The effects of intradiscal methylene blue injection on discogenic low back pain

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List of abbreviations

AF	annulus fibrosus
cGMP	cyclic guanosine monophosphate
CT	computed tomography
DLBP	discogenic low back pain
DRG	dorsal root ganglion
EP	endplates
FGF	fibroblast growth factor
IL-1	interleukin 1
IL-6	interleukin 6
IL-8	interleukin 8
IVD	intervertebral disc
LBP	low back pain
MB	methylene blue
MRI	magnetic resonance imaging
NADPH	nicotinamide adenine dinucleotide phosphate-oxidase
NGF	nerve growth factor
NO	nitric oxide
NOS	nitric oxide synthase
NP	nucleus pulposus
ODI	Oswestry Disability Index
sGC	guanylate cyclase
TGF-β	tumor growth factor β
TNF-α	tumor necrosis factor α
VAS	visual analog scale

Abstract

Purpose: This study was designed to evaluate the effect of methylene blue (MB) injection into the intervertebral disc on discogenic low back pain (DLBP) and on the functional disability of DLBP patients.

Subjects and methods: Twenty-four DLBP patients (age: 43 ± 8 y) referred for discography by the neurosurgeons were randomly assigned to either a placebo (n = 13) or a MB (n = 11) group. The pain perception of the patients and their functional disability were monitored by means of visual analog scale scores and the Oswestry Disability Index, respectively. Scoring was performed immediately before the discography procedure and one day, one week and one month after the procedure.

Results: At baseline the mean ± standard deviation (SD) for pain scores was 5.3 ± 2.4 and 5.5 ± 2.2 in the placebo group, respectively the MB group. The functional disability was 41 ± 13 in the placebo group and 40 ± 12 in the MB group. After one month follow-up the mean ± SD for pain scores and for the functional disability were respectively 6.2 ± 2.3 and 51 ± 20 in the placebo group and 5.1 ± 2.1 and 46 ± 20 in the MB group. There were no significant differences observed in pain scores and functional disability between the two groups. In addition, no significant differences were observed between patients treated at one level or at more than one levels. In this study, 6 of the 11 patients treated with MB experienced severe pain immediately after the MB injection. In 3 of them this pain lasted for more than one week.

Conclusion: In this one month follow-up study, intradiscal methylene blue injection did not influence the DLBP nor the functional disability of the patients. Since significantly increased pain may occur after methylene blue injection, no further patients will be included.

Abstract

Doel: Deze studie werd uitgevoerd om het effect van methyleenblauw (MB) injectie in de tussenwervelschijf op discogene lage rugpijn (DLBP) en op de functionele invaliditeit van DLBP patiënten, na te gaan.

Proefpersonen en methode: Vierentwintig DLBP patiënten (leeftijd: 43 ± 8 jaar) doorverwezen voor discography door de neurochirurg, werden willekeurig ingedeeld in een placebo (n = 13) of een methyleenblauw (n = 11) groep. De pijn perceptie van de patiënten en hun functionele onbekwaamheid werden door middel van visuele analoge schaal scores en de 'Oswestry Disability Index' op verscheidene tijdstippen geëvalueerd: vóór de injectie, en 1 dag, 1 week, 1 maand na de injectie.

Resultaten: De gemiddelde beginwaardes ± standaard deviatie (SD) voor de voor pijn waren 5.3 ± 2.4 in de placebo groep en 5.5 ± 2.2 in de MB groep. Voor de functionele onbekwaamheid waren de beginwaardes 41 ± 13 in de placebo groep en 40 ± 12 in the MB groep. Na één maand follow-up waren de gemiddeldes ± SD voor pijn en functionele onbekwaamheid respectievelijk 6.2 ± 2.3 en 51 ± 20 in de placebo groep en 5.1 ± 2.1 en 46 ± 20 in de MB groep. Er werden geen significante verschillen in pijnscores en functionele onbekwaamheid waargenomen tussen de twee groepen. Bovendien werden er ook geen significante verschillen waargenomen tussen patiënten behandeld op één niveau of op meerdere tussenverwelschjfniveaus. In deze studie ervaarden 6 van de 11 patiënten in de MB groep een sterke pijn reactie na de injectie. In 3 van de patiënten hield de pijn langer dan één week aan.

Conclusie: In deze één maand follow-up studie, kon er geen positieve invloed aangetoond worden van methyleenblauw injectie in de tussenwervelschijf invloed op de DLBP en de functionele onbekwaamheid van de patiënten.

1. Introduction

Approximately 80% of the population has low back pain (LBP) at some time in life. It is the most frequent cause of disability under the age of 45 years and a common reason for visiting a doctor (1). In 40% of the LBP patients the pain is generated in an intervertebral disc (IVD) (2). These patients are said to suffer from discogenic low back pain (DLBP).

DLBP belongs to the category of LBP and is clinically defined as chronic pain in the region of the lumbosacral spine which arises from a damaged IVD. It is commonly diagnosed by means of clinical examination, medical history and medical imaging (computed tomography (CT), magnetic resonance imaging (MRI)). Discography is a minimally invasive procedure that is used to correlate the DLBP of the patient with a specific disc. During this percutaneous procedure a contrast medium is injected into the disc both to evaluate the morphologic condition of the disc and to reproduce the pain felt by the patient by increasing the internal pressure on one particular disc. This subjective test allows the physician to verify that the low back pain of the patient is discogenic and is caused by that particular disc.

The pathophysiology of DLBP is complicated and poorly understood and so far, there is no consensus about the exact pathway causing the pain. Some studies, however, indicate that the pain is caused by damage of an IVD as a result of degeneration or annular disruption (2; 3). Several research groups agree on the fact that painful discs are associated with an increase in the innervation of the annulus fibrosus (AF), i.e. the fibrous ring surrounding the nucleus pulposus of the IVD (4; 5; 6). It is suggested that damage of the IVD may trigger the nerves and increase the innervation in the AF, resulting in pain. It is assumed that DLBP may reduce or disappear if the nerve endings, which are causing the pain, are destroyed.

Methylene blue (MB) is a substance which has been used in different areas of clinical medicine for therapeutic and diagnostic procedures. Its local injection has been used for the treatment of painful ailments such as pruritus ani (7; 8). Different studies suggest that MB may directly or indirectly lead to reduced pain (9; 10).

In this chapter we will focus on the anatomy, function and innervations of a normal and degenerative intervertebral disc, on the pathology of IVD degeneration, on conservative treatment methods, on the role of MB in different areas of medicine and on MB injection as a

potential strategy to improve DLBP.

1.1. Structure and function of the intervertebral disc

An IVD lies between two adjacent vertebral bodies. In the lumbar spine the IVDs are approximately 7-10 mm thick with a transverse diameter of about 4 cm (Fig 1A, B) (11; 12).

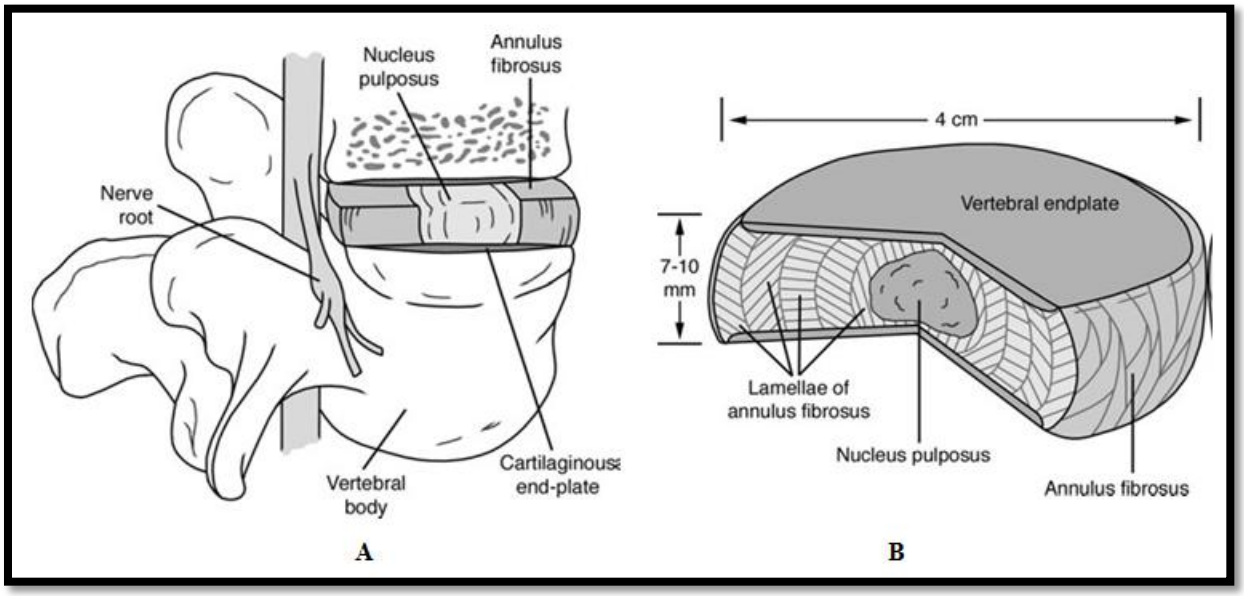

Figure 1: (A) A spinal segment consisting of two vertebral bodies and an intervertebral disc sandwiched between them. (B) A cut out portion of a normal disc which shows the nucleus pulposus, vertebral end plate and the architecture of the annulus fibrosis (13)

The IVD consists of a thick outer ring of fibrous cartilage, known as the AF, which surrounds a more gelatinous core termed the nucleus pulposus (NP). The NP is sandwiched superiorly and inferiorly by the cartilaginous endplates (EP) of the vertebral bodies.

