International Orthopaedics (2019) 43:797–805
https://doi.org/10.1007/s00264-018-4106-5

REVIEW ARTICLE

Ossification of the posterior longitudinal ligament in the cervical spine: a review

Barrett S. Boody[1] · Mayan Lendner[1] · Alexander R. Vaccaro[1]

Received: 25 July 2018 / Accepted: 8 August 2018 / Published online: 16 August 2018

Abstract

Ossification of the posterior longitudinal ligament (OPLL) is a rare pathologic process of lamellar bone deposition that can result in spinal cord compression. While multiple genetic and environmental factors have been related to the development of OPLL, the pathophysiology remains poorly understood. Asymptomatic patients may be managed conservatively and patients with radiculopathy or myelopathy should be considered for surgical decompression. Multiple studies have demonstrated the morphology and size of the OPLL as well as the cervical alignment have significant implications for the appropriate surgical approach and technique. In this review, we aim to address all the available literature on the etiology, history, presentation, and management of OPLL in an effort to better understand OPLL and give our recommendations for the treatment of patients presenting with OPLL.

Keywords Ossification · Posterior longitudinal ligament · Cervical · Spine

Introduction

Ossification of the posterior longitudinal ligament (OPLL) is a pathologic process of lamellar bone deposition at the site of the posterior longitudinal ligament (PLL) and can cause reduced range of cervical motion and spinal cord compression. The PLL originates from the dorsum of C2 vertebral body with its superficial fibres confluent with the tectorial membrane, coursing distally towards the sacrum and closely opposed to the superior and inferior of the vertebral bodies and discs [1]. The function of the PLL is to resist hyperflexion and distraction.

In Japan, the incidence of OPLL among individuals presenting for evaluation with spinal disorders is between 1.9 and 4.3%, and in other Asian countries, the incidence is similarly reported up to 3.0% [2, 3]. Conversely, a much lower prevalence of 0.1 to 1.7% is described in comparable North American and European cohorts [4–6]. OPLL is more frequently seen in older adults (40–60 years old) and in males, with a reported male-to-female ratio of 2:1 [7]. OPLL has been associated with other ossifying spinal disorders, as Ehara found diffuse idiopathic skeletal hyperostosis (DISH) and ossification of ligamentum flavum (OLF) present in 25 and 21% of patients with OPLL, respectively [1].

✉ Mayan Lendner
mayan.lendner@rothmaninstitute.com

[1] Rothman Institute, 125 S. 9th St. 10th Floor, Philadelphia, PA 19107, USA

Etiology

The pathophysiology of OPLL remains poorly understood, but may share similarities to a similar ossifying condition, diffuse idiopathic skeletal hyperostosis (DISH) [8]. Early histologic changes include fibroblast and chondroblast-like proliferation and small vessel infiltration followed by endochondral ossification. Subsequent expression of BMPs within the PLL promotes further growth, maturation, and remodeling into lamellar bone [4, 9]. While environmental and genetic risk factors have been identified, recent research has identified multiple genes (BMP4, BMP9, COL6A1) potentially responsible for the familial inheritance patterns seen [3, 8, 10]. The etiology of OPLL is multi-factorial with both genetic and environmental factors playing a role and is still poorly understood. What is known can be divided into primary and secondary aetiology.

Primary (idiopathic) OPLL

Comorbid conditions found to be associated with idiopathic OPLL include age, diabetes mellitus (DM), and obesity while environmental factors such as exercise, abnormal

mechanical stress to the head, and a vitamin A-rich diet have been associated with OPLL [11–13]. OPLL has also been linked to diffuse idiopathic skeletal hyperostosis (DISH), ossification of the ligamentum flavum (OYL), ankylosing spondylitis, and potentially schizophrenia [14].

A significant genetic association has also been reported. In one study of 347 patients treated for OPLL, a prevalence of OPLL of 26% in parents and 29% in siblings was found [15]. Another study on the families of OPLL patients found an association between OPLL and human leukocyte antigen (HLA) haplotypes such that siblings sharing more identical HLA haplotypes had a higher prevalence of OPLL between siblings [16]. Many linkage and association studies have been conducted with many more still being investigated. Of note, a recent genome-wide association study found six loci more common in patients with OPLL with *HAO1A*, a gene most commonly expressed in the liver and pancreas, being the most common [17]. Furthermore, several genes at these loci were found to promote ossification. *HAO1, RSPO2,* and *CCDC91* may promote endochondral ossification while *RSPH9* and STK38L may promote membranous ossification resulting in OPLL. To date, few other large scale studies have been conducted; however, smaller studies have shown some genes/loci associated with OPLL including *TLR5*, *RXRB*, *COL11A2*, *RUNX2*, *Il-1B*, *ENPP1*, *ESR1*, *IL-15RA*, *BMP9*, *VDR*, *BMP4*, *TGFB3*, *TGFB1*, *BMP2*, and *COL6A1* [11]. Further, large-scale studies are needed to expand upon these results as most current research has focused on examining a small number of sequence variants in a small sample of patients.

Several hormones are theorized to play a role in the pathogenesis of OPLL, yet there is minimal high level-of-evidence data to support this claim. Insulin was once thought to play a role similar to DISH in the severity of ossification but, despite the association of obesity, DM, and OPLL, hyperinsulinemia does not seem to be clearly related to level of ossification [13]. Leptin, which functions both in fat metabolism and bone formation, was found to have an indirect association with level of ossification in OPLL as serum leptin levels were positively correlated with OPLL in females [13]. The effect of hyperglycemia on the extracellular matrix of renal and skin fibroblasts is theorized to have a similar effect on spinal ligament fibroblasts [13]. While growth hormone may also play a role, as acromegaly has been associated with OPLL, this potential association is not yet fully understood. Imbalanced sex hormones in males have been shown to correlate to extent of spinal ossification, with serum total estrogen levels positively correlating with the extent of ossification [13]. However, this correlation has not been found in females despite females' more frequent and marked changes in sex hormones.

