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Therapeutic Periradicular Injections: It's a Gas!

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MR Imaging Studies after Epidural Injections: What Are We Really Imaging?

Although epidural anesthesia is generally considered safe, severe complications may rarely occur. With the increasing use of epidural injections for pain management, the number of cases with complications has steadily increased. Complications reported in the literature have been noted in different compartments of the spine, including the vertebrae and intervertebral disk spaces, the epidural space, the intradural extramedullary space, and the cord itself. Infectious, inflammatory, and vascular causes have been implicated as etiologies (1). Examples of these complications reported in the literature include diskitis and vertebral osteomyelityis, subarachnoid cysts and irregularities of the surface of the cord consistent with arachnoiditis, spinal cord lesions such as syrinxes, epidural or subdural hematomas, and finally, spinal epidural abscesses (SEAs).

Several hypotheses have been postulated as to the mechanism for the above complications. Spinal cord abnormalities may be secondary to ischemia, infarction, or edema. This ischemia may be related to venous stagnation due to the injection of anesthetic into the epidural space, thus interfering with flow in the epidural veins. This may be aggravated by lumbar stenosis in which there is a restricted epidural space. In addition, in patients with coincidental dural arteriovenous fistulas, further venous engorgement may produce spinal cord hypoxia.

In light of the serious consequences of the above complications, it becomes very important to diagnose these clinical complications in a timely fashion, because early diagnosis may change the outcome in many cases. The clinical symptoms of spinal infectious, inflammatory, and vascular processes may be nonspecific, especially in the early stages. However, MR imaging findings for infections, hematomas, and arachnoiditis have been well described in the literature, and application of these findings may help in narrowing the differential diagnosis. Nonetheless, one factor that may contribute to some uncertainty in the MR imaging diagnosis is the lack of scientific documentation of normal MR imaging findings following uneventful spinal injections. The article by Ikushima et al in this issue of the *AJNR* assesses the spinal MR findings associated with continuous epidural anesthesia in five patients with clinically uneventful spinal injections. Posterior epidural lesions were identified in all five cases similar to those in patients with epidural abscesses. In three of the patients, laboratory results ruled out infection. In the other two patients who did not undergo microbiological tests, the presence of infection was ruled out by their clinical course.

The authors of this article attempt to characterize the disease of the catheter-related lesions, but no pathologic specimens of these posterior epidural space lesions were obtained in this series. Several reports have described inflammatory mass lesions at the tip of intraspinal drug administration catheters (especially after infusion of high doses of morphine) in patients with long-term therapy. Surgical specimens have revealed noninfectious chronic inflammation, granuloma formation, and fibrosis or necrosis. Ikushima et al claim that their lesions are probably highly vascularized granulation tissue with increased water content because their lesions were CSF equivalent on T2-weighted images and granulomas are usually not as hyperintense as CSF. The authors also compare their lesions with SEAs, because MR imaging is very useful for the diagnosis of SEA (2). In the literature, catheter-related SEAs have been located in the posterior epidural space at the site of catheter tip insertion. The location, shape, and enhancement pattern of the cases by Ikushima et al were similar to those of chronic-phase catheter-related SEAs, but the SEAs usually do not have CSF-like high T2-weighted signal intensity. It is important to look for these differences in evaluating patients who have received continuous epidural anesthesia, because management would be completely different between sterile collections and SEAs.

The findings described by Ikushima et al are of great value to radiologists interpreting MR studies obtained in patients receiving continuous epidural anesthesia. It is important to remember, however, that some epidural injections are not continuous, especially those given for pain management where only a few milliliters are injected at one time. Findings here may be quite different. In our own experience, these epidural injections for lumbar back pain have produced subtle MR imaging findings. Prospective controlled studies with a larger series of patients are needed in the future to establish a normal baseline of MR imaging findings following uneventful epidural injections. Also, in the future, diffusion-weighted imaging may be used more frequently in examining patients with a question of infection. Until recently, only a few published reports have described the use of diffusion-weighted imaging to evaluate disease processes of the spine, but as experience with diffusion-weighted imaging of the spine increases, information about the findings of common spinal abnormalities such as infections will be more widely available. Eastwood et al (3) reported findings in spinal epidural abscess sim-

ilar to those of abscess cavities in the brain. These further studies may aid in increasing the sensitivity and accuracy of diagnosing epidural catheter-induced lesions.

