

Ossification of the Posterior Longitudinal Ligament (OPLL) in the Cervical Spine: Past, Present, and Future

Chang-Hyun Lee*

Department of Neurosurgery, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Republic of Korea

***Corresponding Author:** Chang-Hyun Lee, Assistant Professor, Department of Neurosurgery, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Gyeonggi, Republic of Korea.

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Collagen and elastin fibers are densely concentrated centrally in the posterior longitudinal ligament, beginning at the clivus and extending to the sacrum [1]. This ligament is widest at the disc spaces and narrowest at the mid-vertebral levels. It is approximately 1 to 2 mm thick centrally and thins out laterally [1]. Ossification of the posterior longitudinal ligament (OPLL) is an ectopic ossification that can cause significant amount of chronic pressure on the spinal cord and result in myelopathy [2,3]. In the past, OPLL was regarded as an East Asian disease due to the low prevalence of OPLL in the North American Caucasian population, which has been reported to be as low as 0.12% [4]. However, more recently, Epstein [1] has reported that as many as 25% of North American and Japanese patients presenting with cervical myelopathy have some evidence of OPLL.

Classical probable mechanism of OPLL

Although the origins and pathophysiological mechanisms of OPLL are not well understood, the ossification process in OPLL is thought to occur through the endochondral mechanism, but the involvement of multiple etiologic factors in the development of OPLL has been suggested, including genetic factors, dietary habits, metabolic abnormalities, some local factors, and spinal instability [5,6]. These pieces of clinical evidence support the hypothesis that the mechanical stress that acts on the posterior ligaments acts an important role in the progression of OPLL [5]. Previous papers reported that OPLL may progress by any of the following mechanisms: (A) direct stimulation of ligaments by surgical invasion, (B) mechanical stress induced by postoperative structural changes, (C) spontaneous increases in ossification, and (D) ossification caused by postoperative instability [7,8].

New era of OPLL research: genomic approach

Over the past several decades, however, a variety of genetic investigations, including pedigree studies, twin studies, and detailed molecular analyses, have documented many genes or gene loci of interest involved in mediating the molecular and genetic pathobiology of OPLL [9]. As OPLL is believed to arise because of endochondral bone formation, each of the aforementioned genetic targets have been shown to critically regulate a crucial step in chondrogenesis, osteogenesis, or bone mineralization [9]. Two single nucleotide polymorphisms related to the collagen 6A1 gene (*COL6A1*/Intron 32(-29)) and the collagen 11A2 gene (*COL11A2*/ Intron 6(-4)) have been associated with an approximate 2-fold increased risk of developing OPLL in multiple studies and may be associated with its development [9,10]. Several genes and proteins have emerged over the years as promising targets for future investigation and intervention: *NPPS*, *BMP-2* and *TGFβ* [9].

OPLL can be a progressive and catastrophic disease of spinal cord compression. Ossification is not abnormal protein like a cancer, but a normal tissue. So, key genomic aberrations of OPLL may lie on the regulatory genes in intron rather than protein coding genes in exon. Genomic analysis about intron is limited because of huge amount data and few knowledges to interpret. Advancement of whole genome sequencing and epigenomic studies may lead to find out pathophysiology and treatment of OPLL.

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