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CASE REPORT

Association of Accelerated Switch From Vertebral End-Plate Modic I to Modic 0 Signal Changes With Clinical Benefit of Intradiscal Corticosteroid Injection for Chronic Low Back Pain

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Modic I vertebral end-plate signal changes detected by magnetic resonance imaging (MRI) are associated with chronic low back pain. Typically, Modic I signal changes in untreated patients switch to non–Modic I signal changes within 3 years, which reflect spontaneous healing. Recent findings suggest that Modic I signal changes may be related to local inflammatory changes, providing a rationale for treatment with intradiscal injections of antiinflammatory drugs. In the present report, we describe a 31-year-old man with 1-year history of chronic low back pain associated with vertebral end-plate Modic I signal changes, who received 1 intradiscal corticosteroid injection in L5–S1. Local treatment led to rapid pain relief and was associated with an accelerated switch from Modic I to Modic 0 signal changes, as seen on lumbar MRI at 1-month followup. This is the first report of an effective local treatment for both the symptoms and the structural changes of chronic low back pain that are associated with Modic I signal changes. Additionally, this case reinforces the hypothesis that local inflammation has a pathogenic role.

De Roos et al (1) and Modic et al (2) described changes of the vertebral end-plate bone marrow magnetic resonance imaging (MRI) signal anecdotally present in an asymptomatic population but specifically observed in patients with nonspecific chronic low back pain (3–5). Modic 0 signal changes are the normal vertebral body signal. Modic I signal changes correspond to vertebral end-plate edema. Modic II signal changes are characterized by disruption of the end-plates as well as fatty degeneration of the adjacent bone marrow. Modic III signal changes are characterized as sclerosis that is evident on radiography. Modic II and Modic III signal changes, which are assumed to correspond to stages of spontaneous healing, usually occur within 1–3 years after Modic I signal change (6). Recent findings suggest that Modic I signal change may be related to low-grade systemic inflammation (7), along with local inflammatory changes. Biopsy studies have shown replacement of vertebral end-plate bone marrow with richly vascularized fibrous tissue (2), increased levels of interleukin-6 (IL-6) (8), and a higher number of tumor necrosis factor α (TNFα) immunoreactive cells (9).

The hypothesis that a local inflammatory reaction occurs in the subchondral bone marrow adjacent to the end-plate has provided a rationale for local injection of corticosteroids to treat nonspecific chronic low back pain associated with vertebral end-plate Modic I signal changes. In a recent open study assessing the association of severity of inflammatory end-plate changes identified on MRI and clinical response to intradiscal corticosteroid injection in nonspecific chronic low back pain, the reduction in pain score at 1 month was significantly higher in patients exhibiting Modic I signal changes than in those with Modic II signal changes (10). This finding suggests that intradiscal injection of corticosteroids could be an appropriate treatment for patients with nonspecific chronic low back pain and predominantly inflammatory end-plate signal changes. However, little is known about the evolution, after intradiscal corticosteroid injection, of local inflammatory structural features that are visible on MRI.

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We report here our findings on the effectiveness of intradiscal corticosteroid injection, on both symptoms and structural changes, in treating nonspecific chronic low back pain associated with lumbar vertebral end-plate Modic I signal changes in a 31-year-old man. Patient-oriented end points included relief of low back pain assessed on visual analog scale (VAS), and disease-oriented end points included MRI study of lumbar vertebral end-plate signal changes.

CASE REPORT

The patient, a 31-year-old athlete, had experienced nonspecific chronic low back pain for 1 year. His medical history was unremarkable, and treatment with short-acting opioid analgesics, nonsteroidal antiinflammatory drugs, physical therapy, and 2 injections of corticosteroid (prednisolone acetate 25 mg/ml [1 epidural, and 1 facet joint injection]) was not effective despite satisfactory self-reported compliance, and interfered with daily activities. The patient was not treated with any other concomitant medication. No remarkable findings were noted on physical examination, and inflammatory back pain related to ankylosing spondylitis was ruled out, based on medical history and clinical findings. The results of laboratory examinations performed at baseline, including C-reactive protein level and complete blood cell count, were within normal limits.