Secondary OPLL

In contrast, secondary OPLL is often associated with hypophosphatemic rickets caused by several genetic mutations, with X-linked hypophosphatemic rickets being the most common, and endocrine disorders such as hypoparathyroidism and acromegaly [11]. In one study of 17 consecutive patients with hypoparathyroidism, nine (53%) had various forms of paravertebral ligamentous ossification (PVLO) with a significant correlation between the time it took for the patient to receive treatment for hypoparathyroidism and the incidence of ossification [18]. While all patients with PVLO did experience ectopic calcification; serum calcium, phosphate, and calcium-phosphate product levels did not seem to influence the incidence [13, 18]. Furthermore, correction of serum calcium and phosphate levels has been shown to aggravate ossification rather than preventing or reversing it [13]. To date, no studies have been able to identify the underlying mechanism for the correlation between OPLL and these diseases.

Natural history

Patients with OPLL should undergo a complete history and physical examination to determine the proper course of treatment. Although 5% of patients diagnosed with OPLL may not note subjective disability, surgeons should evaluate for subtle signs or symptoms of neurologic compression [3]. Physical examination should include the Romberg and tandem gait tests for early signs of gait disturbance or imbalance. Brisk reflexes in the upper and lower extremities and positive pathologic reflexes (Hoffman's and inverted radial reflexes) suggest upper motor neuron lesion.

Symptomatic spinal cord or nerve compression can present clinically as axial neck pain, radiculopathy, and myelopathy. Cervical radiculopathy from OPLL can present as pain, diminished sensation, and motor weakness found within the distribution of the compressed cervical nerve. Cervical myelopathy can present as changes in balance or gait stability, loss of fine manual motor control or dexterity, nonspecific upper and lower extremity weakness, paresthesias, and pain. Upwards of 40% of patients presenting for spine evaluation will exhibit signs and/or symptoms of myelopathy, with progression of neurologic symptoms closely linked to presenting neurologic status [19]. At a mean follow-up of 17 years, Matsuanga reported 64% of myelopathic patients had progression of symptoms [2]. Risk factors for myelopathy include less than 6 mm space available for spinal cord, increased cervical range of motion, laterally deviated OPLL lesions, and > 50–60% canal occupancy [2, 20–22]. As the majority of research on OPLL is published by Japanese physicians, a commonly scoring system used to improve physician communication is the Japanese Orthopaedic Association score (JOA score) for cervical myelopathy. The

scoring system uses a max score of 17, grading motor dysfunction in both upper and lower extremities, sensory disturbances, and sphincter dysfunction. The term "recovery rate" of JOA score is used to help describe the extent of improvement seen between pre- and post-operative scores (post-operative-pre-operative score/17-pre-operative score).

Imaging

Imaging of OPLL should begin with upright X-rays with AP, lateral, and flexion/extension views. On the lateral view, ossification can be seen located posteriorly to the vertebral bodies along the course of the PLL In order to improve clinical and research communication, OPLL is classified morphologically into one of four types: localized (*confined to disc space*), segmental (*fragmented ossification located posterior to vertebral body*), continuous (*ossification extends across several vertebrae*), and mixed (*combination of segmental and continuous*) [23] (Fig. 1).

Additionally, the lateral view is critical for understanding the cervical alignment and sagittal balance, both of which can dictate surgical approach. The kyphosis line or "K-line" is a straight line connecting midcanal C2 to C7 used as a radiographic predictor of successful posterior based decompression. Patients with a K-line positive lateral X-ray (i.e., the OPLL does not extend dorsal to the K-line) are associated with improved outcomes after posterior-based decompressions [24].

Since OPLL can be difficult to observe and diagnose on the lateral X-ray view, the CT scan can be helpful adjunct imaging for diagnosis and evaluation of patients with suspected OPLL.

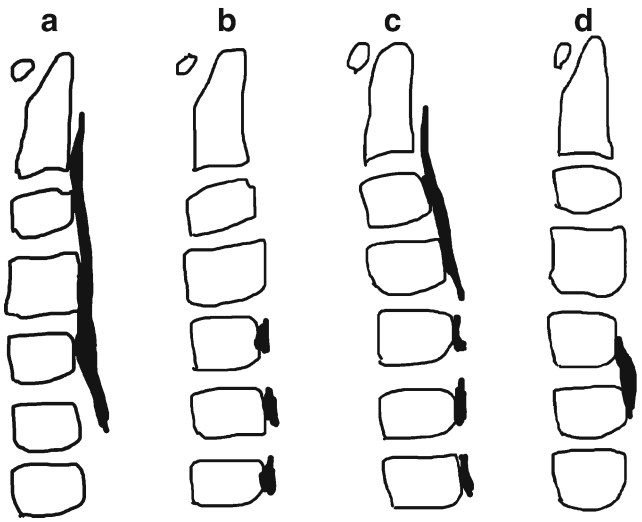

Fig. 1 OPLL is classified morphologically into one of four types: continuous (**a**) (ossification extends across several vertebrae), segmental (**b**) (fragmented ossification located posterior to vertebral body), mixed (**c**) (combination of segmental and continuous), and localized (**d**) (confined to disc space)

Additionally, CT assists with characterizing the morphology in the axial plane. OPLL can demonstrate "plateau" features, a broad base lesion, or "hill", with a narrower base but more pronounced extension posteriorly into the canal. Chang reported the inter- and intra-observer kappa values of 64 and 77% for the diagnosis of OPLL with X-ray, with improvement in kappa values using 2D CT images to 85 and 93%, respectively [25]. Furthermore, while an MRI is commonly obtained for patients with neurologic compression, obtaining a CT in patients suspected of having OPLL is helpful in determining the extent and location of compressive ossification [17].

Additionally, understanding the morphology of the OPLL can predict dural ossification [26]. Mizuno described three basic types of dural ossification: "isolated" type found at a distance from OPLL, "double layer" found posterior to OPLL lesions, and "en bloc" found in continuity with the OPLL lesion [27]. Specifically, the "double layer" sign on CT axial cuts has been well described as a predictive factor for OPLL defects with the dura, as Min reported dural defect rates of 52 and 14% for double- and single-layer signs, respectively [28].

