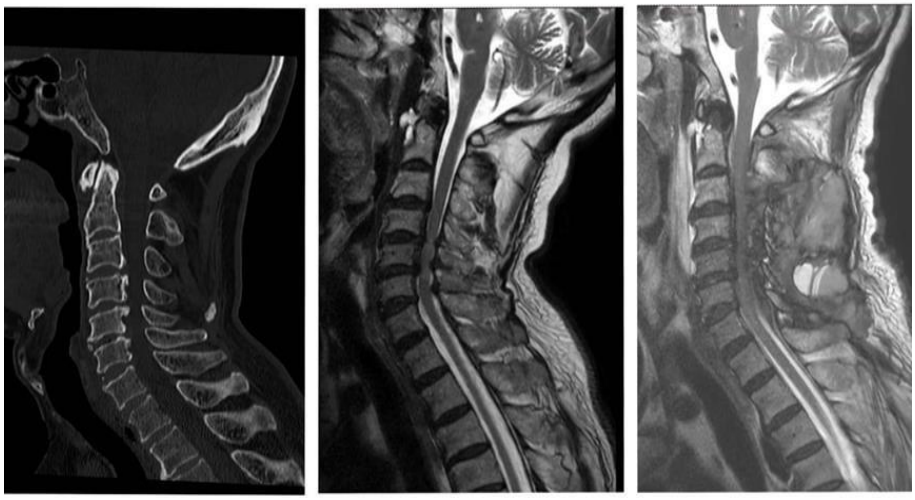

Figure 3: Shows examples of posterior approach, images from left to right, 1: preoperative CT, 2: preoperative MRI, 3: post-operative MRI.

DISCUSSION

Progression of OPLL was defined as below,

- Increased thickness or sagittal extend of OPLL more than 2 mm or more.
- An increase in longitudinal extend of ossification by 2 mm or more.
- Appearance of a new lesion.
- Forming a continuous segment by bridging of 2 or more existing lesion. All these cases significantly reduce the space available for spinal cord. [52]

Additionally, factors such as Diabetes, BMD changes, DISH, Elevated plasma pentosidine level, Flavum Ligament ossification, hypothyroidism, increased prostaglandin, high glucose level and increased body mass are correlated in progression of OPLL. CXCL7 deficiency in OPLL is suggestive of target degradation by the ubiquitin-proteasome by phosphorylation of E3 ubiquitin high factors for OPLL progression which means OPLL progression was significant higher in type 2 and type 3 then type 1. Similarly, ligament thickness is more common in type 2 and type 3 compared to type 1. [53]

Patients with different types of OPLL had different surgical outcomes, different risk of complication and progression rate, for example, patients with K-line + had significant higher rate and post-operative JOA score, in comparison to patients with K-line negative.[54, 55, 56] Complication were more common in anterior approach group compared to posterior approach such as CSF leakage, C5 palsy and neurological compromise. [Table: 2] Risk factors includes old age, end plate removal and non-union after surgery foranterior corpectomy and fusion. [57] The rate of all surgical complications including CSF leak, graft extrusion, or incomplete fusion was reported 23%. [58] For patients undergoing OPLL surgery the complication rate was 21.8%. [59] CSF leakage

was (5.1%), implant complications (3.5%), and hoarseness, dyspnea, and dysphagia (03%) were more common with anterior approach. C5 nerve palsy (42%) and axial pain (35%) were more common with posterior approach. [60] On the other hand, a single-institution study of 1,994 patients undergoing cervical spine surgery, the prevalence of CSF leakage was noted. In this series, patients with OPLL were 137 times more likely to have a CSF leak compared with patients without OPLL. [61, 62]

Anterior Corpectomy & Fusion	**Posterior Laminoplasty**
Advantages	**Advantages**
1. Improved myelopathy score	1. Decreases approach complication
2. Direct removal of pathology	2. Better tolerated in patients >65 YO
	3. Improved stability
Disadvantages	**Disadvantages**
1. Higher complications	1. Increased neck pain
2. Anterior approach related (dysphagia, hoarseness, prolonged intubation)	2. Less improvement in myelopathy score
3. Graft expulsion	3. Persistent ossified bar / ligament
4. C5 root palsy	4. C5 root palsy

Table 2: This figure describes advantages and disadvantages of anterior and posterior approach.

CONCLUSION

OPLL is a progressive disease which thickens and ossifies the posterior ligamentous tissue in the spine, it is the most common cause of myelopathy and it is more common in Asian population compared with Americans or Europeans. Patients in early stages can be treated with conservative management but developed OPLL patients may require surgical management. Studies have proven that the best diagnosis and classification way is to use 2-dimentional or 3-dimentional CT imaging. OPLL has 4 types (segmental type, continuous type, mixed type and circumscribe type) there are 3 surgical approaches (anterior approach, posterior approach and combined approach), surgeons might choose the surgical approach by locating the OPLL with the help of CT, MRI and X-ray. The K-line is equally very important in choosing surgical approach in cervical. In Comparison laminectomy and fusion is a better choice in maintaining cervical lordosis and Laminoplasty revealed lower surgical trauma. Anterior approach has more surgical complication than posterior approach. Pathology of OPLL is still not clear but there are few factors that has been pointed out in this study which might progress OPLL growth. [Fig: 2] Our previous study revealed that anterior approach was an alternative to posterior approach for

single level OPLL and posterior approach was an alternative to anterior approach for multilevel OPLL. [63]

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