

Clinical Significance of Protrusion Edge Enhancement Using Contrast-Enhanced Magnetic Resonance Imaging in The Conservative Treatment of Giant Lumbar Disc Herniation: A Prospective Observational Study

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Research article

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Abstract

Background: Contrast-enhanced lumbar spine magnetic resonance imaging (MRI) was used to predict the efficacy of conservative treatment of giant lumbar disc herniation.

Methods: From June 2017 to June 2019, 30 patients with giant lumbar disc herniation with positive and negative bull's eye signs on contrast-enhanced lumbar spine MRI were assessed to measure differences in the rate of intervertebral disc herniation, rate of protrusion absorption, treatment effect, protrusion rate, and curative effect according to the lumbar Japanese Orthopedic Association (JOA) score before and after treatment.

Results: Thirty patients with positive and negative bull's eye signs (36 men and 24 women) aged 19 to 58 years (mean, 36.37 ± 9.56 years) were included. All patients were followed up for more than 1 year, and at least one MRI review was conducted within 1 year of treatment. The results of the first and final MRI examinations were compared. The protrusion rate was $82.16\% \pm 14.58\%$ before treatment and $32.20\% \pm 30.80\%$ after treatment, and the absorptivity of the protrusion was $59.48\% \pm 38.62\%$. There was no statistically significant difference in the general data before treatment between the positive and negative groups ($P > 0.05$). After treatment, the protrusion rate in the positive and negative bull's eye sign groups was $14.41\% \pm 14.37\%$ and $49.99\% \pm 32.70\%$, respectively ($P < 0.05$). The absorptivity in the positive and negative bull's eye sign groups was $83.09\% \pm 15.54\%$ and $35.87\% \pm 40.49\%$, respectively ($P < 0.05$). There was no statistically significant difference in the JOA score between the two groups before treatment ($P > 0.05$); however, there was a statistically significant difference in the JOA score between the two groups at 3 months ($P < 0.05$) and 1 year ($P < 0.05$) after treatment.

Conclusions: Conservative treatment of giant lumbar disc herniation has a satisfactory clinical effect. Contrast-enhanced MRI can be used to predict the resorption of giant lumbar disc herniation. Protrusion resorption is more likely to occur in patients with than without a bull's eye sign.

Trial registration: Chinese Clinical Trial Registry (No. ChiCTR1900022377). Retrospectively registered 08 April 2019.

Background

After conservative treatment, the size of a lumbar disc herniation may decrease for a long period of time with improvements in symptoms and function [1]. Approximately 20–60% of patients with giant lumbar disc herniation develop herniated disc resorption after conservative treatment [2, 3]. Panagopoulos et al. [4] reported that in patients with lumbar disc protrusion, magnetic resonance imaging (MRI) within 1 year showed that 15–93% of herniated discs decreased in size or disappeared. For patients with nerve root compression, MRI within 1 year showed that 17–91% of herniated discs decreased in size or disappeared. Giant lumbar disc herniation itself is not an indication for surgery [5]; however, symptoms of pain and nerve injury necessitate surgical treatment. Clinical management of patients with indications for surgery who have a risk of resorption after conservative treatment is very difficult.

Contrast-enhanced MRI can extract substantial information from images to excavate advanced and deep features, which has great value for the diagnosis of spinal diseases and has been widely used to predict treatment effect and prognosis [6, 7]. Contrast-enhanced MRI in spinal surgery has provided relatively in-depth information in tumor studies; however, other studies are still in their preliminary stages. Studies have shown that enhanced MRI in patients with spinal disease may be more accurate than conventional MRI in identifying the blood supply [8, 9]. Circular enhancement of a herniated disc on enhanced MRI is called the bull's eye sign [10]. If this characteristic feature appears on enhanced MRI, the rate of resorption is higher and conservative treatment is thus preferred, especially for larger lumbar intervertebral disc protrusions. If the patient exhibits no progressive impairment of movement or symptoms of cauda equina syndrome, observation can be performed for 3 to 6 months. Macki et al. [11] emphasized that contrast-enhanced MRI should be used as a prediction method and a means to evaluate the efficacy of free disc resorption. Kawaji et al. [12] studied 65 patients with large lumbar disc herniation showing the bull's eye sign on enhanced MRI; 21 patients underwent conservative treatment and 44 underwent surgical treatment. Among the patients treated conservatively, contrast-enhanced MRI was performed before and after treatment at the onset and remission of symptoms. The results showed that the protrusion volume decreased and that resorption occurred after conservative treatment, indicating that enhanced MRI is an effective method of predicting resorption.

However, no studies have been performed to assess the predictive effect of lumbar enhanced MRI on conservative treatment of giant lumbar disc herniation, especially herniation showing the bull's eye sign. We performed a rigorous prospective observational study to observe and compare the change in herniated disc size and the clinical treatment efficacy in patients with giant lumbar disc herniation and to investigate the clinical prognostic significance of lumbar enhanced MRI in conservative treatment.

Materials And Methods

Study design and population

This was a rigorous prospective observational study. Sixty patients with giant lumbar disc herniation treated at the outpatient clinic of Suzhou TCM Hospital Affiliated to Nanjing University of Chinese Medicine from June 2017 to June 2019 were enrolled. According to imaging results interpreted by two spinal surgeons, the patients were divided into the positive bull's eye sign group and the negative bull's eye sign group (30 patients in each group) according to the imaging results interpreted by two spinal surgeons. The change in size of the herniated disc before and after treatment and the clinical treatment efficacy were observed and compared, and the predictive significance of lumbar enhanced MRI in the conservative treatment of giant lumbar disc herniation was studied.