MRI is useful for understanding the degree of central and foraminal spinal cord compression, concomitant degenerative spondylotic changes, and myelomalacia [17]. Reviewing preoperative MRIs, Koyangi noted associated disc protrusions in 60% of patients with OPLL and upwards of 81% for the segmental classification of OPLL [29]. OPLL will appear hypointense on T1 and T2 imaging, with small lesions appearing similar to disc-osteophyte complexes. High intensity T2 and low intensity T1 spinal cord signal changes and triangular deformation of the spinal cord (angular lateral and flat anterior surfaces) in the presence of OPLL lesions are associated with more severe pre-operative neurologic deficits and inferior outcomes after surgical decompression [22, 29–31]. Matsunaga reported all (39 of 39) patients with > 60% canal stenosis demonstrated myelopathy compared with 49% (57 of 117) of patients with < 60% canal stenosis [22]. Reviewing symptomatic patients with OPLL, Chang noted patients with or without myelopathy (neck pain ± radiculopathy) had a mean maximal compression ratio of 53.3% (SD 12.1%) versus 41% (SD 14.1%), respectively ($p = 0.03$). Additionally, cord signal changes were found in 61% of myelopathic patients versus 15% without ($p = 0.01$) [19].

Non-operative management

Non-operative management can be undertaken for asymptomatic patients without severe cord compression or myelomalacia on CT or MRI scans [32]. Conservative strategies in patients with OPLL included physical therapy, cervical orthoses, non-steroidal anti-inflammatories, and activity modification with avoidance of high-risk activities. Asymptomatic

patients with OPLL should be followed closely and given return to clinic instructions for signs of myelopathy, since approximately 17% of asymptomatic patients develop myelopathy at a mean of 14.6 years [32]. Although prophylactic surgery for asymptomatic patients is not routinely recommended, patients with severely stenotic cervical segments and cord signal changes should be closely monitored and questioned for signs or symptoms of myelopathy [33]. Additionally, patients conservatively managed for OPLL should be educated about an increased risk of spinal cord injury secondary to trauma [32, 34]. In patients with cervical spondylotic myelopathy (CSM), Chen reported OPLL to be a risk factor for SCI (hazard ratio 2.24, $p = 0.007$) and surgical management to reduce the risk of SCI (hazard ratio 0.52, $p < 0.001$) [35]. Furthermore, Wu reported patients conservatively managed with OPLL had a 4.8-fold higher risk for cervical SCI compared to an age- and sex-matched population without OPLL [34] (Fig. 2).

Surgical management

Surgical intervention should be considered for patients with neurologic symptoms such as myelopathy or radiculopathy and evidence of spinal cord compression. A variety of surgical approaches have been described utilizing anterior, posterior, and combined anteroposterior approaches, each with unique risks and benefits. Physicians and patients should decide on management after individualizing the benefits of surgical decompression against the potential medical and surgical complications. Pre-operative factors adversely affecting clinical results include increased age at operation, increased severity of pre-existing myelopathy and a history of trauma [36]. Complications from surgical management of OPLL are closely associated with the surgical complexity of the procedure. Li's systematic review of OPLL management found a 21.8% complication rate with similar rates between anterior and posterior procedure. C5 palsy and neck pain were more common

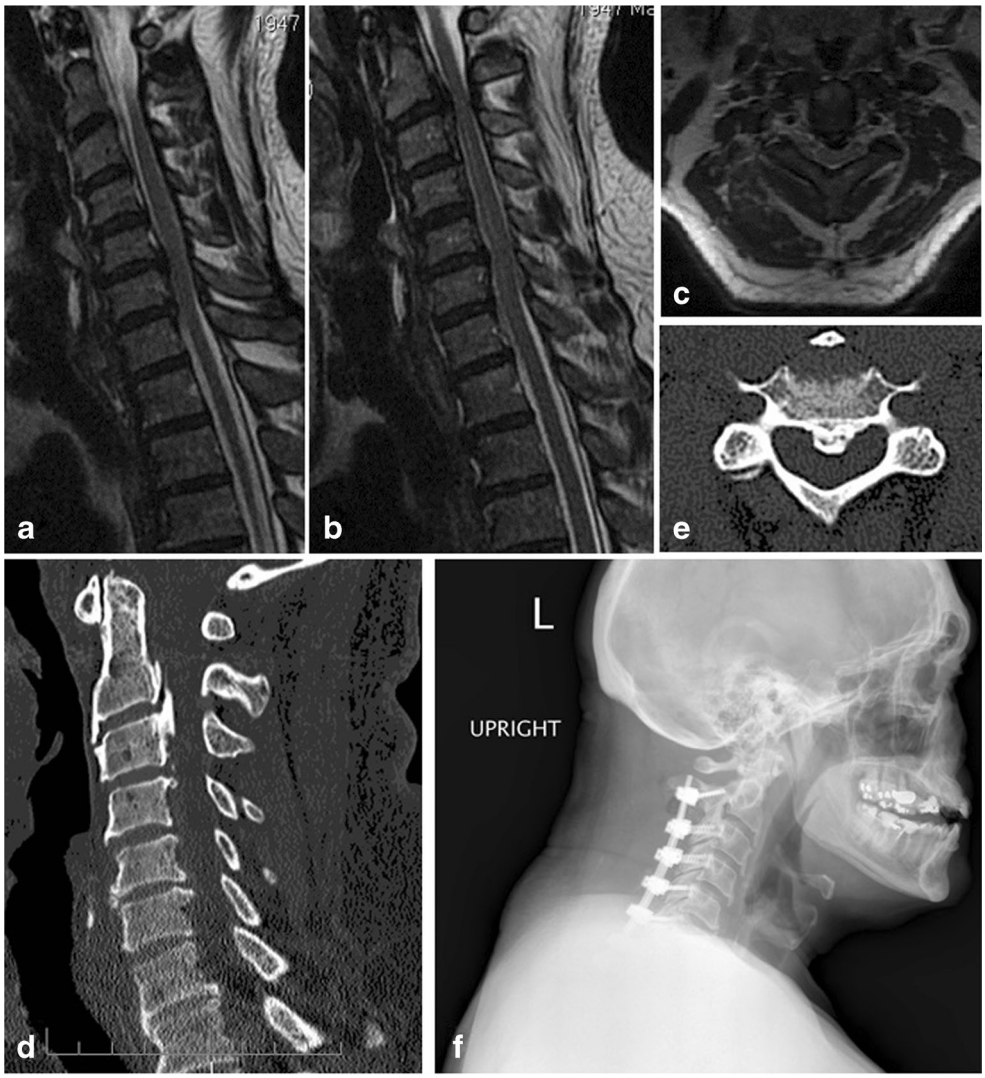

Fig. 2 A 54-year old female after a low speed motor vehicle accident presented with central cord syndrome. Sagittal MRI cuts (**a**, **b**) demonstrated multilevel cord compressions from C3–C7 and T2 hyperintensity within the spinal cord at C4/5. Axial MRI cuts at C4/5 (**c**) demonstrated severe cord compression and T2 hyperintense cord signal changes. Axial (**d**) and sagittal (**e**) demonstrated segmented OPLL from C4–C7. The patient underwent a C3–C7 posterior cervical decompression and C3–T1 posterior spinal fusion

