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Research Paper Review

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Do intervertebral discs degenerate before they herniate, or after?

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ABSTRACT

The belief that an intervertebral disc must degenerate before it can herniate has clinical and medicolegal significance, but lacks scientific validity. We hypothesised that tissue changes in herniated discs differ from those in discs that degenerate without herniation. Tissues were obtained at surgery from 21 herniated discs and 11 non-herniated discs of similar degeneration as assessed by the Pfirrmann grade. Thin sections were graded histologically, and certain features were quantified using immunofluorescence combined with confocal microscopy and image analysis. Herniated and degenerated tissues were compared separately for each tissue type: nucleus, inner annulus and outer annulus.

Herniated tissues showed significantly greater proteoglycan loss (outer annulus), neovascularisation (annulus), innervation (annulus), cellularity/inflammation (annulus) and expression of matrix-degrading enzymes (inner annulus) than degenerated discs. No significant differences were seen in the nucleus tissue from herniated and degenerated discs. Degenerative changes start in the nucleus, so it seems unlikely that advanced degeneration caused herniation in 21 of these 32 discs. On the contrary, specific changes in the annulus can be interpreted as the consequences of herniation, when disruption allows local swelling, proteoglycan loss, and the ingrowth of blood vessels, nerves and inflammatory cells.

In conclusion, it should not be assumed that degenerative changes always precede disc herniation.

ANALYSIS

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Background Information
Do intervertebral discs degenerate before they herniate, or after? This, in many ways is the classic 'chicken and egg' question – Which came first? This is a very important concept, particularly in the personal injury arena, where patients with a symptomatic disc herniation can be denied personal injury compensation if the herniated disc was deemed to be previously degenerated, therefore prone to herniation even if 'the injury' had not occurred.

The nucleus pulposus contains a high concentration of hydrophilic proteoglycan. Once a herniation occurs, the tissue swells between 2 to 3-fold within hours. Swelling allows fragmented proteoglycan

to be lost, and the herniated tissue becomes a collagen-rich and proteoglycan-poor mass. This 'crabmeat'-like substance could point towards the characteristic degenerative changes in disc tissue that occur after herniation. Or at least, this is what the authors of this study suggest in their hypothesis:

The changes in herniated discs differ from those found in degenerated discs, and are consistent with being a consequence rather than the cause of herniation.

They evaluated this concept by looking at disc tissue harvested at surgery from 21 herniated discs and 11 non-herniated discs of similar degeneration as assessed by the Pfirrmann grade (3).

PERTINENT RESULTS

- The herniated discs (n = 21) were fully extruded through the posterior annulus at operation (10 had lost continuity with the rest of the disc [sequestered] and 11 were in contact with the nerve root). The degenerated disc tissue were removed from discs (n = 11) that were neither herniated nor bulging, and so were structurally continuous with the rest of the disc.

- No significant differences were seen in the nucleus tissue from herniated and degenerated discs.

- The annulus section of the disc told a different story, however. Compared with the degenerated discs, the herniated tissues showed significantly greater proteoglycan loss in the outer annulus. Further, blood vessel formation (neovascularization) was only found in the annulus of the herniated discs. They often accompanied inflammatory cells near matrix fissures and on free surfaces. Finally, the cells staining positive for the matrix-degrading enzymes (matrix metalloproteinases - MMP1, MMP2 and MMP3) were more common in herniated discs compared with the degenerative discs. However, the differences only reached significance in the annulus.

CLINICAL APPLICATION & CONCLUSIONS

This novel study is the first direct comparison between herniated intervertebral disc tissues and tissues that have reached a similar grade of degeneration without herniating. The results demonstrated that herniation involved distinct tissue changes compared to degeneration, and differences were usually most pronounced in outer annulus fibrosus tissue and least in nucleus pulposus tissue.

In general, accelerated degeneration is usually most advanced in the nucleus pulposus. The similarities in nucleus pulposus tissue between the two groups suggest that herniation did not represent an advanced or accelerated stage of normal disc degeneration in two-thirds of the discs studied. These findings suggest that it is unlikely that advanced degeneration caused herniations in the majority of the discs examined. Rather, local swelling, proteoglycan loss, and the ingrowth of blood vessels, nerves and inflammatory cells may very well be *consequences* of the herniation.