Inclusion and exclusion criteria

The inclusion criteria were (1) fulfillment of the diagnostic criteria for lumbar disc herniation, consistency of the disc herniation segments with the positioning of symptoms (including lower back pain accompanied by continuous severe lower limb pain, muscle weakness, and lower limb paresthesia), and

a positive straight leg raise test [13]; (2) protrusion rate of $\geq 50\%$ on lumbar MRI and patient willingness to undergo conservative treatment and contrast-enhanced MRI; and (3) availability of medical history and current condition information and willingness to complete follow-up as required.

The exclusion criteria were (1) a history of spinal surgery, scoliosis, spinal cord injury, tuberculosis, tumor, lumbar osteoporotic fracture, severe degeneration, lumbar spondylolisthesis, or cauda equina syndrome (associated with progressive motor nerve injury signs and symptoms) and (2) conservative treatment within 1 year and aggravation of symptoms by surgical treatment.

Treatment protocol

The conservative treatment options included one or more of the following: (1) absolute bed rest for 2 to 6 weeks; (2) administration of the traditional Chinese medicine preparation Xiaosui Huahe, including roasted *Astragalus* (20 g), raw *Astragalus* (20 g), *Angelica sinensis* (10 g), *rhizoma Atractylodis macrocephalae* (10 g), *Ligusticum wallichii* (10 g), pawpaw (10 g), *radix Stephaniae tetrandrae* (10 g), *Lumbricus* (10 g), *Brassica alba boiss* (6 g), leech (6 g), and *radix Clematidis* (10 g) decocted in water and taken orally for 8 to 16 weeks [14]; and (3) administration of celecoxib at 0.1 g twice daily if pain was not relieved within the first 1 to 2 weeks following an acute episode. The indications for surgical treatment were (1) failure of conservative treatment for 3 to 6 months, (2) progressive exacerbation of root symptoms, (3) cauda equina syndrome at any time during treatment, and (4) an unchanged or increased protrusion size on MRI.

Imaging

The protrusion percentage and absorption percentage were calculated in accordance with the method described by Yu et al. [14] and Benson et al. [15]. The upper vertebral body wall after the halfway point of the trailing edge to the vertebral canal length was set as a (spinal canal diameter), the prominence peak to the vertebral canal wall distance was set as b , and the protrusion percentage was calculated as follows: $[(a - b) \div a] \times 100\%$ (Figure 1). The absorption percentage was calculated as follows: (protrusion percentage before treatment - protrusion percentage after treatment) \div protrusion percentage before treatment. The bull's eye sign [10] was defined as protrusion edge enhancement on MRI. Contact between the free disc and the epidural space caused an autoimmune reaction, leading to inflammation.

Granulation tissue developed around the herniation, which manifested as ring enhancement, while the central free disc was not enhanced; these changes presented as the bull's eye sign (Figure 2). The bull's eye sign was considered absent if no protrusion edge enhancement was observed on MRI (Figure 3).

Statistical analysis

Statistical analyses were performed using SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA). Continuous data are presented as mean \pm standard deviation, and categorical data are presented as frequency. The paired-samples t test was used for intra-group comparisons, and the independent-samples

t test was used for inter-group comparisons. The X^2 test was used for comparison of count data. A P value of <0.05 was considered statistically significant.

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki (World Medical Association) and the International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS). This study was reviewed and approved by the Ethics Committee of Suzhou Hospital of Traditional Chinese Medicine (approval number 2020-LYP-034).

Results

General data and statistical analysis

Sixty patients with giant lumbar disc herniation underwent more than 1 year of conservative treatment and continuous follow-up. All patients had at least one MRI review within 1 year of treatment, and the results of the first and final MRI examinations were compared. Thirty-six men and 24 women ranging in age from 19 to 58 years (36.37 ± 9.56 years) were enrolled in the study. The protrusion rate before treatment was $82.16\% \pm 14.58\%$, the protrusion rate after treatment was $32.20\% \pm 30.80\%$, and the protrusion absorption rate was $59.48\% \pm 38.62\%$. The Japanese Orthopedic Association (JOA) score before treatment was 11.15 ± 3.06 , the JOA score 3 months after treatment was 18.70 ± 3.78 , and the JOA score 1 year after treatment was 23.47 ± 4.14 .

All 60 patients were divided into the positive bull's eye sign group ($n = 30$) and the negative bull's eye sign group ($n = 30$). There were no statistically significant differences in the patients' general pretreatment data, including sex, age, and protrusion rate, between the two groups ($P > 0.05$). After treatment, the protrusion rate in the positive and negative bull's eye sign groups was $14.41\% \pm 14.37\%$ and $49.99\% \pm 32.70\%$, respectively ($P < 0.05$). The absorptivity in the positive and negative bull's eye sign groups was $83.09\% \pm 15.54\%$ and $35.87\% \pm 40.49\%$, respectively ($P < 0.05$) (Table 1).

