



Vertebral endplate (modic) changes and the treatment of back pain using antibiotics

Practice points

- Vertebral endplate changes/modic changes (MC) are the MRI-images of inflammatory vertebral endplate damage that are often related to general disc degeneration.
- In patients with prolonged back pain, the prevalence of MC is 40%.
- In individuals with MC, more than 90% will have back pain within 1 year.
- MC often causes localized pain 24/7.
- Nocturnal pain is the rule rather than the exception.
- New MC type 1 occurs frequently during the course of a disc herniation.
- There are currently no better diagnostic methods in MC than MRI and a case story of the typical inflammatory back pain pattern and the likely presence of a disc herniation within the recent few years.
- In biopsies from prolapsed disc mass, bacteria – most commonly *Propionibacterium acnes* of the oral cavity class – are found in at least 40% of patients.
- In a MC subgroup with persistent back pain after a disc herniation and emerging MC type 1, it is relevant to consider: 'disc infection'.
- In one high quality RCT, including a subgroup of post-prolapse/MC patients with chronic pain, demonstrated clinically significant improvements in more than 50% of the patients after 3 months of treatment with a broad spectrum antibiotic.
- MC type 1 are generally considered to be an important prognostic marker of a poor prognosis.

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Vertebral end-plate changes/modic changes are the MRI-image of inflammatory vertebral endplate damage, most often related to general disc degeneration. However, in a subgroup of patients disc infection may be the causal factor. In patients with prolonged back pain, the prevalence of modic changes (MC) is 40%. In most cases, nocturnal pain is the rule and MC causes highly localized pain 24/7. There are currently no better diagnostic methods than MRI and case history findings. In persistent back pain after a disc herniation and emerging MC type 1, it is relevant to consider: 'disc infection'. Most commonly, *Propionibacterium acnes* is involved. Long-term antibiotics may be effective.

Keywords: antibiotics • back pain • chronic pain • disc prolapse • discitis • modic changes • vertebral endplate

Modic *et al.* [1] defined three types of vertebral endplate (modic) changes as visualized on MRI in 1988 and in 2001, Stirling [2] cultured bacteria in disc biopsies from more than 50% of patients investigated who had

undergone surgery for a prolapsed disc. By combining these findings researchers from The Spine Center of Southern Denmark established a hypothesis in 2008 regarding MC including its prevalence, etiology,

pathogenesis, clinical features, diagnosis, treatment and prognosis [3]. Several years of research focusing on MC has resulted in new important scientific discoveries. Further research in MC is now ongoing in many spine research departments around the world.

Background & definitions

Degeneration of the intervertebral disc can be complicated by partial degradation and cracking of the adjacent vertebral end plate structures and intravertebral edema as well as vascular inflammatory granulation tissue in the involved bone marrow may be found. This degenerative process was first identified on MRI in 1988 by the American radiologist, Michael Modic and his research colleagues [1]. He described, how

on occasion, the MRI scans of the lumbar vertebrae, demonstrated signal changes in the endplates and the adjacent bone marrow. MC type 1, type 2 and type 3 were then defined. Type 1 is characterized by high signal changes on T2-weighted images (Figure 1) and low signal changes on T1-weighted images. The extent of each MC can vary from a narrow fringe that simply involves the endplate of the vertebra to spreading into large parts of the adjacent vertebra. MC type 2 is characterized by high signal changes on both T1- and T2-weighted images. MC type 1 contains vascular tissue and active inflammatory components, type 2 contains granulation tissue infiltrated by significant amounts of fat cells, as demonstrated by biopsy studies. MC Type 3 are rare and represent subchondral bony sclerosis with low T1 and T2 signal changes.

Prevalence

In the general population, MC are found in 5–10% of adults [4]. The prevalence increases with age. Thus, the phenomenon is quite rare at the age of 20 years, but up to 20% have MC at age 60 and it occurs most frequently in the lumbar region and especially in the L4/L5 and L5/S1 segments, presumably arising secondarily to significant mechanical forces present in the lower lumbar spine [5]. MC are normally seen at the same vertebral level as disc degeneration. MC can be interpreted as a complication to normal age-related disc degeneration and spondylosis. In groups of patients referred to a spine center due to significant pain for months or years, prevalence rates can be as high as 40% [6]. MC type 1 and type 2 occur in roughly equal proportions [6]. Therefore, MC in low back pain patients are a frequently observed phenomenon.