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Therapeutic Periradicular Injections: It's a Gas!

Radiology departments and imaging centers nationwide are experiencing an increased demand for image-guided spine injection procedures. The use of spine injections for diagnosis and treatment of neck, back, and radicular pain has gained increased popularity with the advent of advanced imaging technology, an increased understanding of the pathophysiology of pain, the demand for less-invasive interventions, and demographic factors. Most individuals will experience neck and low back pain during their lifetime, and with increased age comes a greater number of potential patients with these symptoms.

Therapeutic spinal injections have been performed for more than half a century, and for more than 3 decades selective nerve root injections have been performed for the evaluation and treatment of patients with radicular pain or failed spine surgery. Nerve root injections can be performed for diagnostic preoperative evaluation, to confirm imaging findings, or to solve discrepancies between imaging and clinical findings. Selective nerve blocks and transforaminal epidural injections are also performed for pain management. Local anesthetic and steroids are administered to target the biochemical factors that result in nerve irritation and enhanced nociception. The mechanism for pain relief following steroid administration in this fashion is attributed to its anti-inflammatory effects. By inhibiting the production of phospholipase A and other substances that cause perineural inflammation and pain generation, anti-inflammatory substances suppress the local biochemical cause for pain due to disk degeneration. Steroids also inhibit the activity of nociceptive C fibers, which suppresses the transmission of pain impulses to the CNS. The prolonged therapeutic effects of these blocks may keep the patient pain free for weeks to months. This can result in delay or possible avoidance of surgery.

In this issue of *AJNR,* Bonetti et al report a prospective blinded study comparing intraforaminal infiltration of O_2/O_3 versus periradicular steroid injections for lower back pain. They compared the short-, medium-, and long-term outcome of patients with lower back pain and radicular symptoms. The patients were stratified into two groups, those with pain attributable to primarily disk disease and those with nondiskogenic spinal column degenerative changes. The authors found that patients in both groups responded very well to both modalities (ozone and steroid administration) at short-term follow-up; however, they describe a statistically significant long-term advantage in the ozone therapy group versus the steroid recipients. Bonetti et al postulate that the benefits of the ozone injections are linked to the inhibition of E2 prostaglandins and A2 phospholipase, similar to the therapeutic effects of steroids.

There is a paucity U.S. literature regarding the use of ozone as a therapeutic agent for spinal injections. Several articles appear in the European literature, but many are in obscure journals and do not represent randomized controlled studies. The mechanism of action for the relief of radicular pain may be attributable to one of several biochemical actions exhibited by ozone. Among these, analgesic and anti-inflammatory effects are probably the most important. Additional chemical properties of ozone have been described, including enhancement of glycolysis, hematologic effects, and even bactericidal, fungicidal, and virustatic effects. These mechanisms of action were reviewed in an investigation published last year in the *AJNR* (1). Andreula et al evaluated the effects of intradiskal ozone alone versus an adjunctive periradicular steroid injection. Animal studies have confirmed the offect of ozone on cytokine production (2). There are additional therapeutic mechanisms of action that are currently being investigated. These include localized improvement of microcirculation, resolution of venous stasis, and the direct effect of ozone on mucopolysaccarides associated with herniated disks.

The diverse affects of ozone are dependant on the concentration, or relative strength of the preparation, which have been studied by using animal and cadaveric investigations. The dose-dependent behavior of ozone mixtures mandates accurate photometric control and the production of precise ozone concentrations for any equipment used for medical purposes. Unfortunately, this is difficult to confirm when reviewing the literature, and published values must evaluated in light of the technique and quality of instrumentation.