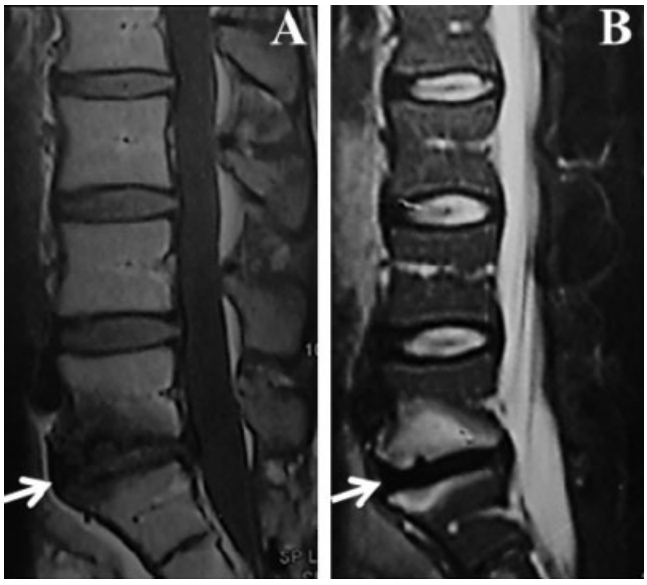

Figure 1. Magnetic resonance imaging of the lumbar spine performed prior to intradiscal corticosteroid injection, showing typical features of vertebral end-plate Modic I signal changes at the L5–S1 level (**arrows**). Hypointense and hyperintense signal changes are visualized in T1-weighted (**A**) and STIR-weighted (**B**) sequences, with edema involving the adjacent vertebral end-plates and bone marrow.

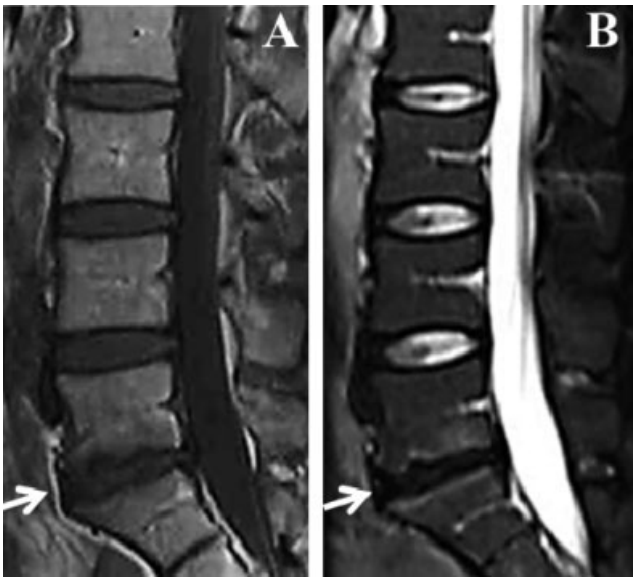

Figure 2. Magnetic resonance imaging of the lumbar spine performed at 1-month followup, showing an early switch from vertebral end-plate Modic I to Modic 0 signal changes (**arrows**), with complete regression of vertebral end-plate and bone marrow edema, as visualized on T1-weighted (**A**) and STIR-weighted (**B**) sequences.

Results of lumbar spine plain radiographs and computed tomography (CT) scans were normal, and lumbar MRI revealed Modic I signal changes in the L5–S1 vertebral end-plate with typical hypointense and hyperintense vertebral end-plate bone marrow changes on T1- and STIR-weighted sequences (Figure 1). The Modic I vertebral end-plate bone marrow MRI signal changes were asymmetric, and involved the whole L5 vertebra inferior end-plate and S1 vertebra superior end-plate in the anteroposterior axis, one- to two-thirds of the L5 vertebra height, and less than one-third of the S1 vertebra height. The vertebral end-plate signal changes in L5–S1 were associated with degenerative discopathy, including intervertebral space narrowing, nucleus pulposus hyposignal on T2-weighted sequences, and intervertebral disc protrusion.

Because previous treatments had not alleviated symptoms, we treated the patient with intradiscal corticosteroid injection, as previously described (10), after having ruled out contraindications to local corticosteroid injection. Discography was performed under CT guidance, using a posterolateral approach. After we ascertained the proper needle-tip positioning into the L5–S1

intervertebral disc center using anteroposterior and lateral views and opacification of the disc, prednisolone acetate (25 mg/ml) was injected into the intradiscal space. No adverse events were noted during or after the procedure. Within 24 hours after injection, the patient reported complete relief of low back pain. Strikingly, a lumbar MRI performed at 1-month followup showed an early switch from vertebral end-plate Modic I to Modic 0 signal changes, as visualized on T1- and STIR-weighted sequences (Figure 2). At the last followup (9 months after injection), the patient was experiencing no pain (as assessed by pain VAS) and was able to participate in his usual athletic activities.