in posterior approaches, whereas CSF leakage, implant complications, dysphagia, dysphonia were more common in anterior exposures [37].

Anterior approaches

Anterior approaches for decompression using cervical discectomies and/or corpectomies allow for direct decompression of the spinal cord by the impinging OPLL and address concomitant compressive spondylosis, followed by fusion and instrumentations of the segments involved. In cases of cervical kyphosis, the anterior approach is superior for restoring lordosis and adequate spinal canal decompression [38, 39]. While the anterior cervical approach is useful for significant canal stenosis (> 60%) due to direct decompression of the compressive OPLL, a higher rate of dural tears and limited to pathology below C2. Additionally, while anterior discectomy is a common and familiar approach to many spine surgeons, the access is largely limited to pathology occurring at the disc space and difficulty with safely resecting adherent ossification to the dura with the limited visualization.

Multiple studies have suggested patients with canal occupancy of 60% undergoing either anterior or posterior decompression for OPLL, anterior approaches resulted in superior clinical outcomes, with similar complication rates for either approach [40]. Iwasaki noted better neurologic outcomes with anterior approaches for OPLL occupying ratio of > 60% when compared with laminoplasty, although graft complications occurred in 15% and re-operation in 26% of anterior approaches [41]. Similarly, Mizuno and colleagues reported 89% excellent or good outcomes and 97% fusion rate in anterior approaches with direct removal of the ossified mass for 107 myelopathic patients [38].

Whereas historically surgeons have attempted to remove the ossified PLL, more recent techniques focus on "floating" the ossified mass, since approximately 13–15% of all OPLL lesions will have dural adhesions [6, 27]. The "floating" method is performed by resecting the overlying vertebral body and releasing the ossified PLL from its vertebral body and/or disc attachments, allowing the OPLL to "float" anteriorly into the space created by the corpectomy [42]. The anterior "floating" method requires the OPLL to be thinned to < 5 mm and a minimum of 20 mm width of decompression. The OPLL is circumferentially released from the vertebral bodies and/or discs, first at its cephalad and caudad margins followed by creation of lateral troughs in order to create a free-floating segment. Because the OPLL remains attached to the dura, this reduces the risk of dural tear [17]. Following circumferential release, the OPLL lesion will translate or "float" anteriorly away from the spinal cord posteriorly [42]. Matsuoka reported good outcomes and preserved long-term maintenance of outcomes for the anterior floating method, with 59.3% improvement in JOA scores over baseline preoperative scores out to 13 years post-operatively [43].

Complications of anterior based surgery can be a result of the surgical approach, decompression of spinal cord, or instrumented fusion. Dural tears are encountered in up to 20% of patients due to the attenuation and/or adherence of the ventral dura to the OPLL [6, 38, 41]. Primary repair with dural sealants should be attempted when possible; however, autogenous fascial or synthetic collagen grafts may be necessary with larger defects. Lumbar drainage for CSF diversion can be considered for tenuous repairs. Nerve root palsies are reported from 4%–17% of anterior approaches, most commonly in the C5 distribution [5, 6, 41, 43]. For postoperative nerve palsies resulting in significant weakness, urgent MRI should be considered to rule out epidural haematoma as well as sufficient decompression of surgical levels. If the levels appear appropriately decompressed and no epidural haematoma is present, conservative management should be undertaken [26]. Additionally, pseudarthrosis and graft migration have been reported in up to 15 and 11%, respectively [6, 38, 41]. Postoperatively, serial cervical spine X-rays should be performed in the outpatient clinic to ensure bony union and monitor for graft and instrumentation complications.

Circumferential approaches should be considered in properly selected patients at risk for complications with a single approach [44]. Anterior approaches can benefit from an adjunct posterior instrumented fusion when the anterior approach extends two vertebral levels or more to prevent graft related complications and reduce the risk of pseudarthrosis. Son and colleagues utilized circumferential cervical surgery in 12 patients for > 60% cord compression at three or more segments with mushroom or hill-shaped OPLL lesions, reporting 91.6% good or excellent results and no major surgical complications [44].

Posterior approaches

Posterior-based approaches are useful for longer segments (3 or more levels) of spinal cord compression in K-line positive patients [24]. Although laminectomy results in a 70 to 80% increase in canal volume [45], the decompression is imparted indirectly through posterior drift of the spinal cord away from OPLL lesions. Pre-operative cervical kyphotic alignment precludes posterior spinal cord drift and minimizes the decompressive effect of posterior approaches. Furthermore, while laminectomy is a procedure familiar to many surgeons and preserves cervical range of motion, patients are at postoperative risk of cervical kyphosis due to disruption of the posterior ligamentous and paraspinal muscle attachments. Lee found that the loss of cervical lordosis with laminectomy is often mild, with only 3/34 patients progressed to kyphotic alignment. Similarly, although Cho demonstrated that 92% of

patients exhibited postoperative reduction in cervical lordosis, all patients maintained their neurologic post-operative improvement [46].

