Hernia (2011) 15:53–58
DOI 10.1007/s10029-010-0735-3

ORIGINAL ARTICLE

Nerve degeneration in inguinal hernia specimens

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Received: 8 June 2010 / Accepted: 17 September 2010 / Published online: 17 October 2010

Abstract
Background The histological study of the herniated inguinal area is rare in the literature. This report is focused on the detection of structural changes of the nerves within tissues bordering the inguinal hernia of cadavers. Their physiopathological consequences are hypothesized.
Materials and methods Primary inguinal hernia was diagnosed in 30 fresh cadavers. Tissue specimens from the inguinal region close to and around the hernia opening were excised for histological examination. A control of the data was achieved through tissue samples excised from equivalent sites of the inguinal region in 15 cadavers without hernia.
Results The detected nerves in the inguinal area demonstrated pathological changes such as fibrotic degeneration, atrophy, and fatty dystrophy of the axons. The thickening of the perineural sheath was constantly seen. These findings were consistently present, independent of the hernia type.
Conclusions The detected nerve alterations lead us to imagine a worsening, or even the cessation, of the nervous impulse to the muscles, leading to atrophy and weakening of the abdominal wall. This could represent one of the multifactorial causes of hernia genesis.

Keywords Inguinal hernia · Etiology · Nerve degeneration · Atrophy · Fibrosis

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Introduction

To date, the precise mechanism of how an inguinal hernia forms is still not clear. Several authors have eluded to the mechanisms [1–3], but a single unified answer has not yet been agreed upon. There have been many studies looking at the molecular biology of collagen formation [4–8] and other studies describing the inactivation or blocking of shuttering mechanisms at the anatomical level [9], but little work has been conducted in the area of histology for inguinal hernia. In a series of ongoing experiments, the authors are looking for histological anomalies to help fill the knowledge gap between the molecular biology and the gross pathological anatomy with regard to hernia genesis. In these studies, the authors have looked at the histological findings with regard to muscles, connective tissue, vascular structures, and nerves. The study series has been performed in both cadavers and clinical patients. In this paper, the authors report the findings from their examinations of the nervous structures in tissues surrounding inguinal hernia from male cadavers.

Materials and methods

Forty-five fresh male cadavers were used for the study. Thirty cadavers were identified to have inguinal hernias and 15 without hernia were used as controls. The authors identified 11 of the hernia cadavers with indirect inguinal hernia type 1 according to Nyhus, eight with indirect inguinal hernia type 2, six direct inguinal hernia type 3a, and five other cadavers had direct inguinal hernia type 3b. The authors chose only primary hernias that had never been operated: the aim was to eliminate false artifacts arising from surgical intervention. The mean age of the sample population was 68 years, with a range of between 45 and 82 years.

Tissue samples were excised from the cadavers following a strict protocol to ensure that samples could be matched for anatomical position between hernia types, within hernia types, and with controls. The need to hit the same anatomical area with and without the same pathological landmarks was a challenge. The authors devised the following protocol to achieve this.

In subjects with hernia, the defect was used as the primary landmark (Fig. 1). Bisecting the hernia defect with a vertical line, a central point of the lower border was designated the starting point. From there, a line was drawn at 45° to the right of vertical, outwards until the upper border of the defect was reached. Distances along this line of 0.5, 1.5, and 2.5 cm away from the border were measured and a full-thickness biopsy of dimensions 0.5 cm × 0.5 cm was taken at each point.

The procedure was repeated at 45° to the left of the vertical; again, a line was drawn along this angle and then measurements were taken along this line, above the hernia border at 0.5, 1.5, and 2.5 cm, at which point biopsies were taken. This procedure was performed in both direct and indirect hernias.

The control group consisted of 15 autopsied male subjects without hernia, with a mean age of 65 years and ranging between 48 and 79 years.

Again, tissue samples were biopsied from the inguinal area. In order to hit similar anatomical areas for comparisons in the absence of a hernia as a key landmark, the following two protocols were followed.