The findings from this study have important implications in the surgical world. Standard discectomy for a first-time lumbar herniated nucleus pulposus may increase the risk of subsequent, same-level lumbar disc degeneration compared with microdiscectomy (1). These days, most disc herniation surgeries involve microdiscectomy, which involves removing the herniated part of the disc and any fragments that are putting pressure on the spinal nerve. The findings from this study confirm and support the choice of microdiscectomy over standard complete discectomy. Further, it emphasizes the importance of surgically managing the disc herniation with care. Minimizing any pathology to the annulus fibrosus, through surgery, can avoid or diminish future degeneration, local swelling, proteoglycan loss and ingrowth of any painful blood vessels or nerves.

This study also has important implications in the fields of tissue engineering and regenerative medicine. Current research focuses on regeneration of the nucleus pulposus, while less attention has been directed to the repair or regeneration of the annulus fibrosus (2). This study highlighted the importance of repairing, regenerating or restoring the function of the annulus fibrosus *and* nucleus pulposus when attempting to treat low back pain of discogenic origin.

Clinically, distinctions between disc herniation and degeneration are important. Discs that degenerate *in situ* often cause no major symptoms, whereas many herniated discs result in severe pain, sciatica and so on. This becomes the focus of many medicolegal cases. Some herniated discs may possibly herniate because of degenerative changes and genetic factors. However, some discs also herniate for other reasons, including injury, meaning some degenerative changes evident during surgery are the consequences rather than causes of herniation. This concept should be kept in mind when reading or interpreting results from your patients' X-ray or MRI studies.

EDITOR'S NOTE: A further take-home point from this (and other) papers is that disc herniations are complex and multi-factorial. The idea of degeneration preceding herniation has not been fully elucidated and more work needs to be done. To further 'muddy the waters' of causation, it is possible that a patient may have a genetic predisposition that leads to molecular changes within important disc-centric molecules that fail or 'degenerate' and in so doing predispose the disc to failure (herniation/degeneration)…could such a disc be considered to be in a state of 'pre-degeneration'? Check out Additional Reference #4 below for more on this idea.

STUDY METHODS

Herniated disc material that was removed during surgery was compared with specimens from discs that had degenerated *in situ*, without herniation. 21 herniated discs and 11 non-herniated discs were obtained for the purposes of this study.

To ensure that similar discs were analyzed between the two groups, a Pfirrmann grading system was used. The Pfirrmann grading system assesses lumbar disc degeneration and ranges in grades from 1 to 5 (3).

Thin sections of each specimen were graded histologically, and certain features were quantified using immunofluorescence combined with confocal microscopy and image analysis. The nucleus pulposus, inner annulus and outer annulus from the herniated and degenerated tissues were compared separately.

Statistical Methods
Mann-Whitney U tests were used to compare average values between herniated and non-herniated in situ tissues in the nucleus pulposus, inner and outer annulus fibrosis regions. Spearman's rank correlation was used to examine associations between histological variables assessed on ordinal scales. A p-value < 0.05 was considered to indicate statistical significance.

STUDY STRENGTHS/WEAKNESSES

Strengths

- The same grades of disc degeneration were used in both groups.
- The same techniques and reagents on both samples of discs were utilized.
- The use of laser confocal microscopy to examine multiple thick sections of tissue reduced the sampling problems inherent in conventional histological assessment.
- The use of automatic quantitative image analysis was used to minimize the risk of subjective bias.

Limitations

- Since degenerative changes start in the nucleus, it seems unlikely that advanced degeneration caused a herniation in 21 of these 32 discs. Since the number of discs examined is a small sample size, further work needs to confirm these findings.
- Furthermore, 11 of the discs did not follow this pattern and more work needs to be done to understand the complexities of the relationship between disc herniation and disc degeneration.
- The clinically relevant experience of the patient is not incorporated into the results of the study. Future studies like this one would do well to incorporate the patient's pain and function in relationship with the objective histological and radiological study results.

Additional References:

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