Bendix *et al.* have shown that there may be a significant difference between low- and high-field MRI regarding the overall prevalence of any MC and therefore, the MRI unit should be taken in consideration when classifying MC types 1 and type 2 for the individual patient [7]. Studies including cohorts re-imaged one or several years later indicate that while small MC sometimes may spontaneously disappear, major MC are usually more persistent [7]. MC Type 1 can change over time to Type 2 and *vice versa* [8].

It has been shown that the emergence of MC type 1 is often a sequel to a herniation of the adjacent disc segment [9]. Two studies have demonstrated that up to 40% of patients following disc herniation may develop new MC type 1 changes in the adjacent vertebra [9,10], and that undergoing surgery may be associated with a higher prevalence compared with conservative treatment regimens [10]. It has also been shown that MC are generally associated with back



Figure 1. A MRI T2-weighted image: typical vertebral endplate (modic) changes type 1 (high signal) in a lumbar segment.

symptoms and that up to 90% of individuals with MC suffer from back discomfort or pain [11–13]. These percentages should be compared with a typical one year prevalence of 50% for low back pain in the general population.

Etiology & pain

The most common reason for MC is in all likelihood that the normal disc degenerative processes are complicated or initiated by damage and microfractures to the vertebral endplates (Figure 2; no. 0–1–2). In some patients, the degenerative process results in the development of edema and inflammation of the involved vertebra. Many factors may be involved. New research results have shown that in patients with disc herniations the ingrowth of capillaries and inflammatory mechanisms may be important ingredients of the development of pain and MC in the involved spinal structures [14]. Additional observations point to a possible association between the high proportion of hyaline cartilage in the herniated disc mass and the development of MC in the adjacent segments [15]. As the bony endplates normally have a rich supply of small free nerve endings, degenerative developments and inflammation can trigger a localized inflammatory pain pattern [5,16]. Typically, the pain is exacerbated by physical stress or exercise, and it is often worse at night. Considerable subjective stiffness of the affected disc segment especially in the morning is commonly reported by patients.

In the patient's medical records, suspicion or evidence of a former or an actual disc herniation of the adjacent disc is often present (Figure 2: no. 0–3–4–5). Patients in these cases generally indicate that highly localized back pain developed in the first few months following the herniation. In cases such as these it is relevant to suspect that the development of a bacterial disc infection associated with MC has taken place in the disc segment [18]. It has been demonstrated that the anaerobic *P. acnes* bacteria is often present in the herniated mass following an acute herniation, and that there is an association between an infected herniation and the development of MC type 1 changes and back pain [19].

Symptoms

Classic – but not pathognomonic – symptoms follow an inflammatory pain pattern [16]. The patient report constant back pain, pain at night, morning stiffness and worsening during performance of back exercises and other exercises. There is often restricted movement of one or more segments of the lumbar spine and distinct tenderness on deep palpation of the painful segment (Positive Springing Test).

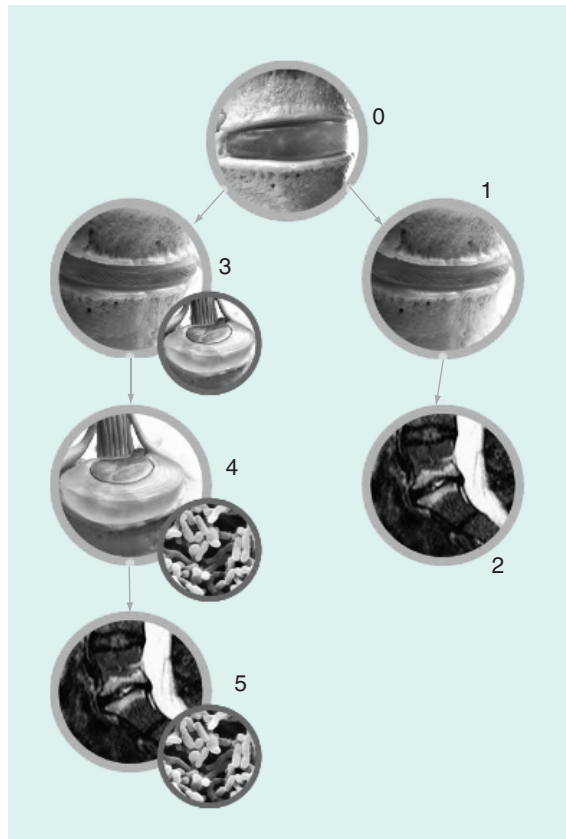


Figure 2. From normal disc to vertebral endplate (modic) changes. Two associated pathways.