Table 1. Comparison of sex, age, protrusion rate, and absorption rate

	Cases		Years	Protrusion percentage before treatment (%)	Protrusion percentage after treatment (%)	Absorptivity (%)
	Men	Women				
Bull's eye sign $\square+\square$	17	13	37.80 \pm 8.65	83.74 \pm 13.68	14.41 \pm 14.37	83.09 \pm 15.54
Bull's eye sign $\square-\square$	19	11	34.93 \pm 10.34	80.59 \pm 15.50	49.99 \pm 32.70	35.87 \pm 40.49
test value	$\chi^2 = 0.278$		t = 1.165	t = 0.834	t = -5.455	t = 5.963
P value	0.598		0.29	0.408	0.000	0.000

The JOA scores were compared between the patients in the positive and negative bull's eye sign groups before treatment, 3 months after treatment, and 1 year after treatment. There was no statistically significant difference in the JOA scores of patients in the two groups after treatment (t = -1.057, P > 0.05). However, there were statistically significant differences in the JOA scores between the two groups 3 months after treatment (t = 4.368) and 1 year after treatment (t = 6.234) (P < 0.05) (Table 2).

Table 2. Comparison of JOA scores before treatment and 3 months and 1 year after treatment

	JOA score		
	Before treatment	Three months after treatment	One year after treatment
Bull's eye sign $\square+\square$	10.73 \pm 3.14	20.57 \pm 2.99	26.07 \pm 1.82
Bull's eye sign $\square-\square$	11.57 \pm 2.97	16.83 \pm 3.60	20.87 \pm 4.19
test value	t = -1.057	t = 4.368	t = 6.234
P value	0.295	0.000	0.000

The JOA scores before treatment were compared with the scores at 3 months after treatment and 1 year after treatment. In the positive bull's eye sign group, a significant difference was found between the pretreatment and 3-month post-treatment scores (t = 12.421, P < 0.05) and between the pretreatment and 1-year post-treatment scores (t = 23.148, P < 0.05). Likewise, in the negative bull's eye sign group, a significant difference was found between the pretreatment and 3-month post-treatment scores (t = 6.182, P < 0.05) and between the pretreatment and 1-year post-treatment scores (t = 9.919, P < 0.05) (Table 3).

Table 3. Comparison of JOA scores 3 months and 1 year after treatment versus before treatment

	Time of therapy	JOA score	Test value	P value
Bull's eye sign(+)	Three months after treatment	20.57 ± 2.99	t = 12.421	0.000
	Before treatment	10.73 ± 3.14		
	One year after treatment	26.07 ± 1.82	t = 23.148	0.000
	Before treatment	10.73 ± 3.14		
Bull's eye sign(-)	Three months after treatment	16.83 ± 3.60	t = 6.182	0.000
	Before treatment	11.57 ± 2.97		
	One year after treatment	20.87 ± 4.19	t = 9.919	0.000
	Before treatment	11.57 ± 2.97		

Case description

A representative case of a patient who underwent dynamic follow-up with enhanced MRI is herein presented. A 38-year-old woman with a 1-year history of lumbago with right lower limb pain developed exacerbation of her symptoms for 1 week in January 2018. The patient visited our hospital. She had no symptoms of cauda equina compression, and the hospital recommended surgical treatment; however, the patient refused surgery.

A physical examination showed right paraspinal tenderness (+) of L5/S1 that radiated to the right lower extremity. In the straight leg raise test, the result on the left side was 70° (-) and that on the right side was 60° (+). The muscle strength in both lower extremities was normal, and tactile sensation in the lateral right lower extremity was decreased compared with the contralateral side. The JOA score was 19. Contrast-enhanced MRI showed no obvious high signal around the protrusion, and the bull's eye sign was absent (Figure 4, A1–A5). After 4 months, reexamination showed no remission in clinical symptoms, imaging showed increased protrusion, the JOA score was 19, the patient still refused surgical treatment, enhanced MRI showed no enhancement around the protrusion, and the bull's eye sign was negative (Figure 4, B1–B). After 9 months, the protrusion was not reabsorbed and the pain was improved. The JOA score was 20, enhanced MRI showed no ring enhancement around the protrusion, and the bull's eye sign was negative (Figure 4, C). After 16 months, the lumbago and leg pain had improved, the radiation pain in the right lower extremity was alleviated, the numbness in the right lower extremity had disappeared, the straight leg test result had increased to 80° on the left (-) and 70° on the right (+), the JOA score was 23, MRI showed partial protrusion resorption, enhanced MRI showed a high-signal shadow around the protrusion, and a positive bull's eye sign was observed (Figure 4, D). After 21 months, the lumbago and leg pain had disappeared completely, the straight leg had increased to 80° on the left (-) and 80° on the right (-), the JOA score was 27, enhanced MRI showed resorption of the L5/S1 giant disc herniation, and the bull's eye sign had disappeared (Figure 4, E).