The addition of posterior instrumented fusion to laminectomy halts the progression of OPLL and maintains intra-operative lordotic cervical alignment but sacrifices cervical range of motion. Chiba found OPLL progression with laminectomy without fusion in 56.5% of patients by two years, with younger patients and mixed- and continuous-type OPLL at higher risk of progression [47]. In patients with lordotic cervical alignment, posterior laminectomy, and instrumented fusion can significantly improve patients' clinical outcome scores. Chen reported a mean improvement in JOA scores of 62% at five years for laminectomy and fusion, with greater improvements in JOA scores associated with greater post-operative lordosis [48]. One of the most commonly described complications is nerve root palsy, reported in up to 12% of patients. The proposed mechanism of nerve root palsy is unclear and potentially multifactorial, either as a result of direct nerve injury or traction as the spinal cord migrates posteriorly. Chen reported an 80% complete recovery of 134 laminectomies and fusions, with ten nerve palsies and two incomplete recoveries [48] (Fig. 3).

Laminoplasty is a motion-sparing alternative to laminectomy for posterior-based decompression of the cervical spine. Laminoplasty uses either open-door or French-door techniques to hinge open the posterior elements, allowing for spinal cord drift posteriorly from the OPLL. Improvement in JOA scores after laminoplasty are reported to be between 43 and 63%, similar to laminectomy and posterior fusion and anteriorly based approaches [49]. Optimal indications for laminoplasty are patients with < 60% occupying ratios and lordotic alignment of the cervical spine. Similar to laminectomy, pre-operative kyphotic alignment is a contraindication to laminoplasty, as the kyphosis does not allow posterior drift of the spinal cord. Whereas multiple studies have suggested higher T1 slope angles to predict greater post-operative loss of cervical lordosis, the association with subsequent increased rates of cervical kyphosis is controversial [50, 51]. Multiple authors have reported the clinical outcomes of laminoplasty to not be associated with mild loss of cervical lordosis [52, 53]. Laminoplasty has been shown to improve JOA scores in patients with neutral and lordotic alignments on upright lateral X-rays [45, 54].

While laminoplasty allows for continued motion of the cervical spine, OPLL has been documented to progress in upwards of 70% of patients [55]. Factors associated with progression include younger age and mixed and continuous types of OPLL. Hori noted the risk of progression of OPLL after laminoplasty was higher in younger patients (53.9 years versus 61.9 years for nonprogression) and OPLL at C3 level [56]. Progression was most frequently noted at C2–4, with most progression seen at C2 (42% of patients) [57].

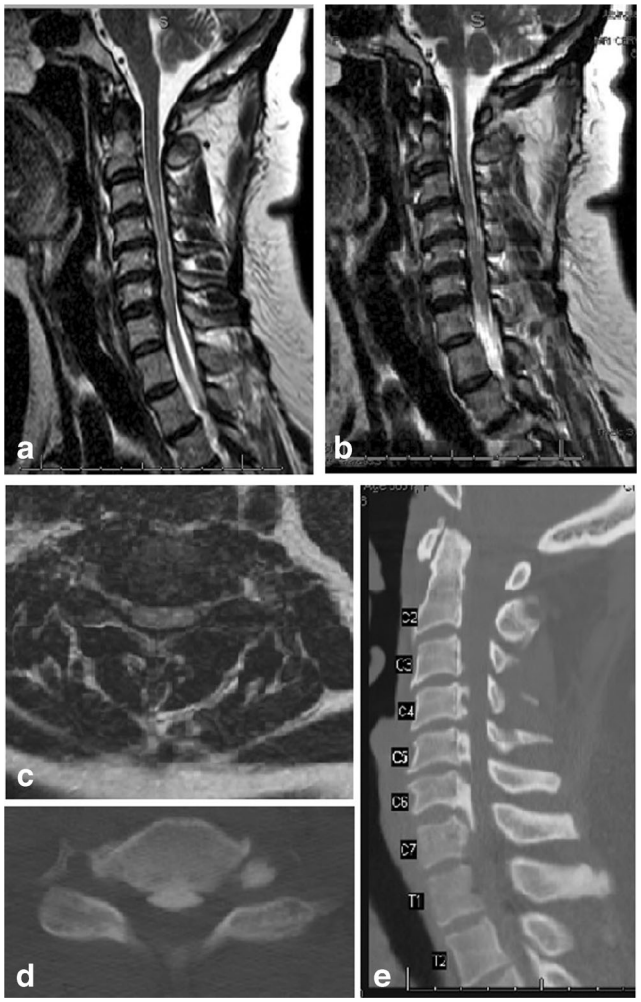

Fig. 3 A 65-year old male presented to clinic with myelopathy. Selected sagittal (**a**, **b**) and axial (**c**) demonstrated cord compression at C2/3, C5/6, and C6/7. Due to retrovertebral cord compression from hypointense masses on T2 imaging, a CT was obtained to evaluate for OPLL. Selected sagittal (**d**) and axial (**e**) cuts demonstrate OPLL at the sites of cord compression. A C2–C7 posterior cervical decompression and C2–T1 instrumented fusion was performed (**f**)

Due to the retained motion with laminoplasty, there is concern that despite K-line positive findings on upright lateral X-rays, cord compression can still result from neck flexion. Takeuchi reported patients with K-line positive upright lateral X-rays but K-line negative on flexion views had significantly lower JOA scores than patients with K-line positive flexion X-rays [58]. Furthermore, in the K-line negative group, 26% (6/23) patient had worsening of JOA scores post-operatively, with four of the six patients having beak-shaped, circumscribed OPLL [58]. Similarly, Maruo found cervical spine pre-operative hypermobility to be a poor prognostic factor for laminoplasty, noting pre-operative C2–7 ROM was significantly greater in patients with poor clinical outcomes (23.1 degrees versus 14.4 for good clinical outcomes, $p = 0.009$) [53].

Complications of laminoplasty include intra-operative spinal cord injury, nerve root injury via direct injury or traction, closure

of lamina, fracture of laminoplasty hinge, progression of OPLL, post-operative kyphosis, and axial neck pain [49]. Recent modifications, such as avoiding laminoplasty at C3 and C7, have led to a decrease in post-laminoplasty neck pain [59]. Patient selection for laminoplasty is critical, as improved outcomes are seen with canal occupancy of < 60%, shorter duration of symptoms (< 1 year), and minimal cord signal change on pre-operative MRI imaging [49]. Sakai reported patients undergoing laminoplasty with < 50% OPLL canal occupancy had equivalent outcomes to anterior procedures with significantly less complications (0% versus 23%, respectively) [39].