The AF is made up of 15-25 concentric rings or lamellae, with collagen fibers lying parallel to each lamella (14). Elastin fibers lie between the lamellae, possibly helping the disc to return to its original arrangement following flexion or extension. In addition, the elastin fibers pass radially from one lamella to the next, probably binding the lamellae together (15). The NP also contains collagen and elastin fibers. The collagen fibers are organized randomly, while the elastin fibers are radially organized (15; 16). Both types of fibers are embedded in a highly hydrated aggrecan-containing gel, which is very important for maintaining the water content of the NP (17). In addition to the collagen and the elastin fibres, the NP also contains several collagen types, small proteoglycans, and other glycoproteins (18; 19). The EP is a thin, less than 1 mm thick, horizontal layer of hyaline cartilage and the subchondral bone plate. This

layer interfaces the disc and the vertebral body. The collagen fibers within it run horizontally and parallel to the vertebral bodies. Some of these fibers extend into the disc (12).

The primary functions of the IVD are to transmit loads and to facilitate movement between vertebral bodies. The NP and the AF allow for pressure dispersal when axial loads are transmitted to the spine (20).

1.2. Nerve and blood supply of the intervertebral disc

It is generally assumed that the lumbar IVD is innervated by dorsal root ganglion (DRG) neurons through the sinuvertebral nerves (Fig. 2) and by branches derived from the ventral rami or gray rami communicantes (21).

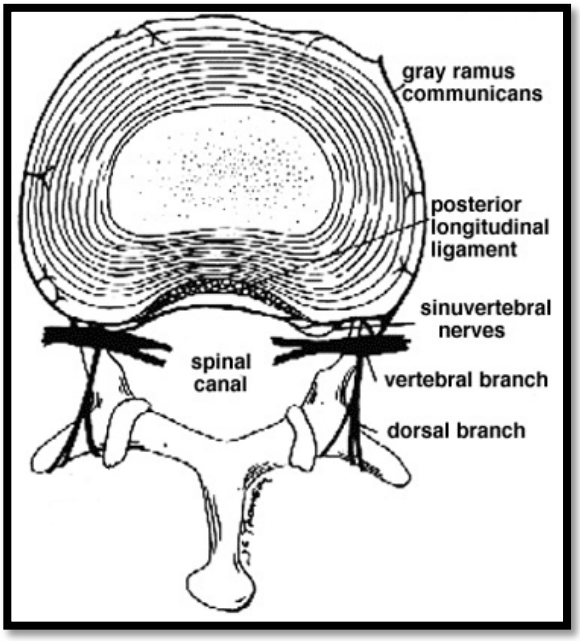

Figure 2: Axial cross-section demonstrating the course of the sinuvertebral nerve (meningeal branch of the spinal nerve) (22)

Several histologic studies have shown the presence of nerve endings in the most superficial layers of the AF (23; 24; 25; 26). Both the free nerve endings and the more complex encapsulated endings are found in the outer layers of the AF. Mechanoreceptors resembling Pacinian corpuscles and Ruffini endings have been considered responsible for proprioception (25; 27). Proprioception is the sensation of motion or location of the different parts of the body and it is the sensory feedback mechanism for motor control and posture. A nociceptive or pain sensation function has been assigned to structures resembling Golgi tendon organs

(28).

Blood vessels are only seen in the outermost layers of the AF (29). Except for the outermost AF, a normal IVD is both avascular and aneural.

1.3. Possible pathogenesis underlying discogenic low back pain

In the last decade, attention has begun to focus on the cellular and molecular activity of IVD tissue in the search for understanding the pathophysiology of DLBP. The following five factors may have a major influence on the IVD and its degeneration:

(i) Genetic factors: Several studies suggest that a significant proportion of IVD degeneration cases can be explained by genetic factors. Candidate genes linked to degeneration of the IVD include collagen I, aggrecan, matrix metalloproteinases, etc (30; 31).

(ii) Ageing: With increasing age, modifications in matrix components such as collagen and proteoglycan occur. The IVD becomes more and more disorganized and disc degeneration may be initiated (32).

(iii) Nutrients and oxygen diffusion to the IVD: While the outer AF is thought to receive its nutrients from the local vasculature, the remainder of the IVD is nourished through nutrients diffusion from the bone marrow. The diffusion pathway (vertebral body, EP, IVD) to cells in the centre of the lumbar disc is long and the nutrient supply to the cells in the NP can be disturbed by factors that affect the blood supply to the vertebral body, such as atherosclerosis and calcification of the EP (33). A decrease in nutrient supply may affect the ability of the disc cells to synthesize and maintain disc's extracellular matrix and may thus lead to disc degeneration (30).

(iv) Soluble factors such as cytokines: Imbalance in the IL-1 isoform system may induce tissue changes associated with degeneration (30). Another cytokine, TNF-α, present in higher levels within the degenerated IVD, is involved in the catabolic processes leading to matrix degradation (30; 34). In addition, TNF-α induces sensory nerve growth into the IVD (35). This is of considerable interest as nerve ingrowth has been described previously as a feature of the painful degenerated IVD (5).

(v) Mechanical load: Abnormal mechanical loads may also result in disc degeneration. Experimental overloading or injury to the disc have been shown to induce degenerative changes (30; 36).

Disc degeneration is a complex process which may be initiated through the combination of the above described factors and possibly also by some other factors.

The first and the most significant change in disc degeneration is the loss of proteoglycan (37). Proteoglycans are necessary to maintain the water content of the disc (38). One of the proteoglycans, aggrecan, regulates the movement of solutes in and out of the disc (39). Because of its high concentration and charge in the normal disc, it prevents movement of large uncharged molecules such as serum proteins and cytokines into and through the matrix (40). Due to the loss of aggrecan, large molecules such as growth factor and cytokines may be able to enter the disc. These molecules may then affect the cellular behavior and possibly lead to the progression of degeneration. Changes in other matrix components such as collagens and fibronectin, and in enzyme activity may also occur and accelerate the process of degeneration (41; 42; 43; 44).

The degenerative changes in the disc lead to a weakening of the nuclear and annular structures, which makes them susceptible to bulging and tears, respectively. Peng B et al. (2005) showed that a characteristic feature of the disc from patients with DLBP is the formation of a zone of vascularized granulation tissue into the annular tear (29). Abundant substance P-immunoreactive nerve fibers, thought to be nociceptive, were found in this granulation tissue. Another study demonstrated abundant macrophage and mast cell infiltrates in the granulation tissue zones in all painful discs (45). Macrophages are phagocytic cells which secrete a large amount of growth factors and cytokines, such as FGF, TGF-β, IL-1, and TNF-α. These factors regulate cell proliferation and differentiation, promote granulation tissue formation, and induce neovascularization. Mast cells are highly specialized mononuclear cells which release substances such as histamine, heparin, TNF-α, proteases, interleukins, etc. They are involved in the process of neovascularization and promote activation and proliferation of fibroblasts as well as the production of fibrosis (46). It has been suggested that mast cells also synthesize, store, and secrete nerve growth factor (NGF), which might be considered an inducer for nerve ingrowth into the inner layer in a painful disc (47). These findings suggest that a granulation tissue occurs in the tears of the painful disc. The factors produced by the macrophages and mast cells in this granulation tissue can mediate cell proliferation and differentiation, promote granulation tissue formation, and induce neovascularization.

A tissue or structure can only serve as a pain generator if it is innervated. Different mechanisms can stimulate or initiate nerve ingrowth into the IVD:
(i) Alteration in IVD matrix: In vitro experiments showed that aggrecan derived from normal IVD inhibits the growth of neurites, while aggrecan that had been deglycosylated to make it more akin to that found in the degenerated IVD, had a reduced inhibitory effect (48). This suggests that changes and loss of aggrecan may result in nerve ingrowth into the IVD.
(ii) Altered IVD cell function: In vitro experiments on the effects of cells derived from normal and degenerated IVD on neurite outgrowth demonstrated that the normal inhibition of neurite outgrowth by aggrecan could be reversed by cells derived from degenerated IVDs (49).
(iii) Angiogenesis: Nerve ingrowth into degenerated IVDs is seen in physical association with ingrowing blood vessels (29). During the process of angiogenesis, endothelial cells, growing into the IVD, synthesize NGF, which stimulates nerve ingrowth (47).

After having analyzed the painful IVD, several research groups described ingrowth of nociceptive nerves into the degenerated IVD (4; 5; 29). These nociceptors within the painful discs can be sensitized through proinflammatory cytokines and mediators, such as prostaglandin E_2, interleukin IL-6 and IL-8, produced by inflammatory cells (50). DLBP might occur when the intradiscal pressure increases with trunk motion such as flexion or extension. In addition, the mechanism of pain during discography could be the same as the pain reproduction might also occur when the intradiscal pressure sharply increases when the contrast medium is injected into the disc.

1.4. Treatment options for discogenic low back pain

Nowadays, DLBP therapy is aimed at relieving symptoms rather than addressing the underlying disease mechanisms. Surgical interventions, such as total disc excision and lumbar fusion surgery, show acceptable improvement but they are expensive and the recovery time is long, further increasing the overall costs. Minimally invasive treatment methods, such as intradiscal steroid injections, intradiscal electrothermal therapy, intradiscal radiofrequency thermocoagulation, and epidural steroid injections, are relatively simple to perform, are less expensive, yield a quicker recovery and fewer long-term side effects. Their efficacy, however, is questioned (51).