Discussion

The reason for annular enhancement with the bull's eye sign may be related to vascularization of lumbar disc herniation and formation of granulation tissue [16]. Matveeva et al. [17] compared lumbar intervertebral discs from 120 patients with lumbar disc herniation and found that 29% of prolapsed lumbar intervertebral discs had new blood vessels and granulation tissue. In patients with giant lumbar intervertebral disc protrusion, [18]. Thus, circular enhancement appears on enhanced MRI. Shamji et al. [19] observed vascular infiltration inside the nucleus pulposus of the degenerative disc, indicating a compensatory reaction inside the degenerative disc with corresponding new granulation and blood vessel growth. After annulus fibrosus damage or cracking, blood vessels may gradually grow from the periphery of the annulus to the internal nucleus pulposus [20]. Therefore, a larger area of intervertebral disc prolapse is associated with a larger area of blood contact and thus a higher risk of entry of new blood vessels, intervertebral disc shrinkage on imaging, and relief of clinical symptoms [21]. Benoist [22] claimed that most of the prominent nucleus pulposus resorption can occur without surgical intervention. With advances in research into heavy absorption, the underlying mechanism can be summarized as follows. (1) New blood vessel ingrowth occurs, triggering an immune response and phagocytosis of macrophages [23], leading to protrusion. (2) The intervertebral disc is exposed to the blood circulation, which causes an immune response, and the disc is then immunodissolved [24]. (3) In the process of intervertebral disc degeneration, the activity of matrix metalloproteinases significantly increases and the content of enzymes that degrade inhibitory enzymes correspondingly decreases, which accelerates degradation of protruding tissues [25]. (4) Finally, the protruding tissue may demonstrate edema or a hematoma after the acute phase, and the protrusion may become dehydrated or undergo hematoma absorption. Splendiani et al. [26] performed a long-term follow-up of 64 patients who underwent enhanced MRI and found that 25 patients developed ring enhancement. After nonsurgical treatment, 23 patients developed resorption, suggesting that the bull's eye sign indicates protrusion resorption. However, Rätsep et al. [27] found that severe disc herniation enhances regeneration of corresponding blood vessels and thus accelerates disc absorption. After the lumbar disc has herniated through the posterior longitudinal ligament, the disc contacts the blood circulation as a foreign body [30], which may result in vascular growth, immune phagocytosis, and stimulation of resorption provides the premise. The presence of granulation and microvessel growth around the protrusion can be used as an important indicator to judge whether the protrusion is prone to resorption. The production and scope of vascularization are closely related to protrusion reduction, the degree of absorption, and the prognosis [31]. In patients with ring enhancement in the bull's eye sign, enhanced MRI shows a marked inflammatory response at the edge of the protrusion, which leads to severe pain in the acute stages of disease because of the severe peripheral inflammatory response [32]. However, the inflammatory response around these protrusions may contribute to heavy disc absorption [33]. Therefore, for patients with mild pain or high pain tolerance, we recommend minimizing the use of anti-inflammatory and analgesic drugs. An objective analysis should be performed in each patient undergoing clinical treatment, and efforts should be made to combine symptoms with imaging to avoid surgery. Minimally invasive treatment to eliminate pain is also more beneficial to patients than open surgery [34].

Conclusion

Conservative treatment of giant lumbar disc herniation has a satisfactory clinical effect. Contrast-enhanced MRI can predict resorption of giant lumbar disc herniation. Patients with a positive bull's eye sign are more likely to demonstrate protrusion resorption.

Abbreviations

MRI = magnetic resonance imaging, JOA = Japanese Orthopedic Association.

Declarations

Ethics approval and consent to participate

The ethics committee of Suzhou Hospital of Traditional Chinese Medicine approved the study (2020-LYP-034). All patients provided written informed consent prior to participation.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

ZM and PY contributed to the statistical analysis and drafted the manuscript. QF was responsible for the assessments, data collection, and data review. YD performed the statistical analysis and assisted with writing the manuscript. XL assisted with drafting the manuscript. ZY contributed to drafting, editing, and

formatting the manuscript. HJ and JL contributed to drafting and editing the manuscript and data review. All authors read and approved the final manuscript.

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Figures

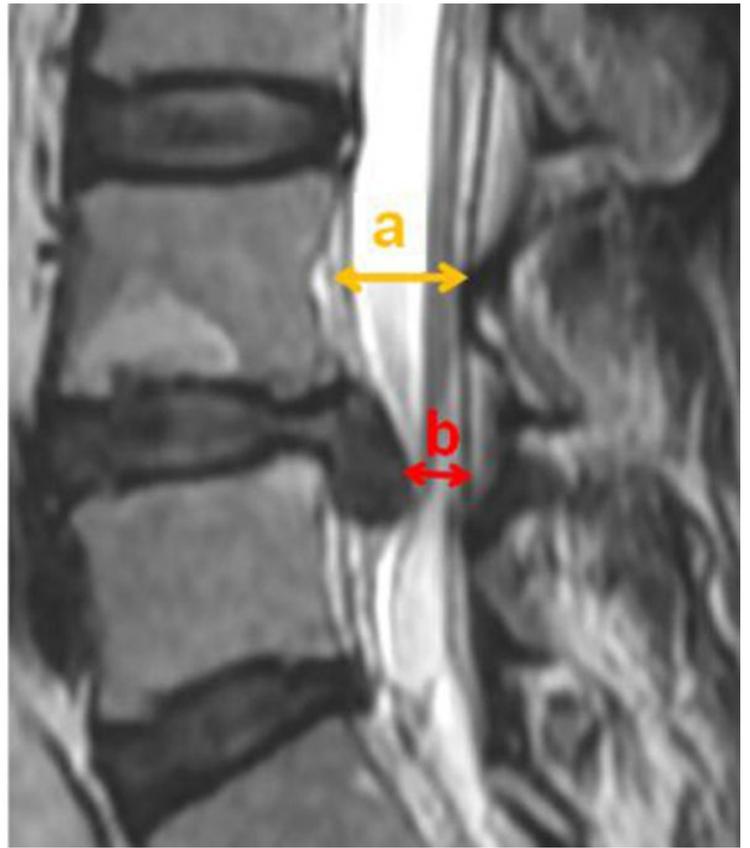
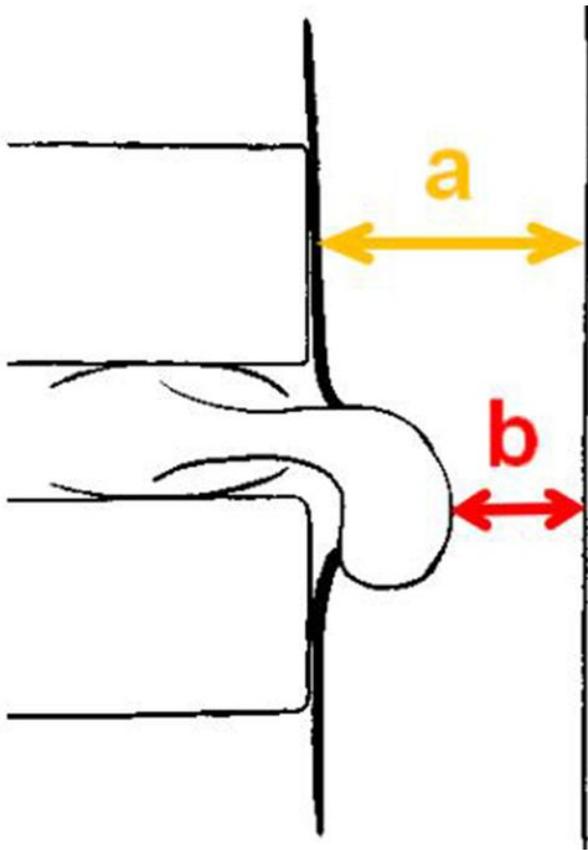