Conclusion

OPLL is a rare but challenging cervical pathology found more commonly in Asian patients and can potentially result in spinal cord compression from ossified PLL masses. While asymptomatic patients may be managed conservatively, patients with radiculopathy or myelopathy should be considered for surgical decompression. Multiple studies have demonstrated the morphology and size of the OPLL as well as the cervical alignment have significant implications for surgical approach and technique. Anterior approaches are superior to posterior techniques for > 60% OPLL canal occupancy with cervical kyphosis. Surgeons should be prepared for dural ossification and/or adherence if removal of OPLL is performed; however, anterior "floating" techniques have reduced the need to resect OPLL to achieve decompression. While laminoplasty retains cervical range of motion compared with laminectomy with instrumented fusion, patients may lose lordotic cervical posture, have continued progression of OPLL, and note increased neck pain.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Ehara S, Shimamura T, Nakamura R, Yamazaki K (1998) Paravertebral ligamentous ossification: DISH, OPLL and OLF. Eur J Radiol 27:196–205
2. Matsunaga S, Sakou T (2012) Ossification of the posterior longitudinal ligament of the cervical spine: etiology and natural history. Spine 37:E309–E314. https://doi.org/10.1097/BRS.0b013e318241ad33
3. Ohtsuka K, Terayama K, Yanagihara M, Wada K, Kasuga K, Machida T, Furukawa K (1986) An epidemiological survey on ossification of ligaments in the cervical and thoracic spine in individuals over 50 years of age. Nihon Seikeigeka Gakkai Zasshi 60:1087–1098
4. McAfee PC, Regan JJ, Bohlman HH (1987) Cervical cord compression from ossification of the posterior longitudinal ligament in non-orientals. J Bone Joint Surgery British Volume 69:569–575
5. Epstein NE (1994) The surgical management of ossification of the posterior longitudinal ligament in 43 north Americans. Spine 19:664–672
6. Belanger TA, Roh JS, Hanks SE, Kang JD, Emery SE, Bohlman HH (2005) Ossification of the posterior longitudinal ligament. Results of anterior cervical decompression and arthrodesis in sixty-one North American patients. J Bone Joint Surgery Am Volume 87:610–615. https://doi.org/10.2106/jbjs.c.01711
7. Maeda S, Koga H, Matsunaga S, Numasawa T, Ikari K, Furushima K, Harata S, Takeda J, Sakou T, Komiya S, Inoue I (2001) Gender-specific haplotype association of collagen alpha2 (XI) gene in ossification of the posterior longitudinal ligament of the spine. J Hum Genet 46:1–4. https://doi.org/10.1007/s100380170117
8. Ren Y, Liu ZZ, Feng J, Wan H, Li JH, Wang H, Lin X (2012) Association of a BMP9 haplotype with ossification of the posterior longitudinal ligament (OPLL) in a Chinese population. PLoS One 7:e40587. https://doi.org/10.1371/journal.pone.0040587
9. Song J, Mizuno J, Hashizume Y, Nakagawa H (2006) Immunohistochemistry of symptomatic hypertrophy of the posterior longitudinal ligament with special reference to ligamentous ossification. Spinal Cord 44:576–581. https://doi.org/10.1038/sj.sc.3101881
10. Tanaka T, Ikari K, Furushima K, Okada A, Tanaka H, Furukawa K, Yoshida K, Ikeda T, Ikegawa S, Hunt SC, Takeda J, Toh S, Harata S, Nakajima T, Inoue I (2003) Genomewide linkage and linkage disequilibrium analyses identify COL6A1, on chromosome 21, as the locus for ossification of the posterior longitudinal ligament of the spine. Am J Hum Genet 73:812–822
11. Ikegawa S (2014) Genetics of ossification of the posterior longitudinal ligament of the spine: a mini review. J Bone Metab 21:127–132. https://doi.org/10.11005/jbm.2014.21.2.127
12. Kalb S, Martirosyan NL, Perez-Orribo L, Kalani MY, Theodore N (2011) Analysis of demographics, risk factors, clinical presentation, and surgical treatment modalities for the ossified posterior longitudinal ligament. Neurosurg Focus 30:E11. https://doi.org/10.3171/2010.12.FOCUS10265
13. Li H, Jiang LS, Dai LY (2007) Hormones and growth factors in the pathogenesis of spinal ligament ossification. Eur Spine J 16:1075–1084. https://doi.org/10.1007/s00586-007-0356-4
14. Saetia K, Cho D, Lee S, Kim DH, Kim SD (2011) Ossification of the posterior longitudinal ligament: a review. Neurosurgical focus, 30:E1. DOI https://doi.org/10.3171/2010.11.focus10276. https://doi.org/10.3171/2011.2.FOC-SpinePeriphSectionabstracts
15. Terayama K (1989) Genetic studies on ossification of the posterior longitudinal ligament of the spine. Spine (Phila Pa 1976) 14:1184–1191
16. Matsunaga S, Yamaguchi M, Hayashi K, Sakou T (1999) Genetic analysis of ossification of the posterior longitudinal ligament. Spine (Phila Pa 1976) 24:937–938 discussion 939
17. Abiola R, Rubery P, Mesfin A (2016) Ossification of the posterior longitudinal ligament: etiology, diagnosis, and outcomes of nonoperative and operative management. Global Spine J 6:195–204. https://doi.org/10.1055/s-0035-1556580
18. Okazaki T, Takuwa Y, Yamamoto M, Matsumoto T, Igarashi T, Kurokawa T, Ogata E (1984) Ossification of the paravertebral ligaments: a frequent complication of hypoparathyroidism. Metabolism 33:710–713
19. Chang H, Song KJ, Kim HY, Choi BW (2012) Factors related to the development of myelopathy in patients with cervical ossification of the posterior longitudinal ligament. J Bone Joint Surgery British Volume 94:946–949. https://doi.org/10.1302/0301-620x.94b7.29018