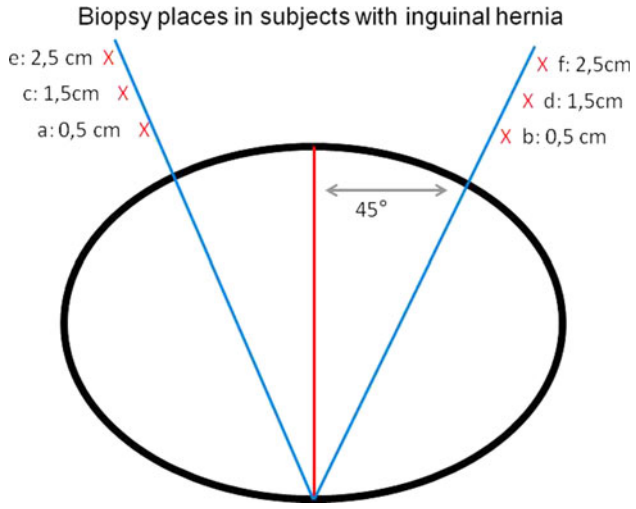

Fig. 1 Biopsy locations in subjects with inguinal hernia. The *black ring* indicates the internal inguinal ring in the case of indirect inguinal hernia and the hernia opening in the case of direct inguinal hernia. A *red line* connects the lowest and the highest point of the hernia opening. Starting from the lowest point, a 45° inclined *blue line* transverses the figure on the right and on the left. Six excisions (*X*) are made: (*a* and *b*) 0.5 cm above the junction of both 45° angled lines, (*c* and *d*) 1.5 cm above the junction of both 45° angled lines, (*e* and *f*) 2.5 cm above the junction of both 45° angled lines

For indirect hernia control, the procedure described above for biopsies with indirect hernia was replicated using the internal ring as the landmark instead of an actual indirect hernia. However, for direct hernia, the sampling technique was modified to mimic the hernia defects of the direct hernia being displaced from the inguinal ring. To make a control sample for direct hernia, the authors used the inguinal ligament as a key landmark. Parallel to this ligament and above it were drawn three lines at distances of 0.5, 1.5, and 2.5 cm. Biopsy samples were taken every 0.5 cm along the three lines, starting 0.5 cm medial from the epigastric vessels to 0.5 cm from the lateral border of the rectus muscle. This achieved an acceptable histological mapping of the entire fossa inguinalis media. Although not a perfect solution, the authors felt that this repeatable measurement method of direct and indirect hernia, and direct and indirect controls gave a meaningful comparison of tissue samples from the same anatomical areas in both subjects and controls. All tissue specimens were biopsied within 24–48 h of death. All tissue specimens were immediately fixed in 10% neutral buffered formalin for at least 12 h. Following routine tissue processing, sections were cut at 4–6 mm and stained with NSE and hematoxylin-eosin. The samples were subjected to histological study.

Results

The excised tissue from the hernia border demonstrated multiple noteworthy histological changes when compared to controls.

As a general observation, independent of the excision site, specimens from cadavers with both direct and indirect hernia demonstrated a constant fibrohyaline degeneration of the myocytes. This was often surrounded by fibroadipose substitution of the muscle fibers (Figs. 2, 3, 4, 5, and 6). There was clear evidence of inflammatory infiltration composed of lymphohistiocytic and plasmacellular elements (Fig. 7). Furthermore, changes of the vascular structures such as a venous congestion, thickening, and sub-occlusion of the arterial walls due to medial hyperplasia were also detected (Figs. 2, 3, and 4).

With specific regard to this study, several motor nerve endings were detected between the altered myocytes. The nervous structures clearly demonstrated fibrotic degeneration and manifest atrophy, as well as focal fatty dystrophy of the axons (Figs. 2, 3, and 4). The thickening of the perineural sheath was frequently seen (Figs. 2, 3, 5, and 6). The described alterations were constantly detected independent of the hernia type (direct or indirect) and biopsy site. In one specific sample, excised at a distance of 1.5 cm from the indirect hernia opening, the detection of a wallerian degeneration of the axons was seen (Fig. 8). Conversely, in the

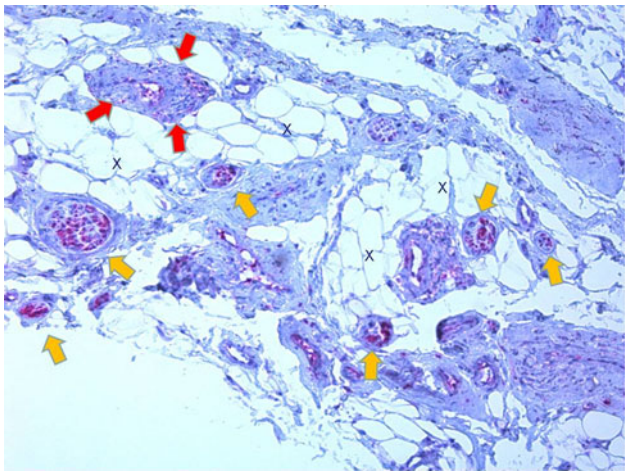

Fig. 2 Biopsy specimen excised 1.5 cm from the border of direct hernia Nyhus type 1. Wide-ranging fatty substitution of the muscle fibers (*X*). Many small nervous trunks showing extensive dystrophic degeneration and fibrotic thickening of the myelin sheath (*yellow arrows*). Arterial sub-occlusion due to medial hyperplasia (*red arrows*). NSE ×2.5