Figure 1

MRI measurement of protrusion percentage. Line a: Length from the midpoint of the posterior margin of the upper vertebral body to the posterior wall of the spinal canal (diameter of the spinal canal). Line b: Distance from the highest point of the protrusion to the posterior wall of the spinal canal; protrusion percentage = $[(a - b) \div a] \times 100\%$.

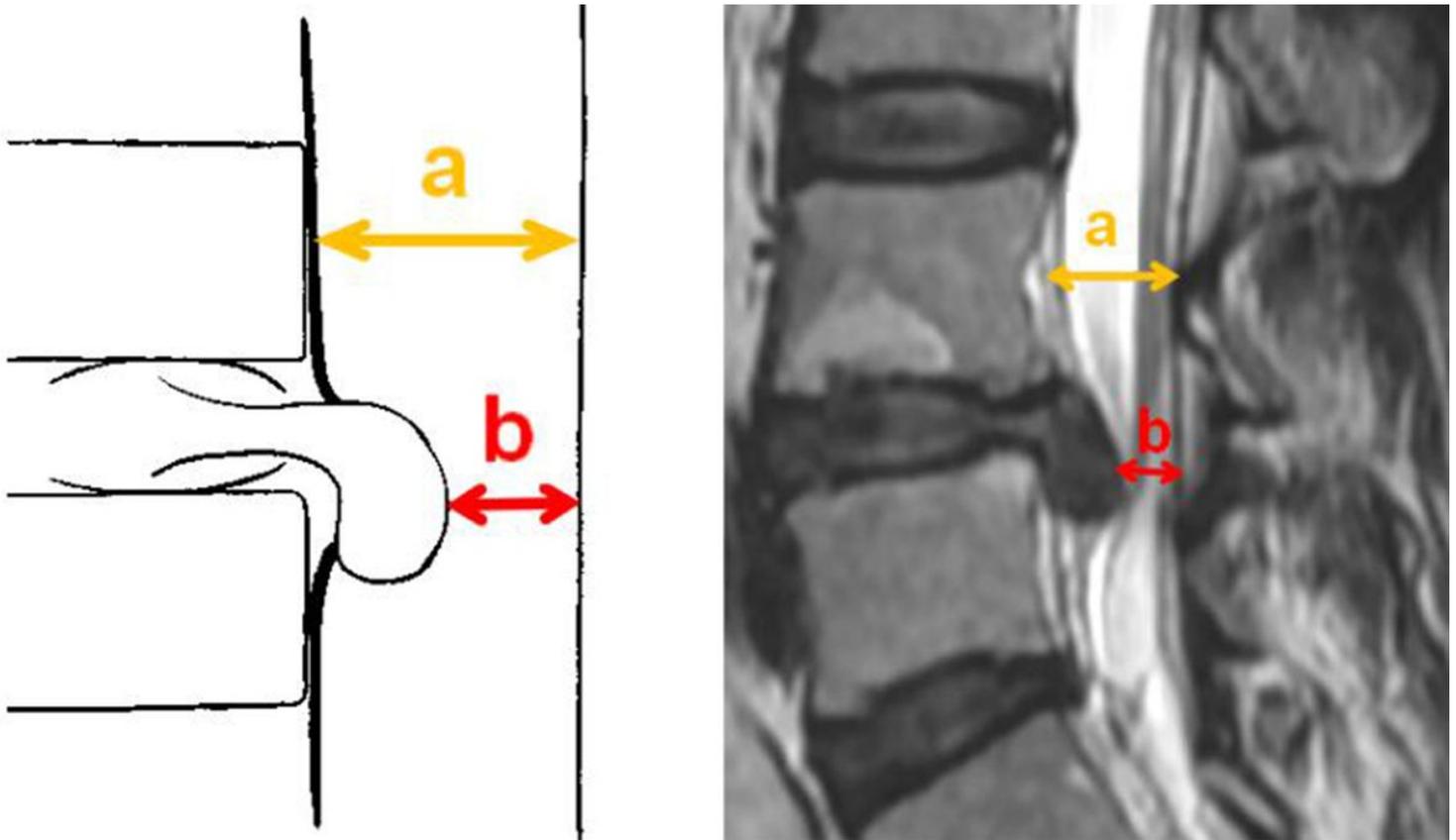


Figure 1

MRI measurement of protrusion percentage. Line a: Length from the midpoint of the posterior margin of the upper vertebral body to the posterior wall of the spinal canal (diameter of the spinal canal). Line b: Distance from the highest point of the protrusion to the posterior wall of the spinal canal; protrusion percentage = $[(a - b) \div a] \times 100\%$.

