INTRODUCTION:
Lumbar spinal canal stenosis is very common degenerative spinal disorder among the elderly population. One of the main causes of the disorder is hypertrophy of the ligamentum flavum (LF). The pathomechanism of the LF hypertrophy is still unknown; despite numerous investigations have been reported. We have previously postulated based on histological analysis that the LF hypertrophy would be caused by the accumulation of scar tissues (fibrosis) in the ligament, especially at the dorsal aspect (1,2,3). In this study, we have evaluated the LF hypertrophy with reference to the pathologic similarity to the hypertrophic scar formation during the cutaneous wound healing process.

METHODS:

Histological analysis
The hypertrophied LF tissue was collected en bloc during posterior decompression surgery for patients with the lumbar spinal canal stenosis. They were 4 males and 1 female. The mean age was 62.3 y.o. (range: 56 – 71). The LF tissue was cut through the sagittal plane, and the plane was subjected to be stained. Three staining techniques were used for evaluation; hematoxylin and eosin (H&E), elastica van Gieson (EVG) stain, and Masson’s Trichrome (MT) stain. To understand the scarring and fibrosis of the LF, MT staining was used. EVG was used to evaluate the state of the elastic fibers.

Immunohistochemistry
For the immunohistochemical, the production of type I and type III collagen was evaluated. Myofibroblast was reported to play an important role for the development of the hypertrophic scar formation, and the α-smooth muscle actin (α-SMA) was reported to be a marker of the myofibroblast. Thus, the production of the α-SMA was also investigated using an immunohistochemical approach.

RESULTS:

Histological analysis
The major extracellular matrix (ECM) of LF tissue is elastic fiber. Thus, most of the LF tissue was strongly stained in black on EVG. In the hypertrophied LF, some area did not show such staining, indicating loss of elastic fiber. Loss of elastic fiber is pronounced at the dorsal aspect of the LF rather than dural aspect. The area showing less elastic fiber was stained in green on MT, indicating the site being scarring (fibrosis). The scarring is pronounced in the dorsal half of the LF rather than the dural side. The mean fibrosis index (0 to 4) was 1.7 at the dural aspect and 3.2 at the dorsal aspect. The difference was significant.

Immunohistochemistry
The ECM of the fibrosis was positively stained by type I collagen. The staining of the type III collagen showed very similar trend to that of type I collagen; however, the staining of type III was stronger and wider than that of type I collagen. In terms of the immune-histochemistry for α-SMA, the most endothelial cells of the vessels were positively stained. Additionally, the fibroblast-like cells in the scarring site were positively stained, indicating the cell to be the myofibroblast. In the dural aspect, only few cells were positive by SMA. However, there were many α-SMA positive cells.

DISCUSSION:
Hypertrophy of LF is one of the main pathological factors causing narrowing neural canal in patients with the lumbar spinal canal stenosis. We hypothesized based on the previous investigations (1,2,3) that the hypertrophy of LF may be the similar condition of the hypertrophic scar which appears during the cutaneous wound healing. Thus, we have conducted the current investigation.

REFERENCES:

The dorsal aspect of the hypertrophied LF tissue showed dense scarring, while the scarring is minimal at the dural aspect even if any. Ogawa (4) stated that one of the risk factors of the appearance of hypertrophic scar is excessive mechanical stress (stretching force) during the cutaneous healing process. Sairyo et al. (1) mathematically calculated the mechanical stress in LF, and clarified that as comparing to the dural aspect dorsal aspect of LF was having 5-fold mechanical stress during the lumbar motion. It seems that over-stretching of the dorsal aspect in LF may relate to the thick scarring in the LF like hypertrophic scars.

It has been reported that type III collagen was positively stained during the wound healing process; then converting to the type I collagen, so that the scar would become maturation (5). In the current study, we have shown that type III collagen was positively, strongly and widely stained in the hypertrophied LF tissue, especially at the site showing scarring. The staining was stronger that the staining of the type I collagen. This histological finding is also compatible of the cutaneous hypertrophic scars.

During the wound healing process, myofibroblast is reported to also play an important role, especially at the immature scar phase. As the maturation of the scar would progress, myofibroblast would disappear. Thus, the continuous appearance of the myofibroblast is the marker of the continuous production of the scar, indicating hypertrophic scar. The α-SMA, which is the marker of the myofibroblast, was stained in the hypertrophied LF tissue, especially at the dural aspect. Thus, it supports that scar accumulation continuously occur in the hypertrophied LF. This is also similar pathology to hypertrophic scars.

Based on the current histological analyses, we can conclude that the pathomechanism of the LF hypertrophy in patient with LSCS is similar to that of hypertrophic scar of the skin. The condition of hypertrophic scars is called as fibroproliferative disorder (FPD). Thus, it seems that LF hypertrophy would also be the FPD in the ligament.