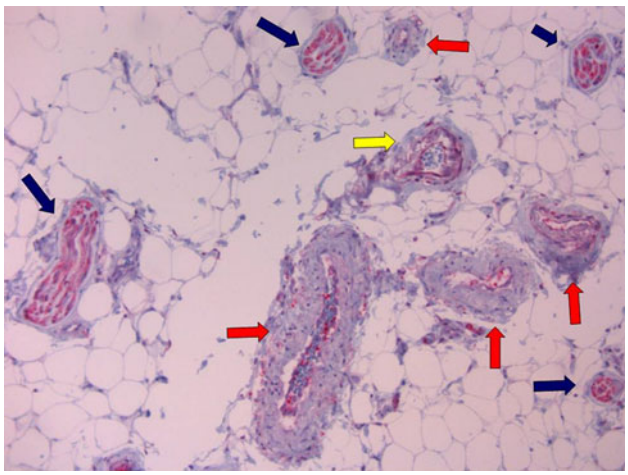

Fig. 3 Biopsy specimen excised 0.5 cm from the border of direct hernia Nyhus type 3a. Several small nervous trunks (*blue arrows*) showing extensive degeneration and fibrotic thickening of the perineural sheath surrounded by fatty substitution of the muscle fibers. Arterial sub-occlusion due to thickening of the media (*red arrows*). Vein with vascular congestion and thickened fibrous wall (*yellow arrow*). NSE ×10

control samples, no comparable degree of structural degeneration of the nerves was found. In some cadavers, a partial spotty fibrotic dystrophy of the axons could be detected, but without a thickening of the myelin sheath. Five representative slides from normal subjects are shown in Figs. 9, 10, 11, 12, and 13 for comparison.

Discussion

The authors would first like to acknowledge several shortcomings in this study design. Firstly, the population samples

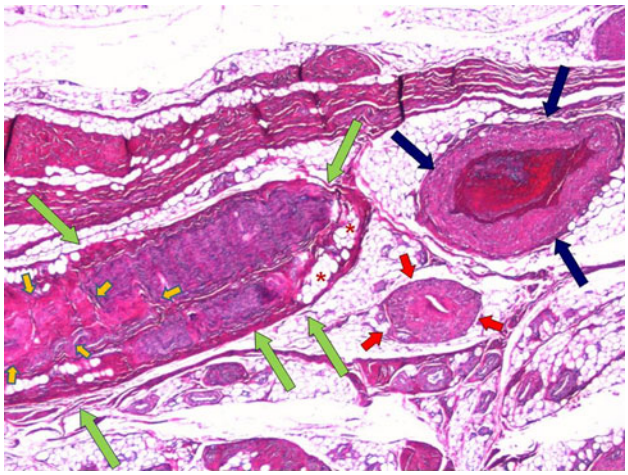

Fig. 4 Biopsy specimen excised 2.5 cm from the border of direct hernia Nyhus type 3a. Large nervous trunk (*green arrows*) showing clear degenerative fibrotic dystrophy (*yellow arrows*) and fatty substitution of the axons (*) with fibroadipose dystrophy of the muscular stroma. Artery with endoluminal thrombus (*blue arrows*). Arterial sub-occlusion due to medial hyperplasia (*red arrows*). Hematoxylin-eosin ×10

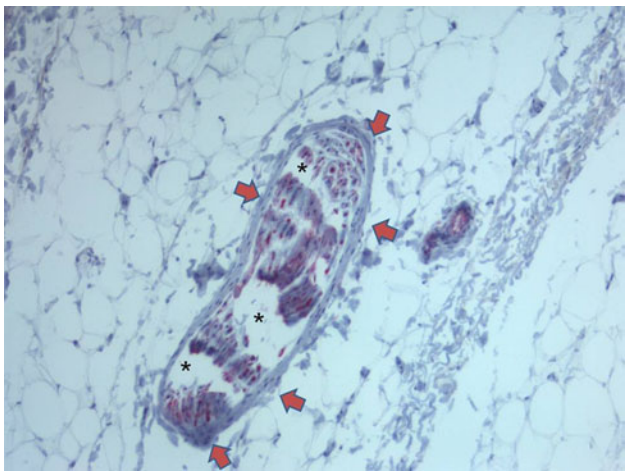

Fig. 5 Biopsy specimen excised 2.5 cm from the border of indirect hernia Nyhus type 2. Severe regressive degeneration of the nerve axons (*) with thickening of the myelinic sheath (*red arrows*). NSE ×10