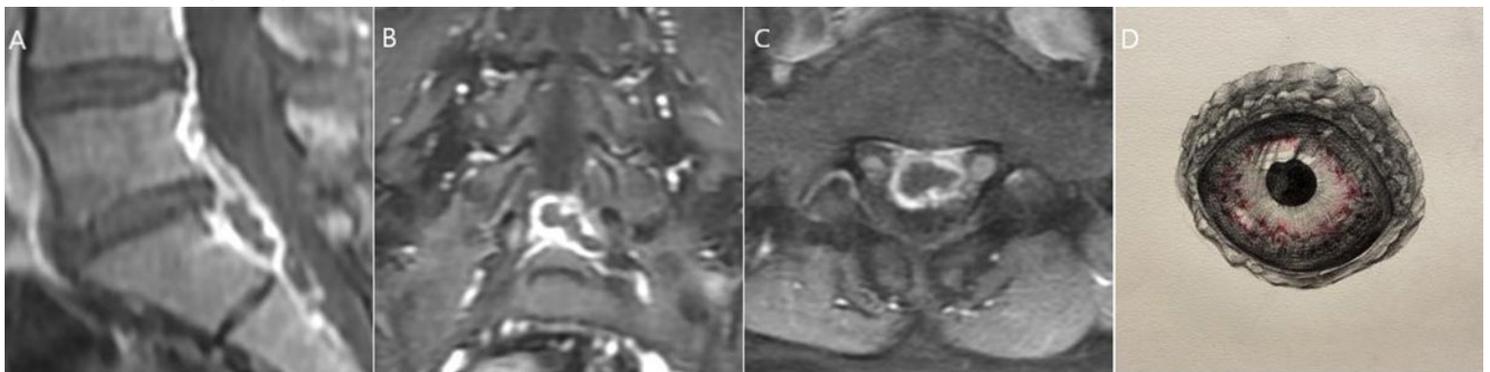


Figure 2

Positive bull's eye sign. Annular enhanced signals are present around protrusions in the (A) sagittal, (B) coronal, and (C) axial planes. (D) These enhanced signals resemble an open bovine eye.

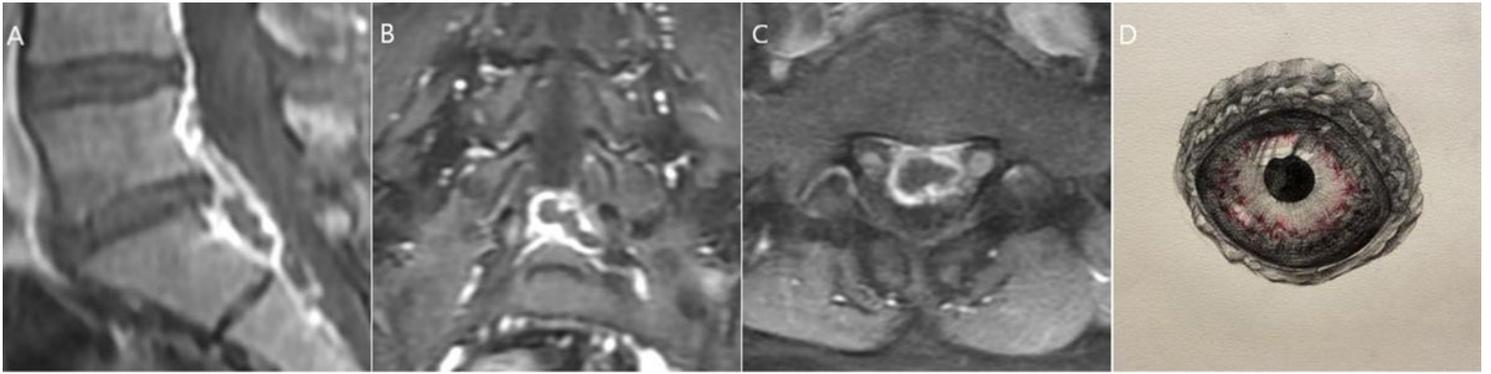


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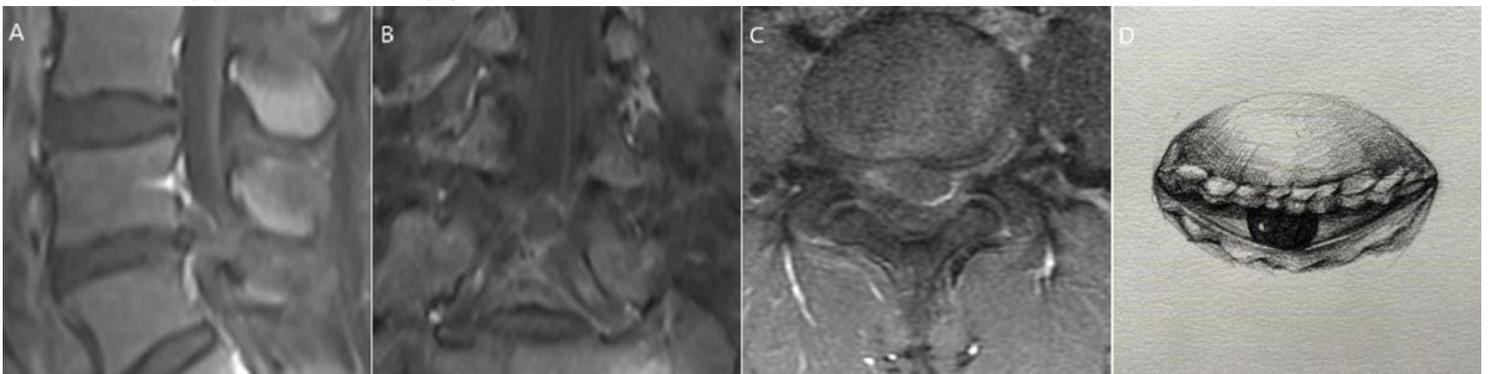