20. Matsunaga S, Komiya S, Toyama Y (2015) Risk factors for development of myelopathy in patients with cervical spondylotic cord compression. European Spine J: Official Publication European Spine Soc, European Spinal Deformity Soc, European Section Cervical Spine Res Soc 24(Suppl 2):142–149. https://doi.org/10.1007/s00586-013-2839-9
21. Matsunaga S, Kukita M, Hayashi K, Shinkura R, Koriyama C, Sakou T, Komiya S (2002) Pathogenesis of myelopathy in patients with ossification of the posterior longitudinal ligament. J Neurosurg 96:168–172
22. Matsunaga S, Nakamura K, Seichi A, Yokoyama T, Toh S, Ichimura S, Satomi K, Endo K, Yamamoto K, Kato Y, Ito T, Tokuhashi Y, Uchida K, Baba H, Kawahara N, Tomita K, Matsuyama Y, Ishiguro N, Iwasaki M, Yoshikawa H, Yonenobu K, Kawakami M, Yoshida M, Inoue S, Tani T, Kaneko K, Taguchi T, Imakiire T, Komiya S (2008) Radiographic predictors for the development of myelopathy in patients with ossification of the posterior longitudinal ligament: a multicenter cohort study. Spine 33:2648–2650. https://doi.org/10.1097/BRS.0b013e31817f988c
23. Tsuyama N (1984) Ossification of the posterior longitudinal ligament of the spine. Clinical orthopaedics and related research:71–84
24. Fujiyoshi T, Yamazaki M, Kawabe J, Endo T, Furuya T, Koda M, Okawa A, Takahashi K, Konishi H (2008) A new concept for making decisions regarding the surgical approach for cervical ossification of the posterior longitudinal ligament: the K-line. Spine 33:E990–E993. https://doi.org/10.1097/BRS.0b013e318188b300
25. Chang H, Kong CG, Won HY, Kim JH, Park JB (2010) Inter- and intra-observer variability of a cervical OPLL classification using reconstructed CT images. Clinics Orthopedic Surgery 2:8–12. https://doi.org/10.4055/cios.2010.2.1.8
26. An HS, Al-Shihabi L, Kurd M (2014) Surgical treatment for ossification of the posterior longitudinal ligament in the cervical spine. J Am Academy Orthopaedic Surgeons 22:420–429. https://doi.org/10.5435/jaaos-22-07-420
27. Mizuno J, Nakagawa H, Matsuo N, Song J (2005) Dural ossification associated with cervical ossification of the posterior longitudinal ligament: frequency of dural ossification and comparison of neuroimaging modalities in ability to identify the disease. J Neurosurgery Spine 2:425–430. https://doi.org/10.3171/spi.2005.2.4.0425
28. Min JH, Jang JS, Lee SH (2007) Significance of the double- and single-layer signs in the ossification of the posterior longitudinal ligament of the thoracic spine. Neurosurgery 61:118–121; discussion 121–112. https://doi.org/10.1227/01.neu.0000279731.21145.45
29. Koyanagi I, Iwasaki Y, Hida K, Imamura H, Abe H (1998) Magnetic resonance imaging findings in ossification of the posterior longitudinal ligament of the cervical spine. J Neurosurg 88:247–254. https://doi.org/10.3171/jns.1998.88.2.0247
30. Yagi M, Ninomiya K, Kihara M, Horiuchi Y (2010) Long-term surgical outcome and risk factors in patients with cervical myelopathy and a change in signal intensity of intramedullary spinal cord on magnetic resonance imaging. J Neurosurgery Spine 12:59–65. https://doi.org/10.3171/2009.5.spine08940
31. Matsuyama Y, Kawakami N, Yanase M, Yoshihara H, Ishiguro N, Kameyama T, Hashizume Y (2004) Cervical myelopathy due to OPLL: clinical evaluation by MRI and intraoperative spinal sonography. J Spinal Disord Tech 17:401–404
32. Pham MH, Attenello FJ, Lucas J, He S, Stapleton CJ, Hsieh PC (2011) Conservative management of ossification of the posterior longitudinal ligament. A review. Neurosurg Focus 30:E2. https://doi.org/10.3171/2011.1.focus10273
33. Yonenobu K (2012) Is surgery indicated for asymptomatic or mildly myelopathic patients with significant ossification of the posterior longitudinal ligament? Spine 37:E315–E317. https://doi.org/10.1097/BRS.0b013e318239ccbd
34. Wu JC, Chen YC, Liu L, Huang WC, Chen TJ, Lo SS, Thien PF, Cheng H (2012) Conservatively treated ossification of the posterior longitudinal ligament increases the risk of spinal cord injury: a nationwide cohort study. J Neurotrauma 29:462–468. https://doi.org/10.1089/neu.2011.2095
35. Chen LF, Tu TH, Chen YC, Wu JC, Chang PY, Liu L, Huang WC, Lo SS, Cheng H (2016) Risk of spinal cord injury in patients with cervical spondylotic myelopathy and ossification of posterior longitudinal ligament: a national cohort study. Neurosurg Focus 40:E4. https://doi.org/10.3171/2016.3.focus1663
36. Kato Y, Iwasaki M, Fuji T, Yonenobu K, Ochi T (1998) Long-term follow-up results of laminectomy for cervical myelopathy caused by ossification of the posterior longitudinal ligament. J Neurosurg 89:217–223. https://doi.org/10.3171/jns.1998.89.2.0217
37. Li H, Dai LY (2011) A systematic review of complications in cervical spine surgery for ossification of the posterior longitudinal ligament. Spine J: Official J North Am Spine Soc 11:1049–1057. https://doi.org/10.1016/j.spinee.2011.09.008
38. Mizuno J, Nakagawa H (2001) Outcome analysis of anterior decompressive surgery and fusion for cervical ossification of the posterior longitudinal ligament: report of 107 cases and review of the literature. Neurosurg Focus 10:E6
39. Sakai K, Okawa A, Takahashi M, Arai Y, Kawabata S, Enomoto M, Kato T, Hirai T, Shinomiya K (2012) Five-year follow-up evaluation of surgical treatment for cervical myelopathy caused by ossification of the posterior longitudinal ligament: a prospective comparative study of anterior decompression and fusion with floating method versus laminoplasty. Spine 37:367–376. https://doi.org/10.1097/BRS.0b013e31821f4a51
40. Fujimori T, Iwasaki M, Okuda S, Takenaka S, Kashii M, Kaito T, Yoshikawa H (2014) Long-term results of cervical myelopathy due to ossification of the posterior longitudinal ligament with an occupying ratio of 60% or more. Spine 39:58–67. https://doi.org/10.1097/brs.0000000000000054
41. Iwasaki M, Okuda S, Miyauchi A, Sakaura H, Mukai Y, Yonenobu K, Yoshikawa H (2007) Surgical strategy for cervical myelopathy due to ossification of the posterior longitudinal ligament: part 2: advantages of anterior decompression and fusion over laminoplasty. Spine 32:654–660. https://doi.org/10.1097/01.brs.0000257566.91177.cb
42. Yamaura I, Kurosa Y, Matuoka T, Shindo S (1999) Anterior floating method for cervical myelopathy caused by ossification of the posterior longitudinal ligament. Clinical Orthopaedics and Related Research:27–34
43. Matsuoka T, Yamaura I, Kurosa Y, Nakai O, Shindo S, Shinomiya K (2001) Long-term results of the anterior floating method for cervical myelopathy caused by ossification of the posterior longitudinal ligament. Spine 26:241–248
44. Son S, Lee SG, Yoo CJ, Park CW, Kim WK (2010) Single stage circumferential cervical surgery (selective anterior cervical corpectomy with fusion and laminoplasty) for multilevel ossification of the posterior longitudinal ligament with spinal cord ischemia on MRI. J Korean Neurosurgical Soc 48:335–341. https://doi.org/10.3340/jkns.2010.48.4.335
45. Manzano GR, Casella G, Wang MY, Vanni S, Levi AD (2012) A prospective, randomized trial comparing expansile cervical laminoplasty and cervical laminectomy and fusion for multilevel cervical myelopathy. Neurosurgery 70:264–277. https://doi.org/10.1227/NEU.0b013e3182305669
46. Cho WS, Chung CK, Jahng TA, Kim HJ (2008) Post-laminectomy kyphosis in patients with cervical ossification of the posterior longitudinal ligament: does it cause neurological deterioration? J Korean Neurosurgical Soc 43:259–264. https://doi.org/10.3340/jkns.2008.43.6.259
47. Chiba K, Yamamoto I, Hirabayashi H, Iwasaki M, Goto H, Yonenobu K, Toyama Y (2005) Multicenter study investigating