DISCUSSION

Herein we provide the first report of local anti-inflammatory treatment showing an effect on both the symptoms and the structural changes in nonspecific chronic low back pain, as evidenced by vertebral end-plate Modic I signal change. The benefit of intradiscal corticosteroid injection for nonspecific chronic low back pain associated with Modic I signal changes has been assessed previously in only a few studies (10,11). Additionally, these studies mainly focused on short- and mid-term clinical outcomes such as pain and function, but did not evaluate the association between clinical response and structural MRI signal change results. Thus, little is known about the evolution of local inflammatory structural changes seen on MRI after intradiscal corticosteroid injection.

The natural course of vertebral end-plate Modic I signal changes has been well described. It is rarely characterized by a return to Modic 0 signal changes, but more frequently exhibits 3 successive stages, occurring within 1–3 years (2,6,12). The first stage, corresponding to Modic I signal changes, is defined by vertebral end-plate bone marrow elementary MRI signal changes as described by Modic et al in the late 1980s (2). They are characterized by low signal intensity on T1-weighted sequences and hyperintense signal on T2-weighted sequences, with enhancement after gadolinium injection, corresponding to bone marrow edema. MRI changes can be asymmetric and can involve a part of or the entire adjacent vertebral end-plate subchondral bone. Histopathologic analysis shows disrupted and fissured vertebral end-plate that is associated with trabecular bone thickening and an increased number of osteoblasts and osteoclasts, suggesting greater bone remodeling as well as replacement of normal bone marrow tissue with richly vascularized granular tissue.

Modic I signal changes are also associated with an active inflammatory process, involving vertebral end-plates adjacent to the intervertebral disc, and stimulated by local proinflammatory mediators and cytokines, including nitric oxide, prostaglandin E_2, IL-6, and TNFα (8,9). Consistently, patients with Modic I signal changes exhibit more frequent clinical and biologic inflammatory features, such as longer duration of morning stiffness, more frequent late night and morning pain, and higher serum levels of high-sensitivity C-reactive protein (hsCRP), than patients with nonspecific chronic low back pain who do not exhibit Modic I signal change (mean $\pm$ SD hsCRP 4.64 $\pm$ 3.09 mg/liter in the Modic I group versus 1.33 $\pm$ 0.77 mg/liter in the Modic 0 group, and versus 1.75 $\pm$ 1.30 mg/liter in the Modic II group; $P = 0.002$, Modic I group compared with Modic 0 and II groups) (7). The next stages, corresponding to Modic II and Modic III signal changes, are considered more quiescent phases of the process, associated with fewer clinical inflammatory features and less painful symptoms (5), and thus may represent the healing stages of the disease. With an understanding of the spontaneous natural course of vertebral end-plate Modic signal change, treatments aimed at accelerating the course of Modic I lesions may be relevant.

This hypothesis is further supported by the results of 2 surgical trials. In an open prospective study of the outcome of Modic I signal changes in 17 patients with nonspecific chronic low back pain after instrumented posterior lumbar arthrodesis, a switch from Modic I to non–Modic I signal changes was found in all patients at 6 months, along with clinical improvement that was maintained at 1-year followup (13). Consistent with these findings, in another open study designed to assess the predictive value of Modic signal changes on clinical outcomes in 60 patients with nonspecific chronic low back pain who had lumbar single-level degenerative disc disease that had been surgically treated (segmental instrumented interbody fusion [n = 22] or posterolateral fusion [n = 38]), initial Modic I signal changes were associated with better clinical outcome after surgery than non–Modic I signal change (14).

In 2 clinical trials, intradiscal injections of corticosteroids have been reported to be more effective in patients with nonspecific chronic low back pain with vertebral end-plate Modic I signal changes than in those without (10,11). In an open study intended to analyze the association between the severity of inflammatory end-plate changes identified on MRI and the clinical response to intradiscal injection of corticosteroids in 74 patients with nonspecific chronic low back pain who showed no response to 3-month conservative treatment, reduction in pain score at 1 month after injection was

significantly better in the group exhibiting Modic I signal changes than in the group with Modic II signal changes at baseline (10). In another study that had been designed to determine the effect of intradiscal injections in 171 patients who had exhibited degenerative disc disease symptoms for >1 year and to determine whether patients with inflammatory end-plate changes are a unique subgroup in terms of treatment response, injection of steroid into discs with concordant pain at the time of discography led to significant improvement in patients with inflammatory end-plate changes, but to only minimal and temporary improvement in patients without end-plate changes (11). However, outcome measures did not include MRI followup, so the association of subjective symptom improvement with objective changes on MRI was difficult to assess.