1.5. Methylene blue

Since the first synthetization of MB in 1876, it has been used in different areas of clinical medicine for therapeutic and diagnostic procedures. MB can be seen as a redox-cycling substrate which is reduced by reducing agents, such as NADPH, to leucoMB. LeucoMB is subsequently oxidized by O_2. Oxidized MB and leucoMB together form a reversible electron donor-acceptor couple. LeucoMB is colorless, uncharged, lipophilic, and enters cells by diffusion across the plasma membrane where it can be re-oxidized to MB and as such is sequestered within the cells (52; 53). MB is able to cross the blood-brain barrier and shows high affinity towards nervous tissue (54; 55). Its ability to permeate cellular membranes (as LeucoMB) and to cross the blood-brain barrier makes MB attractive as a potential therapeutic agent. The mechanism underlying the high-affinity uptake of MB into nervous tissue is not fully understood. MB accumulates in the cytoplasm in the form of large, drop-like structures and binds to material at the plasma membrane (56).

MB is shown to be effective in the treatment of malaria (57). One of the most common clinical applications of MB, however, is to treat methemoglobinemia or to aid localization of the parathyroid glands during surgery (58; 59). MB has shown beneficial effects in brain diseases, such as depression and Alzheimer disease. Its local injection has also been used for the treatment of painful ailments such as pruritus ani (7; 8). It has been suggested that the effectiveness of intradermal MB injection in the treatment of pain and irritation in pruritus ani is due to the destruction of dermal nerve endings (8). Up to now, however, there is no evidence for this (7).

Low concentrations of MB were found to inhibit the hyperalgesia induced by intrathecal injections of prostaglandin E2 and prostaglandin F2 in animal models (60; 61). On the other hand, epidural injections of MB in cats were shown to induce paraplegia, axonal swelling, and inflammation of the leptomeninges (62). Although the mechanism for these detrimental effects of MB is not clear, it is likely that anatomical regions with limited blood perfusion, such as the spinal cord, are highly sensitive to the vasoconstrictive effects of MB (9). As mentioned before, angiogenesis may stimulate nerve ingrowth into the degenerate disc, and this may affect pain perception (29; 47). The vasoconstrictor role of MB may lead to a state which resembles the normal avascular state of the IVD and may thus normalize the changes which occur in the degenerated IVD.

Research over the last decades indicates that nitric oxide (NO) and cyclic guanosine monophosphate (cGMP) essentially contribute to the processing of nociceptive signals in the spinal cord and are also involved in the sensitization during both inflammatory and neuropathic pain. Therefore, blocking their effect or inhibiting the synthesis of NO and/or cGMP can considerably reduce both inflammatory and neuropathic pain (63). MB is able to inhibit guanylate cyclase (sGC), the second messenger which is activated by NO, and it also directly inhibits both constitutive and inducible forms of nitric oxide synthase (NOS) by oxidation of ferrous iron bound to the enzyme. It inactivates nitric oxide (NO) by generation of superoxide anions (10).

1.6. Aim of the study

Until now, a substantial number of DLBP patients undergo invasive surgery (discectomy, disc replacement by prothesis) when all conservative therapeutic measures have failed. Peng et al. (2007) performed a clinical trial in which a group of 24 DLBP patients, who met the criteria for interbody fusion surgery, were treated with an intradiscal MB injection (64). The pain perception of the patients and their functional disability were determined through visual analog scale (VAS) scores and the Oswestry Disability Index (ODI), respectively. 87% of the patients showed a significant improvement of the pain and the functional disability (64). However, since a control group was not included, this study is methodologically less valuable. Nevertheless, the pilot study showed that the intradiscal MB injection procedure is safe and the results of MB treatment of DLBP patients are encouraging.

The aim of this study was to perform a placebo-controlled study to evaluate whether DLBP patients injected with MB during the discography procedure have a better clinical outcome than patients undergoing discography without MB injection. If MB treatment would result in a significant pain reduction, it might become an intermediary, minimally invasive treatment for DLBP between conservative therapy and surgery. This innovative DLBP treatment method may be used to avoid or postpone disc surgery, or could be used as an adjunct therapy on disc levels adjacent to the surgical disc.

2. Subjects and methods

2.1 Subjects

This study was approved by the local Medical Ethical Committee of Ziekenhuis Oost-Limburg. All subjects were informed on the nature and possible risks of the experimental procedures before written informed consent was obtained. The medical history of all patients was evaluated. A total of 24 DLBP patients (43 ± 8 y), referred by the neurosurgery department for discography prior to decision for disc surgery, were included. Patients were randomly assigned to either a MB (n = 11) or placebo (n = 13) group. In the latter group, 7 patients received an injection with contrast agent at one disc level. The other 6 patients were injected in two or more intervertebral discs. In the MB group 3 patients received a MB injection at one level, while the other 8 patients were injected in two or more levels. The patients' characteristics at day 0 are listed in Table 1.

Table 1: Subjects' characteristics

Subjects	Placebo (n=13)	Methylene blue (n=11)
Age (years)	41±9	45±6
VAS scores:		
One level	5.6±2.7	3.5±2.2
Two or more levels	5.1±2.1	6.2±1.8
The whole group	5.3±2.4	5.5±2.2
Disability percentage		
One level	39±10	32±12
Two or more levels	42±16	43±11
The whole group	41±13	40±12

Data represent means ± standard deviation (SD); Data were analyzed by using independent samples t-tests. No differences were observed between the two groups.

2.2 Discography procedure

Discography is an imaging-guided procedure in which a contrast agent is injected into the nucleus pulposus of the intervertebral disc. This imaging technique directly relates the patient's pain response to the morphological appearance of the disc. This procedure should be performed only if the patient has failed adequate attempts at conservative management of

persistent severe back or neck pain and if non-invasive techniques, such as MR imaging, do not provide sufficient information for a definitive diagnosis. Drawbacks of this procedure include the discomfort for the patient related to the eliciting of pain responses, and possible procedural complications such as infection (spondylodiscitis) and dural tear (leakage of cerebrospinal fluid; see also addendum 2). Discography may be necessary to assess painful discs prior to surgical interventions (29; 65).

Immediately after the discography procedure, CT is performed. This is required to confirm contrast injection into the nucleus pulposus. It provides anatomical detail in the axial plane and assesses the degeneration and disruption of the annulus (65).

In this study, patients were interviewed before the discography procedure regarding medical history, pattern and intensity of their low back pain and irradiating pain to the lower limbs before the discography procedure. Patients were positioned prone on the fluoroscopy table. The skin was cleaned and a sterile environment was created for the procedure. Local anesthesia was applied to numb the skin at the entry point of the needle and the tissue down to the disk area. The needle was inserted and, under fluoroscopic guidance (Siemens Axion Artis, Germany), passed into the centre of the intervertebral disc (nucleus pulposus). After all needles (gauge: 18G x 200mm, HS hospital services S.P.A., Italy) were placed (Fig. 3), 1 to 3 cc iodinated contrast medium was injected into the NP to increase intradiscal pressure and in this way possibly elicit pain. Patients had to describe the pain in detail. Patient and interventional radiologist decided whether the pain produced by the discography was concordant pain or not. If a disc level was concordant (reproducing the pain), 1 cc of 1% MB (Sterop-pharmacobel, Belgium) (10 mg) was injected in the MB treatment group. In the placebo group, 1 cc of iodinated contrast medium (Omnipaque-iohexol, GE Healthcare, Belgium) was injected. After X-ray pictures were taken, all needles were removed. Subsequently, a CT scan (Siemens Somatom Definition, Germany) of the injected discs was performed to evaluate for internal structure of the disc and for annular tears.

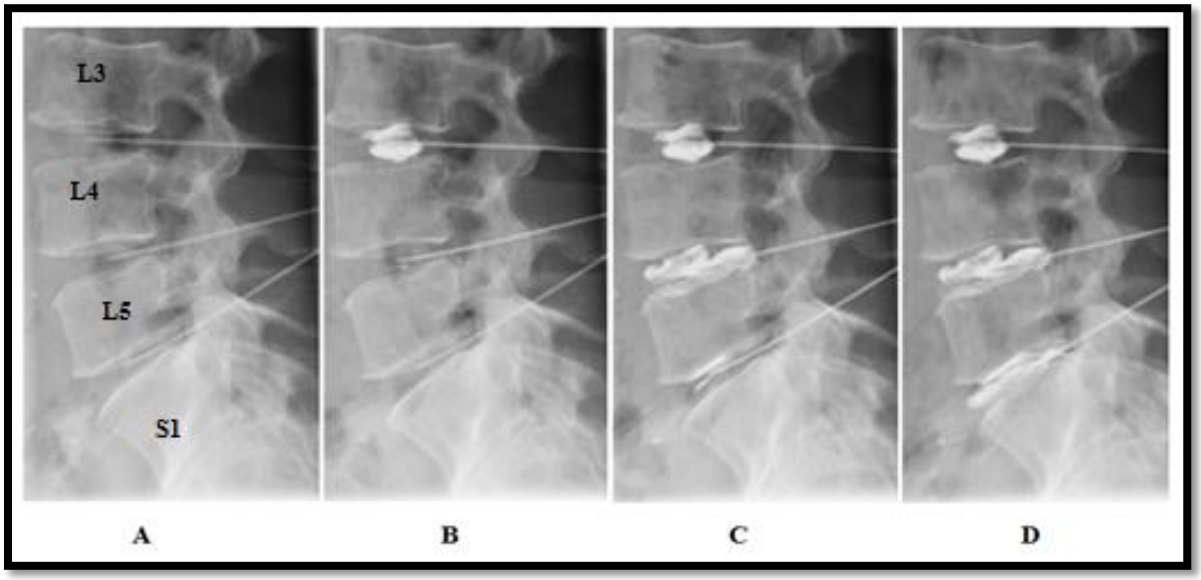

Figure 3: X-ray images taken during the discography procedure. (A) Needles are inserted in the intervertebral discs at levels L3-L4, L4-L5 and L5-S1. Contrast agent is injected at level L3-L4 (B), at level L4-L5 (C) and at level L5-S1 (D).