the postoperative progression of ossification of the posterior longitudinal ligament in the cervical spine: a new computer-assisted measurement. J Neurosurgery Spine 3:17–23. https://doi.org/10.3171/spi.2005.3.1.0017

48. Chen Y, Guo Y, Chen D, Wang X, Lu X, Yuan W (2009) Long-term outcome of laminectomy and instrumented fusion for cervical ossification of the posterior longitudinal ligament. Int Orthop 33:1075–1080. https://doi.org/10.1007/s00264-008-0609-9
49. Matsumoto M, Chiba K, Toyama Y (2012) Surgical treatment of ossification of the posterior longitudinal ligament and its outcomes: posterior surgery by laminoplasty. Spine 37:E303–E308. https://doi.org/10.1097/BRS.0b013e318239cca0
50. Kim B, Yoon DH, Ha Y, Yi S, Shin DA, Lee CK, Lee N, Kim KN (2016) Relationship between T1 slope and loss of lordosis after laminoplasty in patients with cervical ossification of the posterior longitudinal ligament. Spine J: Official J North Am Spine Soc 16:219–225. https://doi.org/10.1016/j.spinee.2015.10.042
51. Kim TH, Lee SY, Kim YC, Park MS, Kim SW (2013) T1 slope as a predictor of kyphotic alignment change after laminoplasty in patients with cervical myelopathy. Spine 38:E992–E997. https://doi.org/10.1097/BRS.0b013e3182972e1b
52. Lee CK, Shin DA, Yi S, Kim KN, Shin HC, Yoon DH, Ha Y (2016) Correlation between cervical spine sagittal alignment and clinical outcome after cervical laminoplasty for ossification of the posterior longitudinal ligament. J Neurosurgery Spine 24:100–107. https://doi.org/10.3171/2015.4.spine141004
53. Maruo K, Moriyama T, Tachibana T, Inoue S, Arizumi F, Daimon T, Yoshiya S (2014) The impact of dynamic factors on surgical outcomes after double-door laminoplasty for ossification of the posterior longitudinal ligament of the cervical spine. J Neurosurgery Spine 21:938–943. https://doi.org/10.3171/2014.8.spine131197
54. Liu X, Chen Y, Yang H, Li T, Xu B, Chen D (2017) Expansive open-door laminoplasty versus laminectomy and instrumented fusion for cases with cervical ossification of the posterior longitudinal ligament and straight lordosis. European Spine J: Official Publication European Spine Soc European Spinal Deformity Soc, European Section Cervical Spine Res Soc 26:1173–1180. https://doi.org/10.1007/s00586-016-4912-7
55. Iwasaki M, Kawaguchi Y, Kimura T, Yonenobu K (2002) Long-term results of expansive laminoplasty for ossification of the posterior longitudinal ligament of the cervical spine: more than 10 years follow up. J Neurosurg 96:180–189
56. Hori T, Kawaguchi Y, Kimura T (2006) How does the ossification area of the posterior longitudinal ligament progress after cervical laminoplasty? Spine 31:2807–2812. https://doi.org/10.1097/01.brs.0000245870.97231.65
57. Hori T, Kawaguchi Y, Kimura T (2007) How does the ossification area of the posterior longitudinal ligament thicken following cervical laminoplasty? Spine 32:E551–E556. https://doi.org/10.1097/BRS.0b013e31814614f3
58. Takeuchi K, Yokoyama T, Numasawa T, Yamasaki Y, Kudo H, Itabashi T, Chin S, Wada KI (2016) K-line (−) in the neck-flexed position in patients with ossification of the posterior longitudinal ligament is a risk factor for poor clinical outcome after cervical laminoplasty. Spine 41:1891–1895. https://doi.org/10.1097/brs.0000000000001660
59. Lee GW, Cho CW, Shin JH, Ahn MW (2017) Which technique is better option for C3 segment in multilevel open-door laminoplasty of the cervical spine?: laminectomy versus Laminoplasty. Spine 42:E833–e840. https://doi.org/10.1097/brs.0000000000001974