In our patient, the striking and rapid efficacy of intradiscal corticosteroid injections both in treating symptoms and in effecting vertebral end-plate MRI changes provides strong evidence that inflammation is part of the underlying pathogenic mechanism of the symptoms associated with Modic I signal changes. This case also confirms the relevance of antiinflammatory nonsurgical local treatments that accelerate the course of Modic I lesions. In contrast with previous studies, in which the benefit of intradiscal corticosteroid injection was barely maintained beyond 3 months, our patient did not report any pain at 9 months. Although MRI was not performed at 9 months, the lack of patient-reported pain suggests that an early switch from Modic I to Modic 0 signal changes may predict prolonged clinical response. Therefore, MRI performed soon after local treatment may be of interest regarding the mid- and long-term prognosis of the disease.

A placebo effect may have contributed to our patient's experience of symptom improvement. However, striking evidence of accelerated vertebral end-plate transformation was shown in a lumbar MRI at 1-month followup. Although this is the first reported case of an effective antiinflammatory local treatment for both the symptoms and the structural changes of nonspecific chronic low back pain associated with Modic I signal change, it reinforces the hypothesis that local inflammation has a pathogenic role. It provides a sound rationale for the further investigation of treatments that target local inflammation in patients with nonspecific chronic low back pain associated with vertebral end-plate Modic I signal changes.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Rannou had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Nguyen, Bénichou, Revel, Poiraudeau, Rannou.

Acquisition of data. Bénichou.

Analysis and interpretation of data. Nguyen, Revel, Poiraudeau, Rannou.

REFERENCES

1. De Roos A, Kressel H, Spritzer C, Dalinka M. MR imaging of marrow changes adjacent to end plates in degenerative lumbar disk disease. AJR Am J Roentgenol 1987;149:531–4.
2. Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. Radiology 1988;166:193–9.
3. Weishaupt D, Zanetti M, Hodler J, Boos N. MR imaging of the lumbar spine: prevalence of intervertebral disk extrusion and sequestration, nerve root compression, end plate abnormalities, and osteoarthritis of the facet joints in asymptomatic volunteers. Radiology 1998;209:661–6.
4. Toyone T, Takahashi K, Kitahara H, Yamagata M, Murakami M, Moriya H. Vertebral bone-marrow changes in degenerative lumbar disc disease: an MRI study of 74 patients with low back pain. J Bone Joint Surg Br 1994;76:757–64.
5. Kjaer P, Leboeuf-Yde C, Korsholm L, Sorensen JS, Bendix T. Magnetic resonance imaging and low back pain in adults: a diagnostic imaging study of 40-year-old men and women. Spine 2005;30:1173–80.
6. Mitra D, Cassar-Pullicino VN, McCall IW. Longitudinal study of vertebral type-1 end-plate changes on MR of the lumbar spine. Eur Radiol 2004;14:1574–81.
7. Rannou F, Ouanes W, Boutron I, Lovisi B, Fayad F, Mace Y, et al. High-sensitivity C-reactive protein in chronic low back pain with vertebral end-plate Modic signal changes. Arthritis Rheum 2007; 57:1311–5.
8. Burke JG, Watson RW, McCormack D, Dowling FE, Walsh MG, Fitzpatrick JM. Intervertebral discs which cause low back pain secrete high levels of proinflammatory mediators. J Bone Joint Surg Br 2002;84:196–201.
9. Ohtori S, Inoue G, Ito T, Koshi T, Ozawa T, Doya H, et al. Tumor necrosis factor-immunoreactive cells and PGP 9.5-immunoreactive nerve fibers in vertebral endplates of patients with discogenic low back pain and Modic type 1 or type 2 changes on MRI. Spine 2006;31:1026–31.
10. Fayad F, Lefevre-Colau MM, Rannou F, Quintero N, Nys A, Mace Y, et al. Relation of inflammatory modic changes to intradiscal steroid injection outcome in chronic low back pain. Eur Spine J 2007;16:925–31.
11. Buttermann GR. The effect of spinal steroid injections for degenerative disc disease. Spine J 2004;4:495–505.
12. Jarvik JG, Hollingworth W, Heagerty PJ, Haynor DR, Boyko EJ, Deyo RA. Three-year incidence of low back pain in an initially asymptomatic cohort: clinical and imaging risk factors. Spine (Phila Pa 1976) 2005;30:1541–8.
13. Vital JM, Gille O, Pointillart V, Pedram M, Bacon P, Razanabola F, et al. Course of Modic I six months after lumbar posterior osteosynthesis. Spine 2003;28:715–20.
14. Esposito P, Pinheiro-Franco JL, Froelich S, Maitrot D. Predictive value of MRI vertebral end-plate signal changes (Modic) on outcome of surgically treated degenerative disc disease: results of a cohort study including 60 patients. Neurochirurgie 2006;52: 315–22.