2.3 Outcome measures

Pain and functional disability of the subjects was monitored at several time points: before the discography, and one day, one week and one month after the discography. The intensity of the pain was determined through a VAS score on which the subject had to score pain between zero and ten. To determine the functional disability subjects were asked to complete the ODI questionnaire. This questionnaire contains 10 multiple choice questions designed to give information about how the back pain is affecting the ability of the patient to manage in everyday life. Each question can be answered by choosing one of the six possible statements. For each question the maximum possible score is 5: the section score is 0 if the first statement is marked, it is 5 when the last statement is marked. After completion of all 10 sections, the percentage of the patient's disability is calculated as follows:

$$\frac{\text{total score}}{(\text{maximum possible score} = 50) \times 100} = \ldots \% \text{ disability}$$

In case one section is not filled in or is not applicable, the percentage of the patient's disability is calculated as follows:

$$\frac{\text{total score}}{(\text{maximum possible score} = 45) \times 100} = \ldots \% \text{ disability}$$

2.4 Statistics

Data are expressed as means ± SD. The baseline characteristics of both groups were compared by means of an independent samples *t*-test. Pre- versus post-intervention data were analyzed using repeated-measures ANOVA with time as intra-subject factor and treatment as inter-subject factor. Statistical significance was set at $p<0.05$. All calculations were performed using the Statistical Package for the Social Sciences 16.0 (SPSS). For two patients in the placebo group and 1 patient in the MB group the follow-up data of day 1, week 1 and month 1 are missing.

3. Results

Due to the limited time period of the senior internship only data from the first month of follow-up are shown in this report. Patients, however, will be further observed for up to one year. Subjects' characteristics prior to intervention are shown in Table 1. No statistical differences were found between the two groups before the discography procedure.

3.1 Visual analogue scale scores

At baseline (day 0), VAS scores did not differ between the placebo and the MB group (Table 2). During the period of one month, no statistically significant changes in VAS scores were found. In addition, there were no significant differences between patients who were injected at one level and those who got an injection at more than one level. There is no time x treatment interaction.

Table 2: Visual analogue scale scores

Subjects	Placebo (n=13)	Methylene blue (n=11)
Day 0		
One level	5.6±2.7	3.5±2.2
Two or more levels	5.1±2.1	6.2±1.8
The whole group	5.3±2.4	5.5±2.2
Day 1		
One level	6.6±1.3	4.7±0.7
Two or more levels	5.3±2.5	6.1±1.2
The whole group	6.1±1.8	5.6±1.2
Week 1		
One level	7.1±1.3	3.9±1.5
Two or more levels	5.1±2.7	5.5±1.6
The whole group	6.4±2.1	5.0±1.7
Month 1		
One level	7.0±1.4	3.6±2.8
Two or more levels	5.1±3.0	5.8±1.5
The whole group	6.2±2.3	5.1±2.1

Data represent means ± SD. Data were analyzed using repeated measures ANOVA.

3.2 Oswestry Disability Index questionnaire

Before the intervention, the percentage of disability did not differ significantly between the two study groups (Table 3). In the placebo group there was a significant ($P < 0.05$) increase in functional disability over time. The functional disability did not change over time in the MB group. Significant differences between the groups were not found. The ODI questionnaire did not reveal any significant differences between patients in each group who were treated at one level and patients who got an injection at more than one level.

Table 3: Oswestry disability index

Subjects	Placebo (n=13)	Methylene blue (n=11)
Day 0		
One level	39±10*	32±12
Two or more levels	42±16	43±12
The whole group	41±13	40±12
Day 1		
One level	49±16*	40±10
Two or more levels	41±27	48±13
The whole group	46±20	45±12
Week 1		
One level	52±15*	34±8
Two or more levels	38±23	48±8
The whole group	47±18	44±16
Month 1		
One level	57±10*	36±26
Two or more levels	42±29	51±18
The whole group	51±20	46±20

Data represent means ± SD. Data were analyzed using repeated measures ANOVA. * indicates significant difference ($P < 0.05$) over time.

4. Discussion

Nowadays a large part of the world population suffers from DLBP and designing an intervention to counteract DLBP is a major challenge. DLBP is a form of chronic low back pain which is difficult to diagnose and to treat. The underlying pathology is not clear. A pathologic feature of discs from DLBP patients was found to be the formation of a zone of vascularized granulation tissue with extensive innervations in fissures extending from the outer part of the annulus into the nucleus pulposus (29). This vascularized granulation tissue is consists of abundant SP-immunoreactive nerve fibers, which have been thought to be nociceptive. Nociceptors within the painful discs can be sensitized through proinflammatory cytokines and other mediators secreted by inflammatory cells (47). Pain may also be caused by an increase in the intradiscal pressure due to trunk motion, such as flexion or extension. During a discography procedure, the injection of contrast medium into the pathologic intervertebral disc causes sharp pain, which is thought to be caused by increasing the local pressure and stimulating the nociceptors (29). If the pain is indeed caused by the nerve endings or the nociceptors, a drug or compound, which is able to destroy these nerve endings or nociceptors, may reduce the pain or even totally cure the patient.

Peng B. and colleagues (2007) treated 25 DLBP patients, who showed no response to various non-surgical treatments and who met the criteria for interbody fusion surgery, with an intradiscal MB injection (64). The clinical outcome was determined by means of VAS sores for pain and the ODI questionnaire for functional disability. According to Peng et al. (2007) 87% of patients treated with a MB injectiond during the discography procedure showed a significant pain reduction and an improved functional disability (64). These results are similar or even superior to those obtained by fusion surgery, which is an invasive surgery used to treat DLBP. It is worthwhile mentioning, however, that a control group was not included.

For this reason, we set up a single blind placebo-controlled single centre study. Patients who were unsuccessfully treated with conservative treatments, such as physiotherapy, medication (ibuprofen, corticosteroids, etc) and back education for more than six months, were referred by the neurosurgeons. Since these patients are candidate for disc surgery and/or disc prothesis, a discography procedure had to be performed for clinical reasons in order to determine/confirm the disc level of discogenic LBP. Patients were included in the study after having given informed consent and were allocated at random to the MB treatment group or

the placebo group. Although the estimated sample size for a power of 0.80 is 25 patients in each group, this report includes data from only 24 patients (13 patients in the placebo group and 11 patients in the MB group) and only data for the one month follow-up are shown due to the limited period of the internship. However, patients will be monitored for up to one year.

In this study, MB injection into the intervertebral disc during the discography procedure did not induce any changes in pain and functional disability when compared to the placebo control group. In the placebo group there was a significant ($P < 0.05$) increase in functional disability over time for patients treated at one level (Table 3). There is no explanation for this increase. Further significant differences in pain scores and functional disability between the groups and over time were not observed. In addition, significant differences between patients treated at one level and at more than one level were not found.

During the period of this internship, Peng B. et al. (2010) published their results of a placebo-controlled MB study (66). The effect of intradiscal MB injection on chronic DLBP was tested in a randomized double-blind placebo-controlled trial. Thirty-six patients received an intradiscal MB injection and 36 a placebo treatment. The primary outcome measures were pain assessment by a 101-point numerical rating scale, and improvement in disability, which was assessed with the ODI questionnaire. Patients were evaluated at baseline and at 6, 12 and 24 months post-treatment. At 6 months, patients treated with intradiscal MB injections achieved a mean reduction in pain of 47.39 scores and a mean reduction in ODI scores of 32.47. There were no statistically significant differences in the evaluation scores at 6, 12, and 24 months. Two years after treatment, 33 (91.6%) patients were completely satisfied in the MB group compared to only 5 (14.3%) in the placebo group All the primary outcome measures were in favour of intradiscal injection of MB, when compared with the placebo treatment.

Peng et al did not describe any adverse effects or complications of intradiscal MB injection (64; 66). This is in contrast to our study, in which 6 of the 11 patients treated with MB experienced severe pain immediately after the MB injection. In 3 of them this pain lasted for more than one week. The pathway for this pain is not clear. It is clear, however, that more attention has to be paid to this adverse effect and that further research is necessary to find out what MB is doing exactly at the molecular level.

In conclusion, in our placebo-controlled study, there seems to be no effect of intervertebral MB injection on any of the outcome parameters. This might be due to the low number of subjects (statistical power is less than 0.80) and the short follow-up period (one month). Significant changes might be observed when having finished the one year follow-up period for more patients. However, since more than 50% of the patients, who received a MB injection, suffered from severe pain immediately after the injection which lasted for more than one week in 3 of them, no further patients will be included in the study. The patients included so far, will be monitored for up to one year. Because of the high incidence and disability rate of discogenic low back pain, it is clear that there is a strong need for further experimental and clinical studies in order to yield an effective and minimally invasive treatment method for DLBP.

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Supplemental information

1. Visual analogue scale score for pain

The VAS score is used to determine the intensity of the pain felt by the patient. The patient is asked to indicate the intensity of the pain on a horizontal line of 10 cm.

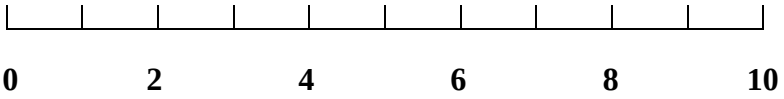
Instructions and the questionnaire:

Indicate how much pain you currently feel by drawing a vertical line between 0 and 10.