Figure 3

Negative bull's eye sign. No enhanced signal is present around protrusions in the (A) sagittal, (B) coronal, and (C) axial planes. (D) This lack of enhancement resembles a closed bovine eye.

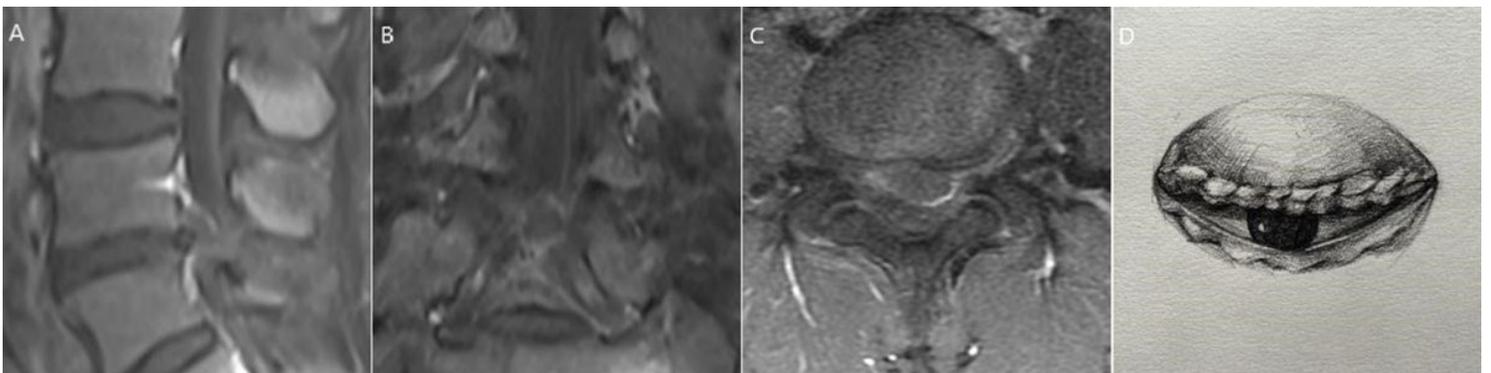


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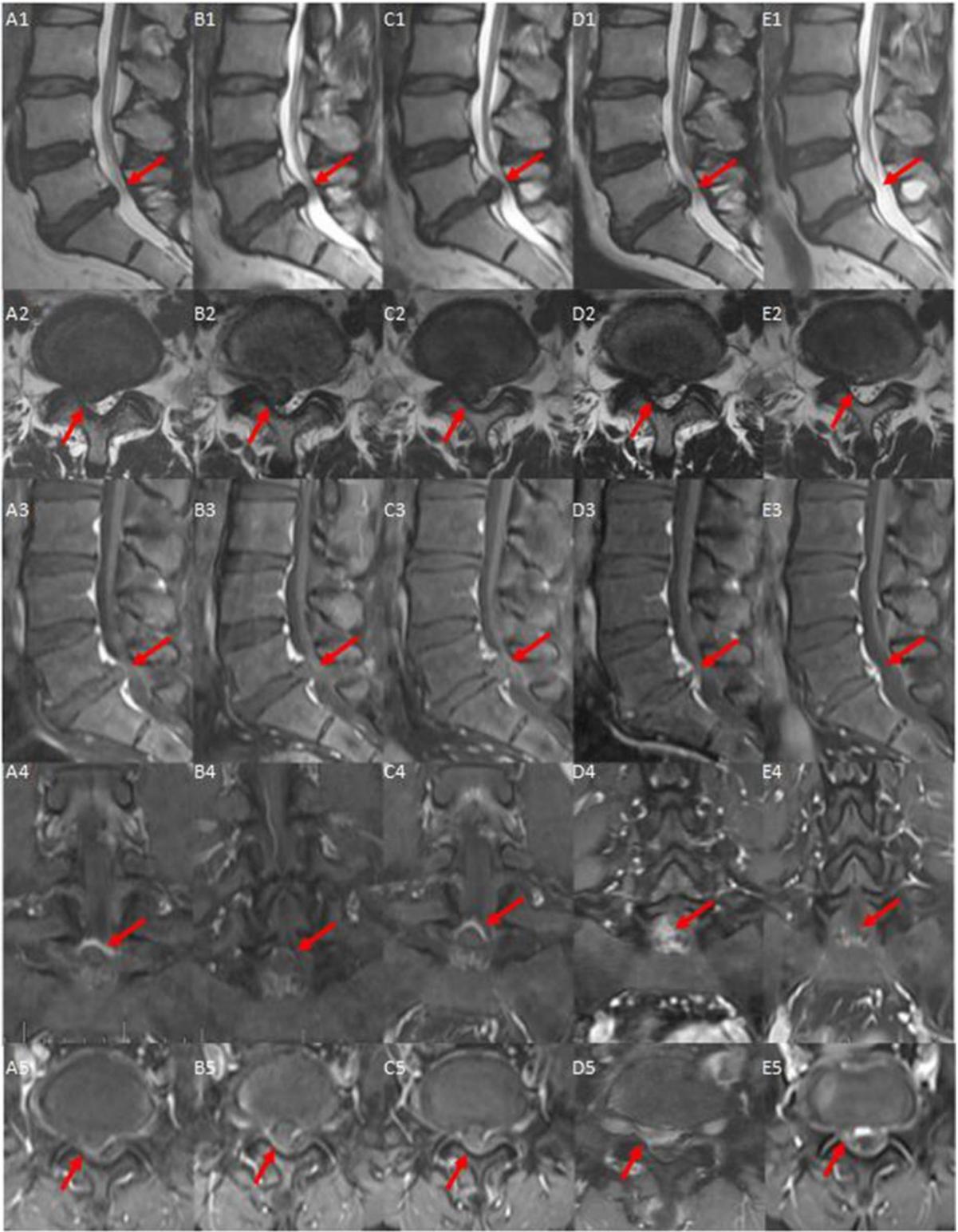