are small. This is mainly due to the fact that finding and identifying hernias in cadavers is very difficult, but to find primary hernias that have undergone no repair is extremely challenging. In order to complete the study in a reasonable time scale, the sample number was set at 30 cadavers.

Secondly, the ability to compare samples within groups and across controls for varying types of hernia presented challenges for the protocol. The authors hope that they have devised a method that adequately achieved this, but acknowledge that it is not perfect. However, there were so few previous histological studies that the authors could not repeat any "gold standard" in terms of methodology.

In a previous article by the authors, descriptions of the histological changes of the muscular tissue excised from

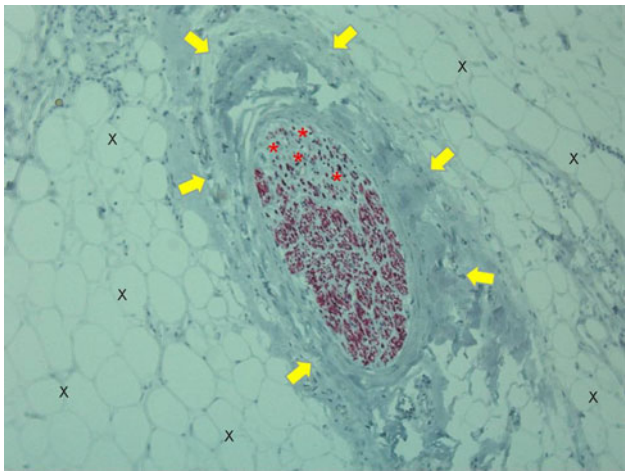

Fig. 6 Biopsy specimen excised 0.5 cm from the border of indirect hernia Nyhus type 1. Fibrotic degeneration of the nerve axons (*) as well as fibrotic thickening of the perineural sheath (*yellow arrows*) surrounded by fibroadipose muscle dystrophy (*X*). NSE ×20

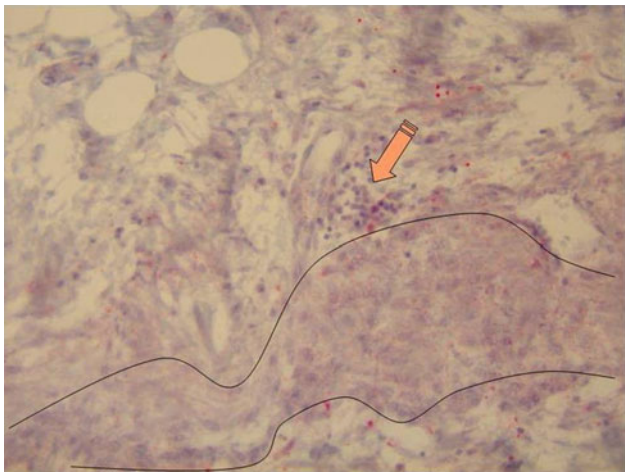

Fig. 7 Biopsy specimen excised 1.5 cm from the border of mixed inguinal hernia Nyhus type 3b. Silhouette of a residual nerve trunk (*black contour*) which has lost its specific immunoreactivity due to degenerative neurodystrophy. The *orange arrow* indicates a lymphohistiocitary cluster. NSE ×20

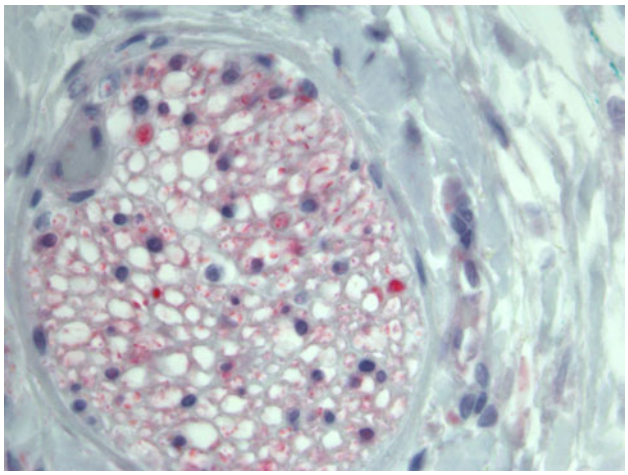

Fig. 8 Biopsy specimen excised 1.5 cm from the border of direct inguinal hernia Nyhus type 2. Wallerian degeneration of a nerve trunk. Almost all nerve axons have disappeared and the Schwann tubes are empty (*white spots*). The rest of the axons show a manifest fibrotic dystrophy (*red spots*). Myelin sheath clearly thickened. NSE ×63