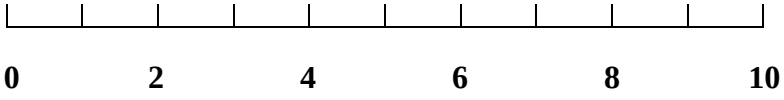
0 = No pain

10 = Worst pain ever

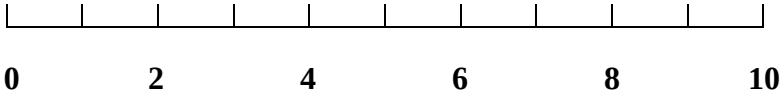
The least pain felt today:



Average pain felt today:



The worst pain felt today:



2. Oswestry Disability Index questionnaire

The functional disability of the subjects was measured through an ODI questionnaire. This questionnaire contains 10 multiple choice questions designed to give information about how the back pain is affecting the ability of the patient to manage in everyday life. Using this questionnaire the percentage of disability is calculated.

Instructions and the questionnaire:

This questionnaire has been designed to give the doctor information on how your back pain has affected your ability to manage in everyday life. Please answer every section, and mark in each section only the one box which applies to you. We realize you may consider that two of the statements in any section relate to you, but please just mark the box which most closely describes your problem.

Section 1: Pain intensity

- ○ I can tolerate the pain I have without having to use painkillers.
- ○ The pain is bad but I manage without taking painkillers.
- ○ Painkillers give complete relief from pain.
- ○ Painkillers give moderate relief from pain.
- ○ Painkillers give very little relief from pain.
- ○ Painkillers have no effect on the pain and I do not use them.

Section 2: Personal care (washing, dressing, etc.)

- ○ I can look after myself normally without causing extra pain.
- ○ I can look after myself normally but it causes extra pain.
- ○ It is painful to look after myself and I am slow and careful.
- ○ I need some help but manage most of my personal care.
- ○ I need help every day in most aspects of self-care.
- ○ I do not get dressed, wash with difficulty and stay in bed.

Section 3: Lifting

- ○ I can lift heavy weights without extra pain.
- ○ I can lift heavy weights but it gives extra pain.
- ○ Pain prevents me from lifting heavy weights off the floor, but I can manage if they are conveniently positioned, e.g. on a table.
- ○ Pain prevents me from lifting heavy weights but I can manage light to medium weights if they are conveniently positioned.

- ○ I can lift only very light weights.
- ○ I cannot lift or carry anything at all.

Section 4: Walking

- ○ Pain does not prevent me walking any distance.
- ○ Pain prevents me walking more than 1 mile.
- ○ Pain prevents me walking more than 1/2 mile.
- ○ Pain prevents me walking more than 1/4 mile.
- ○ I can only walk using a stick or crutches.
- ○ I am in bed most of the time and have to crawl to the toilet.

Section 5: Sitting

- ○ I can sit in any chair as long as I like.
- ○ I can sit in my favorite chair as long as I like.
- ○ Pain prevents me from sitting more than 1 hour.
- ○ Pain prevents me from sitting more than 1/2 an hour.
- ○ Pain prevents me from sitting more than 10 minutes.
- ○ Pain prevents me from sitting at all.

Section 6: Standing

- ○ I can stand as long as I want without extra pain.
- ○ I can stand as long as I want but it gives me extra pain.
- ○ Pain prevents me from standing for more than 1 hour.
- ○ Pain prevents me from standing for more than 30 minutes.
- ○ Pain prevents me from standing for more than 10 minutes.
- ○ Pain prevents me from standing at all.

Section 7: Sleeping

- ○ Pain does not prevent me from sleeping well.
- ○ I can sleep well only by using tablets.
- ○ Even when I take tablets I have less than 6 hours sleep.
- ○ Even when I take tablets I have less than 4 hours sleep.
- ○ Even when I take tablets I have less than 2 hours sleep.
- ○ Pain prevents me from sleeping at all.

Section 8: Sex life

- ○ My sex life is normal and causes no extra pain.
- ○ My sex life is normal but causes some extra pain.
- ○ My sex life is nearly normal but is very painful.
- ○ My sex life is severely restricted by pain.
- ○ My sex life is nearly absent because of pain.
- ○ Pain prevents any sex life at all.

Section 9: Social life

- ○ My social life is normal and gives me no extra pain.
- ○ My social life is normal but increases the degree of pain.
- ○ Pain has no significant effect on my social life apart from limiting my more energetic interests, eg dancing, etc.
- ○ Pain has restricted my social life and I do not go out that often.
- ○ Pain has restricted social life to my home.
- ○ I have no social life because of pain.

Section 10: Travelling

- ○ I can travel anywhere without extra pain.
- ○ I can travel anywhere but it gives me extra pain.
- ○ Pain is bad but I manage journeys over two hours.
- ○ Pain restricts me to journeys of less than one hour.
- ○ Pain restricts me to short necessary journeys below 30 minutes.
- ○ Pain prevents travel except to the doctor or hospital.

Addendum

1. Arain A., Vandevenne J., De Peuter B., Smits J., Weyns F., Palmers Y., Case report: a glomus tumor of the cavernous sinus, Department of Medical Imaging, Campus Sint-Jan, Ziekenhuis Oost-Limburg, Schiepse bos 6, 3600 Genk, Belgium, accepted for publication in Radiological Documents and 'Belgische tijdschrift voor radiologie' (JBR-BTR)