Figure 4

A 38-year-old woman, multiple contrast-enhanced MRI scans revealed disc resorption. Date: (A) January 17, 2018; (B) May 19, 2018; (C) October 17, 2018; (D) May 21, 2019; (E) October 19, 2019.

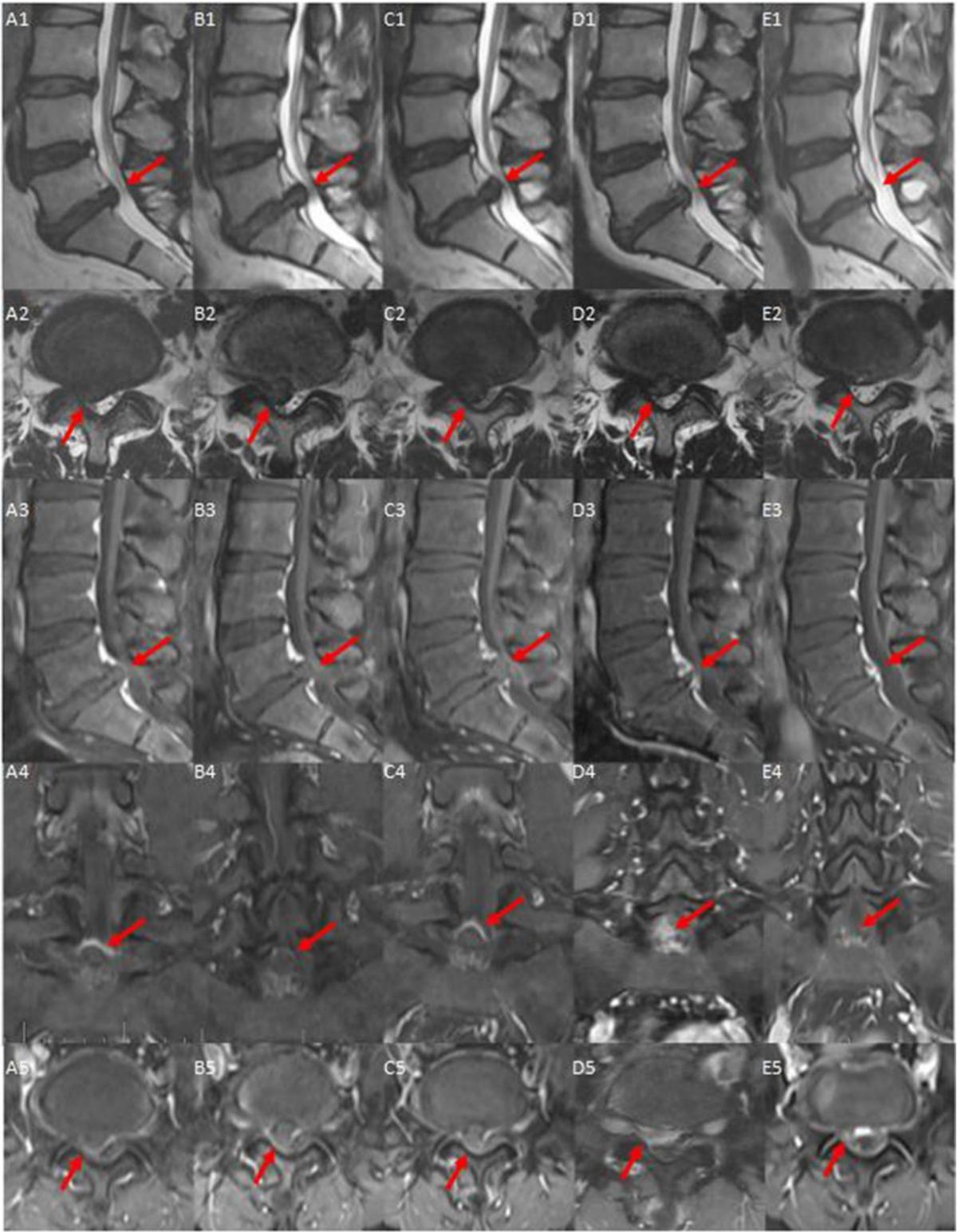


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