Mechanical pathway: 0: normal disc; 1: age-related disc degeneration and the development of spondylosis; 2: endplate damage with development of modic changes type 1. Infectious pathway: 3: disc degeneration with the development of a disc herniation; 4: invasion of bacteria, causing a disc infection; 5: endplate damage and bacteria with the development of modic changes type 1.

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Diagnostic considerations

To establish the diagnosis of MC, an MRI of the lumbar spine (including T2-weighted images or STIR) is required. The typical clinical picture supports the suspicion that MC are implicated in the patient's pain description. If the patient has had a disc herniation at the same level within the last 1–2 years one must consider ongoing disc infection, in most cases caused from *P. acnes* [19]. Recall that a disc herniation may occur silently without the patient's experiencing the classically known symptoms and that it is not the disc in itself that may serve as port of entry for bacteria, but the development of blood vessels required for the process of resorbing the scar tissue.

Biopsy is complicated to perform and unreliable with currently available techniques. Blood tests are not helpful, as they are mostly normal, but consider SR/CRP to rule out other possible diagnoses.

Differential diagnostics

Osteomyelitis is seen in old and weak or immunosuppressed patients, and may be accompanied by fever and a rapid progression of symptoms.

The classical postoperative discitis with virulent streptococcal or staphylococcal bacteria progresses rapidly over the days/weeks following surgery. Fever and perhaps elevated CRP/ SR/ and leukocytosis are commonly seen.

Spondyloarthritis has the following characteristics: familial history, involvement of the sacroiliac joints, extra articular manifestations, positive HLA -B27 and elevated CRP/SR.

Treatment

In most cases, treatment is similar to that recommended for other cases of disc degeneration/spondylosis that are not spontaneously improving. In many cases, no relief is seen following back exercises or general training [20]. If there is a suspicion of a disc infection, prolonged antibiotic therapy may be an effective treatment. A 1-year follow-up RCT tested the efficacy of amoxicillin/clavulanic acid for a 3-month period in post-prolapse patients and modic type 1 changes seen on MRI. In more than 50–60% of these patients clinically relevant and statistically significant improvements were seen at the end of treatment with further improvement in the actively treated group up to 1-year follow-up [21–23]. Another new RCT suggests consideration of bisphosphonates in the treatment of pain associated with MC [24]. However, we need many more clinical studies in this research field before it is possible to establish relevant examination/treatment guidelines regarding MC.

Prognosis

Although scientific differences of opinion exist MC type 1 have been shown to be a negative prognostic finding in two studies in which patients with proven MC type 1 were referred for hospital treatment due to persistent back pain. Patients were encumbered with persistent pain of 1-year duration and a diminished working capacity [25,26].

Conclusion, clinical implications & future perspective

Vertebral endplate (modic) changes are the MRI image of inflammatory vertebral endplate damage, most often related to general disc degeneration, and in many instances MC are not associated with intense pain or pain of a different nature to that which clinicians observe in many back pain patients. However, particularly patients demonstrating MC type 1 appear to constitute a subgroup that is at risk of developing more

frequent pain and have a generally less favorable prognosis than patients with other or unestablished diagnoses. Research activities carried out during the previous 10 years has identified an entirely new research area in spine science including important pathoanatomical and physiological arenas that we had no previous knowledge of. We now have the opportunity of gaining an enhanced understanding of the pathogenesis of back pain in many of our patients, particularly regarding the interplay between discs, vertebral endplates and bone marrow, which can lead to complicated pain syndromes. Furthermore, it has become clear that a discrete subgroup of patients with MR type 1, a previous disc herniation and persistent low back pain has been identified. In these patients, a painful discitis involving *P. acnes* as the active microorganism may develop in the involved segments. Adequate long-term antibiotic treatment can be an effective treatment for many of these patients.

Similar scientific observations have taken place in other disease areas during the past 10 years. *P. acnes* may be involved in several different invasive opportunistic infections, including, prostatitis, sarcoidosis and joint or breast implants [23,27].

It may well be that we can look forward to an era during which we are able to provide patients with a far more precise clinical diagnosis and therefore more effective treatments than at the present time. Prior to GPs considering the usage of antibiotic treatment for patients with low back pain with or without the specific findings reviewed above it is essential that additional pathoanatomically focused and clinically anchored studies are carried out in this area including additional randomized antibiotic trials from other research groups in other countries. We are also in need of improved diagnostic methods in daily clinical practice in order to be more able to identify which patients are likely to be suffering with symptoms due to bacteriological MC type 1.

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