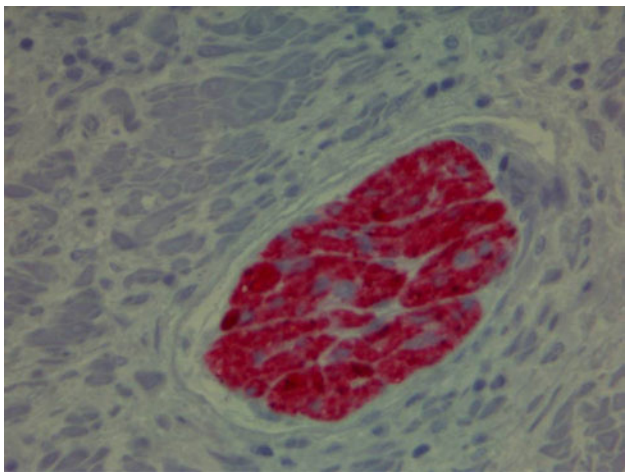

Fig. 9 Control cadaver aged 45 years. Broad, well characterized, and healthy nervous structure. NSE ×20

the internal inguinal ring in living patients having indirect inguinal hernia were reported [10]. In that study, histological changes, such as fibrohyaline and fatty degeneration of the muscle fibers, lymphohistiocytic inflammatory infiltrate, as well as venous congestion were observed. The general findings of this current study confirm and support the previous findings. However, the authors wanted to note these observations as the ability to compare to controls (which did not demonstrate these changes) adds an extra element of scientific knowledge. Indicating the histological changes identified are possibly related to the presence of a hernia.

With specific regard to the aim of this study, the authors detected several histological changes within the nerve structures that were not seen in the controls. This included evidence of fibrotic degeneration, fatty dystrophy, and thickening of the perineural sheath. One possible cause of such alterations has previously been described in the literature [11–13] and was considered to be as a result of compressive damage of the nerve axons. Interestingly, these changes are not seen exclusively in the tissue samples excised from the structures close to the hernia opening, but they are also evident with equivalent extent in the biopsy samples taken at 1.5- and 2.5-cm distances from the hernia border. This potentially eliminates an initial thought by the authors that the compressive damage might have been as a result of the direct compression of the hernia sac and contents on the border of the hernia orifice. This then raises an important question: "Could the histological changes to the

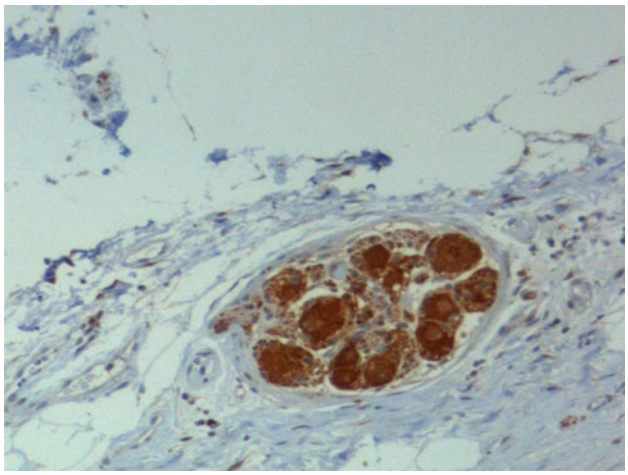

Fig. 10 Control cadaver aged 50 years. Broad nerve ganglion, with no evidence of pathological changes. NSE ×10