Images

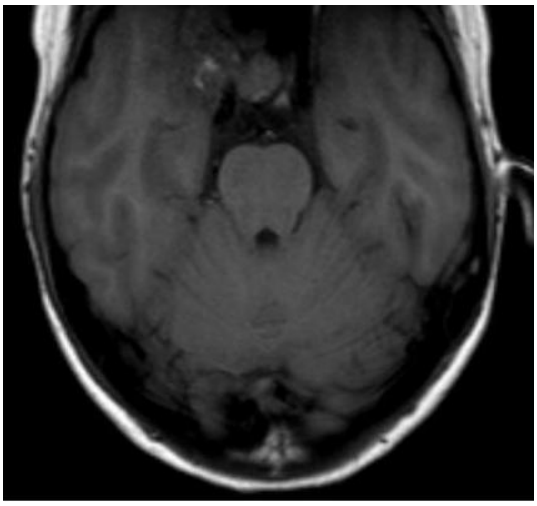


Fig. 1

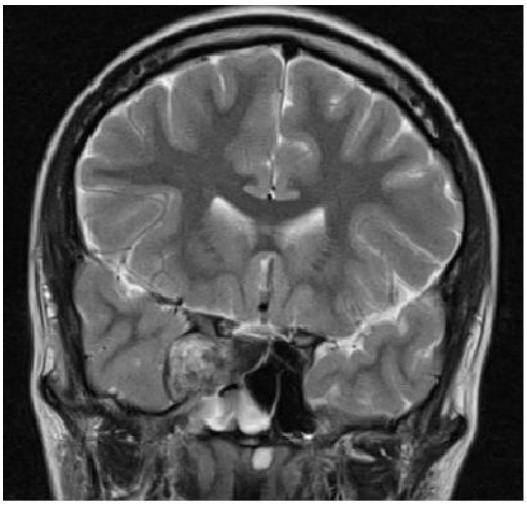


Fig. 2

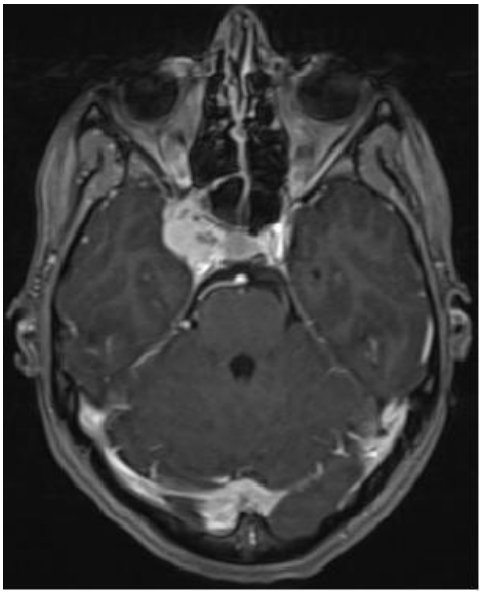


Fig. 3

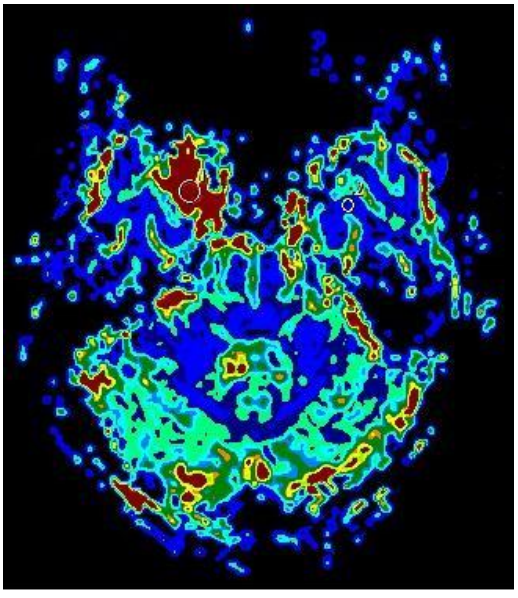


Fig. 4

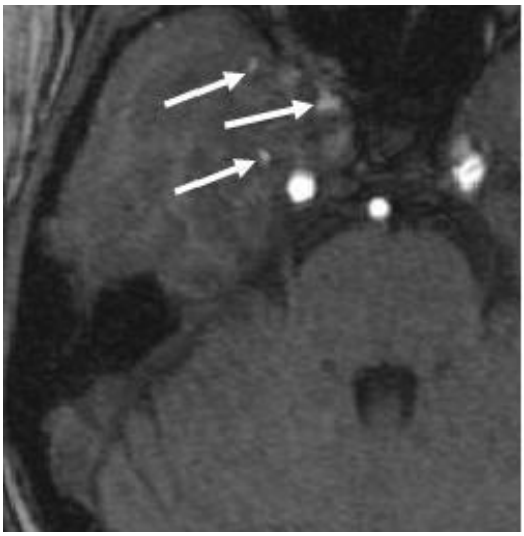


Fig. 5

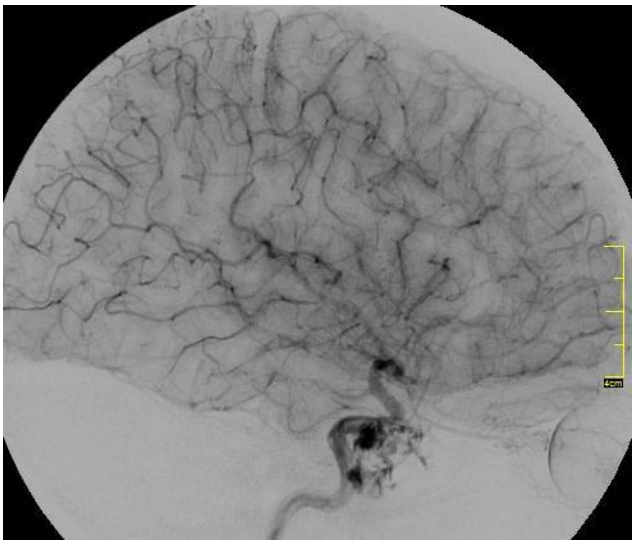


Fig. 6

Clinical History

A 15-year-old girl presented in a Dutch hospital with right-sided trigeminal neuralgia. MR imaging showed a mass lesion in the right cavernous sinus (Fig. 1, 2). The lesion was characterized by a heterogenic or "salt and pepper" appearance. Working differential diagnosis in the Dutch hospital was a meningioma or a schwannoma. The patient was referred to the neurosurgery department of our hospital, and resection of the lesion was planned.

At surgery, the lesion presented as a subdural bulge surrounded by swollen venous structures. The incision of the dura resulted in profuse hemorrhage of arterial origin, and hemostasis was obtained with difficulty. The tumor showed a fibrillar structure and a strong arterial vascularization which was not concordant with a schwannoma. No further exploration of the lesion was performed, and no biopsy was obtained.

To clarify the unexpected surgical findings and to reach a diagnosis without biopsy, pre-operative MR images were reviewed. At perfusion MRI (Fig. 3), the relative cerebral blood volume (rCBV) in the lesion was nine-fold increased compared to normal brain parenchyma, suggesting strong angiogenesis. The TOF MR images demonstrated arterial flow within the lesion (Fig. 4). A postoperative digital subtraction-angiography (DSA) (Fig. 5) demonstrated that the tumor is supplied both by the internal and external (recurrent sphenopalatine branch of internal maxillary artery) carotid artery. The lesion did not take up FDG on the PET scan. Laboratory results showed increased catecholamines in the urine.

Imaging findings

Figure 1: Axial T1-weighted, MR image of the brain. Lesion located in the right cavernous sinus.

Figure 2: Coronal T2-weighted MR image. Heterogeneous lesion in the right cavernous sinus.

Figure 3: Axial contrast enhanced MR image. Strong contrast enhancement of the lesion.

Figure 4: rCVB map of perfusion MRI showing nine-fold increased rCVB in the lesion.

Figure 5: Axial TOF-MR image showing presence of arterial flow (white arrows) within the lesion.

Figure 6: Digital subtraction-angiography (DSA) image demonstrating strong arterial vascularization of the lesion arising both from internal and external carotid artery branches.

The most likely diagnosis is a large, hypervascular paraganglioma or glomus tumor of the cavernous sinus. The strong arterial vascularization as seen on TOF MR images, DSA and surgery together with the 'salt and pepper' appearance on T2-weighted MR images, and the presence of increased catecholamine levels in the urine are the arguments in favor of this diagnosis.

Comment

Paragangliomas are highly vascular neoplasms that arise from paraganglia, which serve as chemoreceptors responsible for monitoring changes in blood pH, carbon dioxide concentration, and rate of blood flow. Approximately 90% of the paragangliomas occur in the adrenal gland (pheochromocytoma), the largest collection of chromaffin cells. The remaining 10% arise from extra-adrenal sites. Most of the extra-adrenal paragangliomas arise in the abdomen (85%), with some in the thorax (12%), and some less commonly in the head and neck area (3%). Paragangliomas of the head and neck (HNP) are rare tumors of neural crest origin, comprising about 0.6% of head and neck tumors and about 0.03% of all tumors. They may occur along the paraganglia's pathway of embryologic migration which extends from the skull base to the pelvic floor.

Radiologic evaluation of glomus tumors aids in differentiating them from other neoplastic processes. Paragangliomas usually show a hyperintense signal on T2-weighted magnetic resonance images (MRI) and a distinct contrast enhancement on T1-weighted images. In larger lesions, On T1-weighted a "salt and pepper" appearance of the tumor matrix on T1- and/or T2-weighted images is characteristic. In this case, the lesion showed a "salt and

pepper" appearance on T2 weighted images. Prominent arterial vasculature associated with the main lesion may also be seen on TOF sequence of MR images. DSA is also useful in the diagnosis giving information about vascularity and feeder vessels. CT is useful as it presents a very sensitive imaging procedure for the diagnosis of bony destructions by the paragangliomas often seen in jugular and tympanic paragangliomas. Histological evaluation is the most reliable way to confirm the diagnosis of a paraganglioma. Microscopically irrespective of the site, paragangliomas have a common appearance. The tumor contains all three elements normally present in a paraganglion (i.e., type I, chief cells or granular cells; and type II, the supporting or sustentacular cells and numerous capillaries).

Paragangliomas are sometimes associated with the secretion of several neuropeptide hormones, such as adrenocorticotropic hormone, serotonin, catecholamine, and dopamine. The incidence of catecholamine secretion is approximately 4%. Frequently, these tumors have a low level of secretion that is not recognized clinically.

The treatment options for head and neck paragangliomas include surgical resection, conventional radiation therapy, stereotactic radiosurgery, permanent embolization or a combination of those modalities. The dose commonly recommended for radiation therapy is 45 to 50 Gy; in stereotactic radiosurgery 12 to 18 Gy are usually applied. In this case the surgical resection is not performed to avoid hemorrhagic complications. Our patient was referred for radiotherapy.

Key words

Cavernous sinus, paraganglioma, glomus tumor

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2. Arain A., Vandevenne J., Meylaerts L., Gelin G., Vanormelingen L., Pictorial review: MR imaging of acquired dural tears in the spine, Department of Medical Imaging, Campus Sint-Jan, Ziekenhuis Oost-Limburg, Schiepse bos 6, 3600 Genk, Belgium, Department of Morfology, Hasselt University

Introduction

Dural tears in the spine may result in leakage of cerebrospinal fluid (CSF) into the extradural space. Such CSF leakages may pass unnoticed, but may be a cause of low-back pain, radiculopathy, subcutaneous swelling, posture related headaches and other sensory or motor dysfunctions. Some causes of acquired dural tears include surgical interventions of the spine, percutaneous interventions involving the spinal canal, trauma of the spine or limbs, and degenerative changes of the vertebrae. The patient's clinical condition and the underlying cause of the dural leak determine choice of treatment. Magnetic resonance (MR) imaging is an excellent modality to diagnose these dural tears and to suggest the underlying cause. The purpose of this pictorial essay is to demonstrate typical MR findings of acquired dural tears in the spine.

Postoperative dural tears

Extradural collections of CSF are uncommon and may result from iatrogenic, traumatic, spontaneous or idiopatic and congenital causes (1). By far the most common cause are iatrogenic events. Different surgical procedures such as laminectomy (Fig. 1), discectomy, and corpectomy have been associated with the development of postoperative dural tears or pseudomeningoceles (2; 3; 4).

CSF leaks are often asymptomatic, but patients may present with low-back pain, radiculopathy, subcutaneous swelling (5; 6; 7; 8; 9). These patients may also present with symptoms seen in those with spontaneous intracranial hypotension such as photophobia, cranial nerve palsies, and tinnitus (10; 11). Larger CSF leaks may lead to intracranial hypotension associated with the typical symptom of posture-related headache, which occurs or worsens in upright position and improves or disappears in recumbent position (12). Patients may complain of cervical or occipital pain with or without nausea and vomiting while in a standing position.

The diagnostic study of choice is MRI because of its ability to visualize the soft tissues in the spinal canal. Pseudomeningoceles are focal extradural CSF collections as a consequence of dural tears; the presentation on MR imaging may be reminiscent of congenital meningoceles (CSF fluid collection lined by meninges and having a focal or wide connection to the contents of the thecal sac). However, pseudomeningoceles are surrounded only by compressed soft tissues lacking any meningeal lining (hence, the prefix ‘pseudo-‘). Signal intensities of pseudomeningocele resemble CSF while the surrounding compressed soft tissues may demonstrate slight rimlike (smooth) enhancement. This may differentiate pseudomeningoceles from postoperative abscesses which often demonstrate thick-walled irregular enhancement. MRI is able to show the location, extent, and internal characteristics of the CSF leak and may demonstrate the level of communication with the thecal sac (13; 14) (Fig. 1, 2).

