Letters to the Editor

Osteopontin Induces the Extension of Epidural Fibrosis into the Spinal Canal

To the Editor:

We read with great interest the recent article by Paulo Pereira and colleagues (1).

In the study, 24 patients with typical symptoms of persistent or recurrent low back and/or leg pain after lumbar spine surgery were reported to have osteopontin (OPN) and an absence of beta3-tubulin. Thus, the study proved an epidural scar does not contain nociceptive fibers that could explain the source of pain associated with epidural fibrosis.

As the authors stated, the limitation of the study was an unavailable control group. In the present letter, related research on rats was undertaken for breaking this limitation.

We have been focusing on epidural fibrosis (EF). Some interventions were tried out, and a certain level of success was achieved (2-4). Being similar with the authors' experience, OPN came into our view since 2011 (5). And to investigate the association between OPN and EF, the following research, which could be a supplement for Paulo Pereira and colleagues, was designed.

As shown in Fig. 1, 15 healthy adult female Wistar

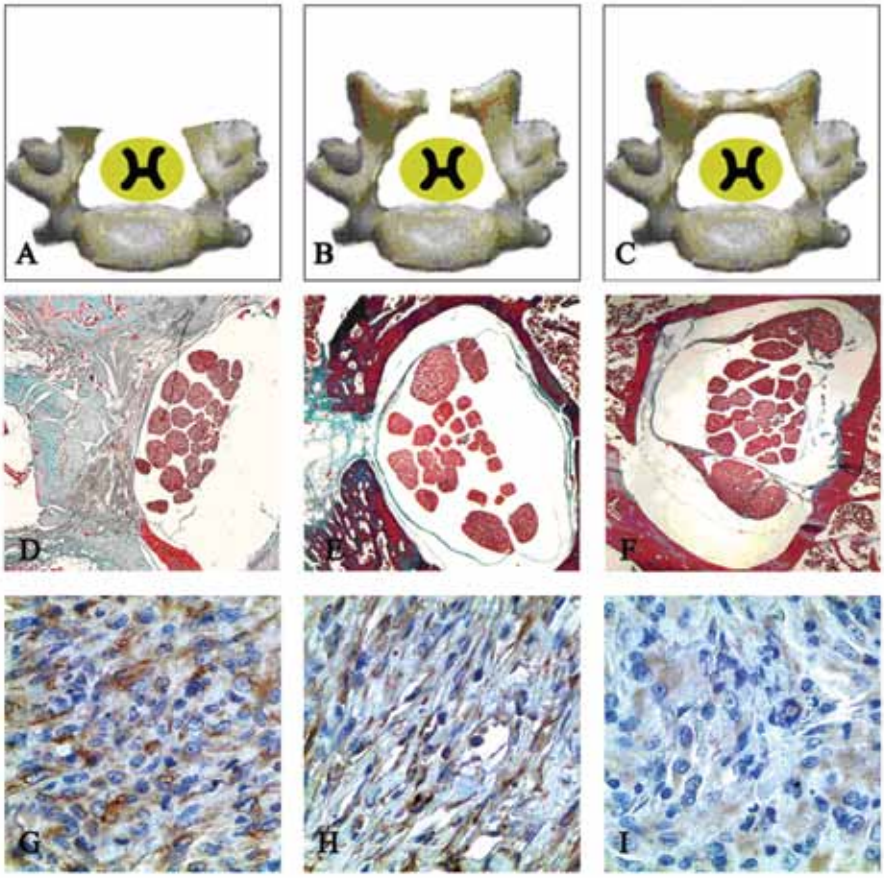

Fig. 1. *A-C: Modeling of laminectomy rats in 3 groups. D-F: Masson's trichrome staining of L1 on post-operative 6 week. G-I: osteopontin immunohistochemistry evaluation of epidural scar tissue (D-F, G-I original magnification 40× and 100×, respectively).*

Table.1. *Rydell classification*.

Group	Grade			
	0	1	2	3
1	0	0	0	5
2	5	0	0	0
3	5	0	0	0

rats (mean weight 220g) were randomly divided into 3 groups (5 rats per group). Group 1: total L1 laminectomy; Group 2: perforation at the L1 level with a microdrill; Group 3: removal of the spinous process with a rongeur. Six weeks post laminectomy, Rydell classification, Masson's trichrome and OPN immunohistochemistry were performed.

As shown in Table 1, Rydell classification showed no significant difference between group 2 and group 3. Still, during the operation we found the hiatus was filled with scar tissue, and some light scar tissue extended into the spinal canal (Fig. 1 E). As shown in Fig. 1 (G, H and I), first of all, a similar result that the OPN was detectable in epidural scar tissue was gained. At the same time, for the condition of groups 2 and 3, the expressional levels of OPN was significantly lower than group 1. The expressional level in group 3 was significantly lower than group 2.

Combined with both Paulo Pereira and colleagues' research and the previous report (4), we hypothesized that OPN, as the major player in the formation of EF, also promotes the extension of epidural fibrotic tissue into the spinal canal. How OPN links adhesion between epidural scars and dorsal root ganglions (DRG) is unclear. Thus, this may explain some if not all of the possible mechanisms that make EF related to persistent or recurrent low back and/or leg pain after lumbar spine surgery. We think we have answered the question Paulo Pereira and colleagues raised in the end of their discussion. OPN could be a good target for preventing and/or treating EF. Undoubtedly, further research will be carried out in the future.

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Conflict of Interests

There are no potential conflict of interests and financial activities related to the present paper to disclose.

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In Response

We deeply appreciate the interest in our article (1]) and the comments related to it. We would also like to highlight the extensive and important research carried out by the authors of this letter on epidural fibrosis and on designing strategies to prevent it [2-4].

In the experiment reported in this letter to the editor, the authors found that the epidural scar tissue was firmly adherent to the dura mater on rats that underwent laminectomy, whereas no adherence between the epidural scar tissue and the dura mater was present on animals whose lamina was left intact or perforated with a micro-drill. Moreover, the authors pointed out that the expression of osteopontin (OPN) in the epidural scar tissue was significantly decreased on specimens with intact laminae in comparison to the laminectomy ones and reached an intermediate level on specimens with a perforated lamina.

While we find these results highly relevant, we would be very pleased to have the opportunity to analyze them in a structured article, since a full explanation of the methods and discussion of the results are beyond the scope of a short report, such as a letter to the editor. In particular, detailed descriptions of the histological sections and the exact location where the epidural scar tissue was collected on rats with intact laminae would certainly be relevant information for the reader.

Our article [1] documented, for the first time, the expression of OPN in human postoperative epidural scar tissue. Animal experiments, such as the one described by the authors of the present letter, offer an irreplaceable opportunity to control for confounding factors and to test strategies drawn to counteract the tethering effect of epidural fibrosis on the neural structures. Hopefully, further research will greatly enhance the scientific knowledge on this matter.

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