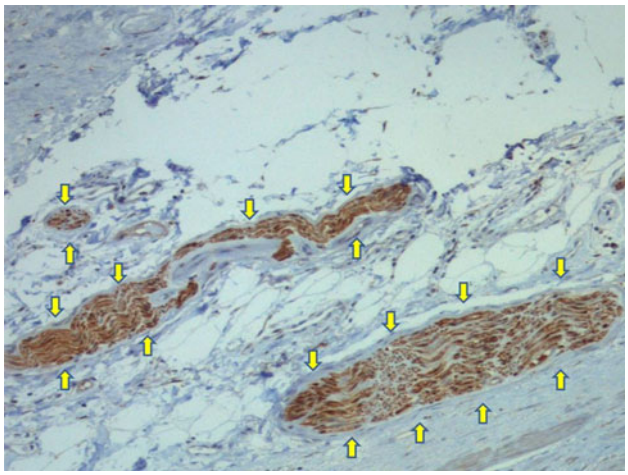

Fig. 12 Control cadaver aged 37 years. Healthy nerve trunks (*yellow arrows*) having normally structured myelin sheath. NSE ×10

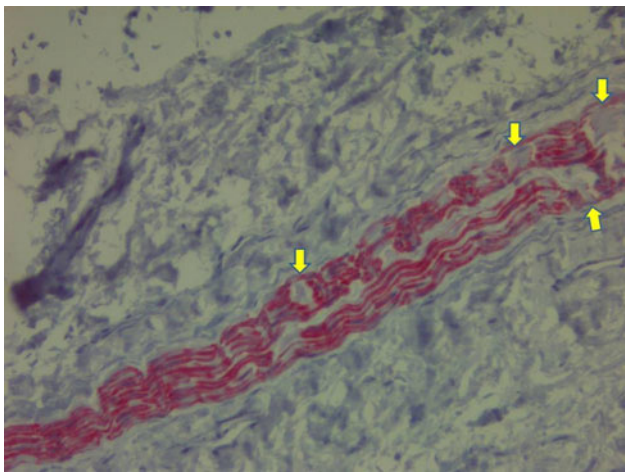

Fig. 11 Control cadaver aged 65 years. Nerve trunk with healthy axons and sporadic evidence of spots of fibrotic dystrophy (*yellow arrows*). The perineural sheath shows a regular contour and thickness. NSE ×20

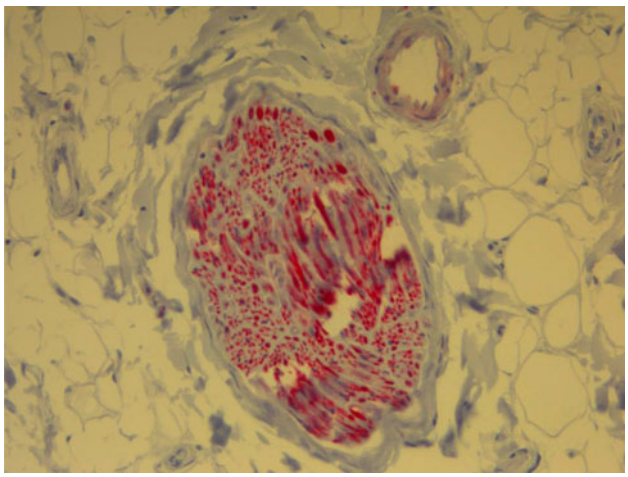

Fig. 13 Control cadaver aged 53 years. Broad nervous structure. Healthy nerve fibers (*in red*) interspersed in fibroadipose connective tissue (*colored in grey*). Normal thickened myelin sheath. NSE ×20

nerves potentially be causal and not consequential to the hernia?"

More evidence of long-term compressive injury arises from the evidence of the nervous trunk with manifest wallerian degeneration found at 1.5 cm from the direct hernia border. This type of histological damage has been described in the literature as a consequence of degeneration of the axon distal to a site of transection [11].

This unusual finding, also known as anterograde nerve degeneration, could also derive from the compressive crushing of the nerve trunk.

The wide range of nerve lesions described in the results would normally lead to a diminished innervation, or even a complete blockade of the nerve action. The authors question what would be the impact of motor nerve damage to the highly contractile inguinal area. Chronic damage to the innervation could potentially lead to atrophic effects on the muscle, which is evident in the more general histological findings of this study. It could also lead to reduced contraction of any protective muscular mechanisms, such as the shuttering mechanisms described in the literature [1–3, 9].

The now open question of the nerve damage being causal or consequential to hernia raises several important questions: does long-term compressive damage to the nerves reduce the ability of the muscles of the inguinal region to contract during stress events such as coughing, and induce a gradual atrophy/thinning of the muscles? Could this be another contributing factor in the "weakness" of the inguinal area leading to hernia?

The authors feel that these initial findings should encourage more groups to conduct histological studies to gain

vital information to support the molecular, biological, and gross anatomical studies regarding the formation of hernia.

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