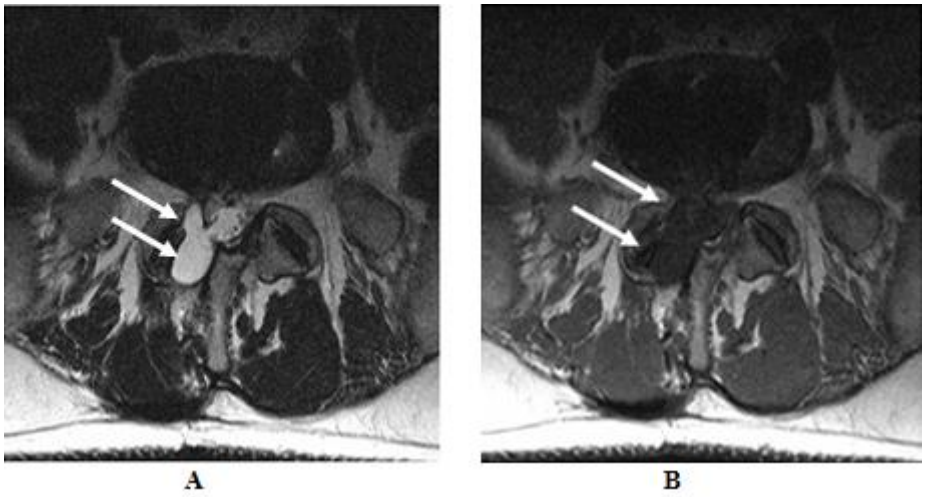

Figure1: Axial T2- (A) and T1-weighted (B) image Small pseudomeningocele (white arrows) after laminectomy. Note the fluid collection laterally to the thecal sac, with a clear connection to the CSF within the thecal sac representing the postoperative dural tear.

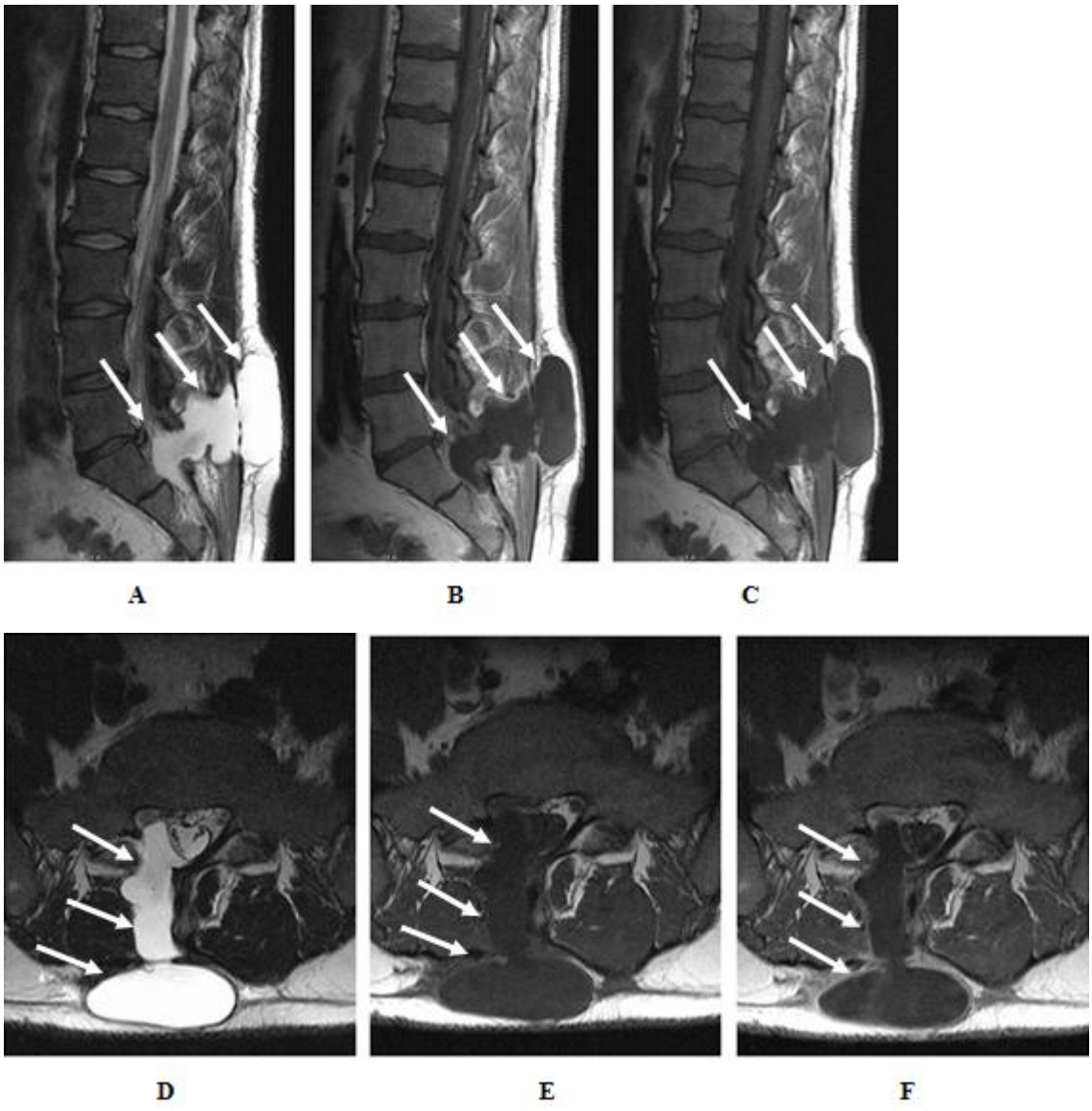

Figure 2: Sagittal (A, T2-weighted, B, T1-weighted, C, T1-weighted gadolinium enhanced) and axial (D, T2-weighted, E, T1-weighted, F, T1-weighted gadolinium enhanced) images of a large pseudomeningocele after laminectomy. Large fluid collection (white arrows) starting laterally of the thecal sac and extending posteriorly through the surgical trajectory in the paraspinal muscles into the subcutaneous fat.

Treatment options for these CSF leaks include conservative management, placement of an epidural blood patch, lumbar subarachnoid drainage, and surgery. Close observation and bedrest are frequently the first steps in the conservative management of pseudomeningoceles and CSF fistulas (15; 16). Epidural blood patches has also been used successfully to treat postoperative CSF fistulas and pseudomeningoceles (17; 18; 19). Surgical repair of the dura is the definitive treatment for CSF fistulas and pseudomeningoceles. Indications for surgery include failure of conservative measures or progressive radicular or signs and symptoms of myelopathy.

Post- epidural puncture CSF leak

Postpuncture CSF leak (Fig. 3) known as post-dural puncture headache (PDPH) is caused by iatrogenic events such as lumbar puncture, discography and inadvertent dural puncture after placement of an epidural catheter (20; 21; 22; 23).

Typical symptoms of PDPH are photophobia, nausea, vomiting, neck stiffness, tinnitus, diplopia, dizziness and often a severe head ache (23).

CSF seaping out of the dural pinpoint defect may not form a focal collection, but rather dissipate circumferentially around the thecal sac and extend cranially and caudally. This way of extradural CSF spread has two consequences. Firstly, the location of the dural defect is difficult to retrieve (no focal collection of CSF at the site of the dural defect). Secondly, the occupied extradural space is a large virtual space extending from the sacrum to the cranial vault that may lead to loss of large amounts of CSF into the extradural space accounting for intracranial hypotension and for compression of the thecal sac.

MR imaging of extradural CSF diffusely spread in the spinal canal has typical features. The hallmark is presence of fluid signal on both the internal and external side of the thecal sack, visible as discrete hypo-intense line surrounding the myelum or cauda equina. The extradural CSF collection may result in compression of the thecal sac, and as a consequence the hypointense line may be closer to the myelum than expected, the thecal sack and myelum may be displaced (anteriorly or posteriorly),and/ or the nerve roots exiting the myelum may become more prominently visible (image resembling an eye) (Fig 3). CSF pulsation artefacts may be visible in the extradural CSF. It is important to recognize that the CSF is in extradural location. Therefore, one should look for the hypo-intense line representing the dura mater on axial T2-weighted sequences with fat saturation.

Apart from the extradural CSF collection in the spine, typical imaging signs of intracranial hypotension may be seen including diffuse dural enhancement, with evidence of a sagging brain, descent of the brain, optic chiasm, and brain stem, obliteration of the basilar cisterns, and enlargement of the pituitary gland (24). MR images of the brain are not shown in this review.

A B

Figure 3: MR images of CSF leak in a young woman after epidural catheter placement just before partus. (A) Axial T2- weighted images with fat saturation. Thecal sac is closer to the myelum (star) than expected due to the surrounding extradural CSF collection (white arrow). Note crowding of cranial nerves in the thecal sac (striped arrow), seen as black spots around the myelum. The image of the thecal sac and contents resembles an eye. (B) Displacement of thecal sac and myelum (arrow head) far anteriorly. Near absence of CSF within the thecal sac. All the CSF fluid (white arrow) seen posteriorly is in extradural location. Note CSF flow voids in the extradural CSF collection.

To limit the symptoms patients can be treated with theophylline, caffeine, and sumatriptan. Also epidural saline and epidural dextran is used which are thought to increase the epidural and subarachnoid pressures and restore normal CSF dynamics. An epidural blood patch (EBP) most commonly is the definite treatment (preferably at the location of the dural tear, or if randomly applied preferably at the dorsolumbar level). EBP shows apparent benefits and there are two theories which explain the underlying mechanism. The first theory is that the autologous blood after epidural injection, forms a clot, which patches the hole. The second theory suggests that the injected blood volume increases the CSF pressure in the epidural space, which results in symptoms relief through reduction in traction of pain sensitive meningeal structures (23).

Nerve root avulsion

The brachial and lumbosacral plexus are anchored between two mobile parts, thus any forceful distraction can stretch either of them and result in nerve root avulsion. Injuries from blunt trauma account for the majority of nerve root avulsion cases. Avulsion of the nerve roots may be accompanied by a tear of one or more dural sleeves resulting in the formation of nerve root pseudomeningoceles (Fig. 4) (25).

Patients may suffer from burning or stinging pain that radiates down one of the limbs and the motor symptoms may range from weakness to complete paralysis (26).

MR imaging will demonstrate the pseudomeningoceles as one or more cylindric CSF collections at the expected location of the nerve roots. The nerve root is usually not visible within the pseudomeningocele. Heavily T2-weighted images preferably with fat saturation or STIR images are most useful (27).

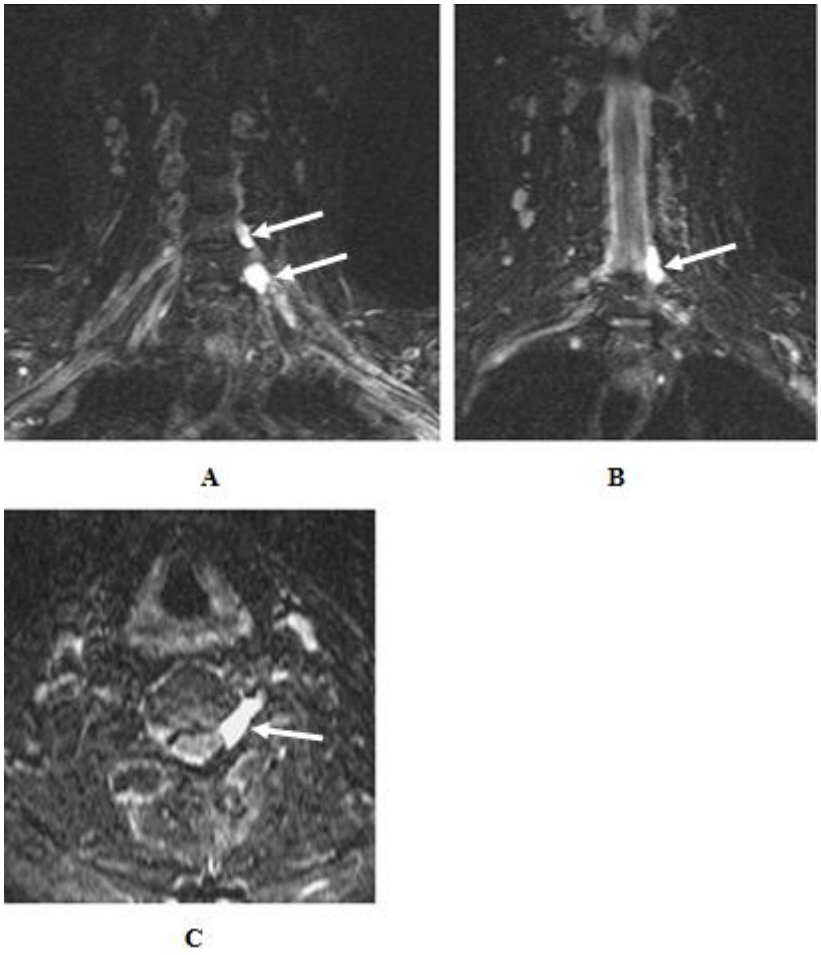

Figure 4: MR images, using short inversion time inversion recovery (STIR) sequence, of post-traumatic nerve root avulsion after a motor-vehicle accident. (A, B) Coronal STIR image showing pseudomeningoceles (white arrows) at the levels C5-C6 and C6-C7. These pseudomeningoceles demonstrate that there is a rupture of the dural sleeve suggestive of nerve root avulsion. (C) Axial STIR image showing CSF collection (white arrow) filling the space which is normally the location of the nerve root leaving the spinal cord.

The treatment method in the case of nerve root avulsion depends on the type of lesion. Treatment of postganglionic (nerve rupture) lesions include nerve grafting and nerve transfer (neurotization) techniques in which intra- and extraplexal donor nerves may be used. In the

case of preganglionic lesions (root avulsion) extraplexal neurotization of key muscles or functioning free muscle transfer (FFMT) is applied (26).

Idiopathic spinal cord herniation

Idiopathic spinal cord herniation is a rare condition which shows a spontaneous displacement of thoracic cord through an anterior dural defect. Almost all spontaneous herniations develop through ventral or ventrolateral dural defects in the upper thoracic or midthoracic region (28; 29). The predominant theory lauds that the naturally ventral positioned thoracic cord, becomes adherent and pushed through (or sucked in) a dural defect due to the cardiac and pulmonary actions as well as CSF pulsations (30; 31). These dural defects sometimes can be related to prominent osteofytes developing on the posterior side of the vertebral endplates.
Symptoms of idiopathic spinal cord herniation progress slowly over years. In more than 70% of the patients, Brown-Séquard syndrome or spastic asymmetric paraparesis is found. This syndrome is characterized by ipsilateral paresis and loss of vibratory and position sense, combined with contralateral loss of pain and temperature sensation. This syndrome results from damage of the lateral funiculus of the spinal cord. In some cases impairment of bladder and/or bowel function is noticed (30; 32).

The typical feature of spinal cord herniation on MR imaging is an anteriorly kinking of the spinal cord with dorsal widening of the subarachnoid space (Fig. 5) (33; 34). Cord displacement is generally limited to one or two thoracic spine segments, most commonly between the levels of the T4 and T7 vertebrae (35; 36). The dorsal widening of the subarachnoid space should not be confused for an arachnoid cyst. Occasionally, an anterior extradural masslike area of signal intensity similar to that of the spinal cord may be seen, representing the herniated spinal cord.

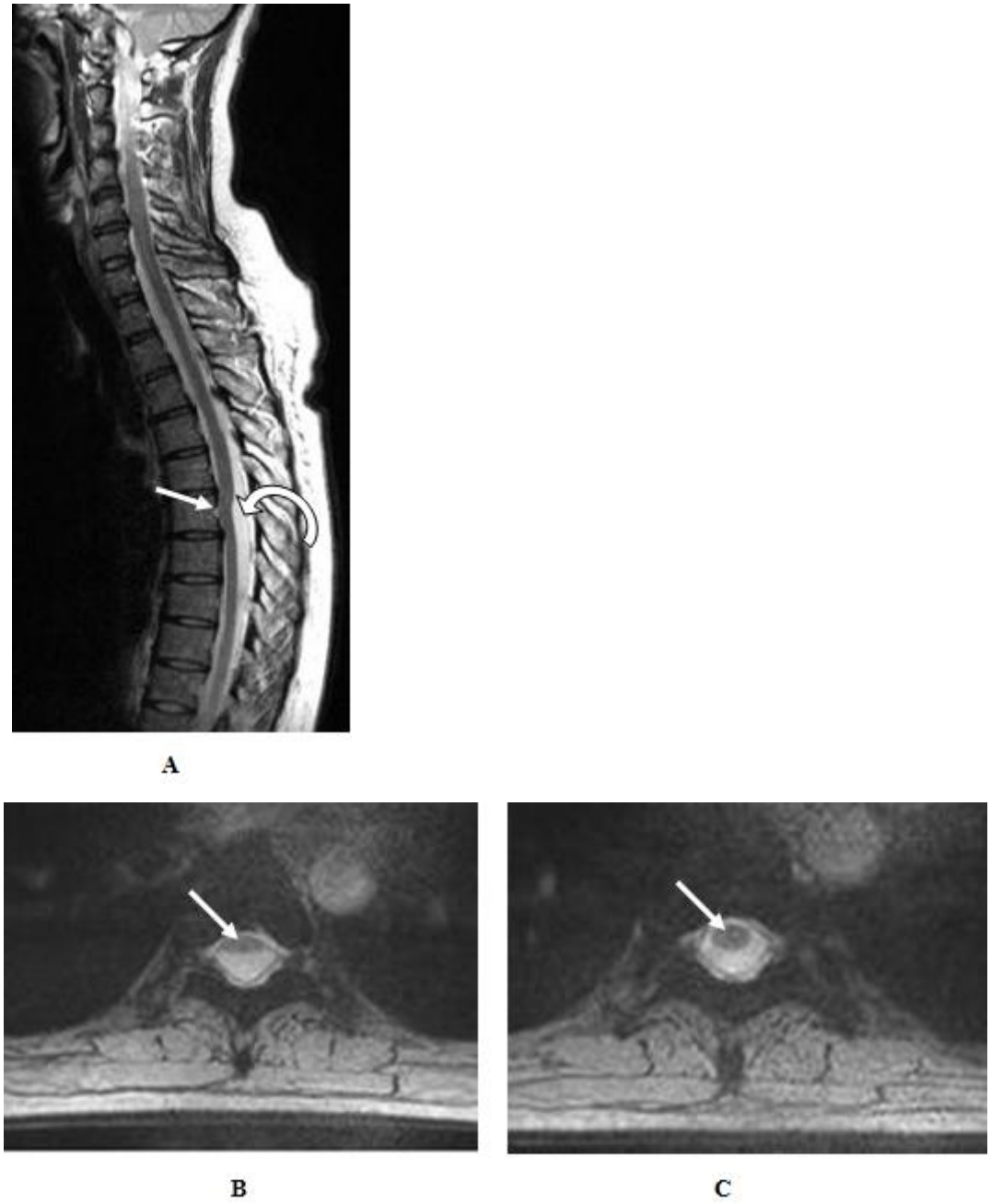

Figure 5: MR images of spontaneous spinal cord herniation. (A) Sagittal T2-weighted image showing a focal anterior displacement (kinking) of the cord (white arrow) at the T6 vertebral level causing a widening of the dorsal subarachnoid space (curved arrow). (B) Axial T2-weighted image at the level of the spinal cord herniation showing flattened spinal cord (white arrow) adherent to the ventral dura. (C) Axial T2-weighted image at a normal level showing the spinal cord (white arrow) in its normal oval shape.

In conclusion, acquired dural tears in the spine may be caused by traumatic, postoperative, post puncture of idiopathic events and present with specific features on MR imaging. Knowledge of these features and the clinical presentation is key to make the specific diagnosis.

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