CT-guided injections were used for all patients in Bonetti et al's series. A brief comment on technique selection is warranted. Proponents of CT guidance for injection procedures cite advantages including the

ability to monitor adjacent structures and confirm precise needle tip location. On the other hand, unlike real-time fluoroscopic monitoring with contrast administration, CT does not allow real-time assessment for intravascular injections, which cannot be excluded on the basis of negative aspiration. Assessing for vascular infiltration is extremely important when injections are performed in the upper lumbar or lower thoracic distribution, potential locations for the artery of Adamkiewicz. In the cervical region, radicular vessels that contribute to perfusion of the spinal cord may also be encountered within the intervertebral foramina. Injection of particulate steroids into these vessels may result in cord infarction and other disastrous outcomes. Direct injection of a particulate steroid suspension or a gas (O_2/O_3) may present the risk of embolization if inadvertent intravascular injection occurs. It is extremely important to be aware of these anatomic considerations when performing transforaminal injections. If O_2/O_3 gas is administered, a slow injection of <10 mL (combined disk and foramen) is recommended to avoid complications (Dr. Mario Muto, personal communication). Another technical consideration is the use of contrast (with CT or fluoroscopy), which maps the subsequent distribution of therapeutic substances.

We would welcome further innovations and techniques (many of which are already popular in other countries) as potential solutions to clinical challenges. On the other hand, we must bear in mind an important axiom for all physicians: "*primum non nocere*" (first, do no harm). It is important to document efficacy and safety before employing any new treatment technique. All treatment modalities should thus undergo well-designed controlled investigations (control for natural history of the condition being treated). Although this novel approach to the treatment of back and radicular pain looks promising, there are a number of important issues that plague ozone's proponents (3). These include a lack of standardized procedures and dosages, problems with calibrations for confirming those dosages (because of variable fidelity of equipment), incomplete understanding of the precise mechanism of action, inherent difficulties by using a gas as a therapeutic substance, and a lack of controlled trials. Further, ozone exposure has been linked to a number of adverse health effects (4). Bonetti et al have moved us closer to addressing a number of these issues, and we look forward to further investigations of this technique.

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Intracranial Atherosclerosis: A Few Good Images?

Lieutenant Daniel Kaffee, U.S. Navy: "I want the truth!"
Colonel Nathan Jessup, U.S. Marine Corps: "You can't handle the truth!"
A Few Good Men, Columbia Pictures, 1992

Physicians want the truth when imaging patients suspected of having intracranial stenosis. Currently, four imaging modalities might be considered as pathways to the truth in cases of intracranial atherosclerosis. These modalities are digital subtraction angiography (DSA), CT angiography (CTA), MR angiography (MRA), and transcranial Doppler (TCD). Bash et al have done an unprecedented comparison of three of these modalities in 28 patients with intracranial stenosis. On the basis of their study, it is clear that, compared with CTA and DSA, MRA generally does not get us as close to the truth about intracranial stenosis.

Should we be surprised that MRA does not accurately depict intracranial atherosclerosis? Not really. It is a firmly established fact that MRA tends to overestimate degree of stenosis (1–3). MRA has poor spatial resolution relative to what is now available for CTA and DSA, so we cannot reasonably expect to image stenotic arteries reliably with a lumen of <1 mm. Three-dimensional time-of-flight MRA is susceptible to artifacts secondary to turbulent flow, and some degree of turbulent flow is generally present with stenotic intracranial atherosclerosis. Even normal arteries can be misrepresented on MRA, because curves in normal arteries can cause turbulence that creates an artifactual stenosis. These artifactual stenoses account for the poor positive predictive value of MRA for intracranial atherosclerosis. No contrast or ionizing radiation is needed for an MRA, but how much harm really comes to patients from the use of iodinated contrast material or ionizing radiation? Have we helped a patient by avoiding iodinated contrast material and radiation in exchange for an inaccurate diagnosis? Patient care based on an incorrect diagnosis, no matter how caring and well intentioned, is much more likely to fail than care based on the correct diagnosis.

DSA has traditionally been the criterion standard for imaging intracranial disease. It offers superb spatial resolution and contrast resolution. But DSA is an invasive procedure that carries a small but real (0.7%) risk of permanent neurologic deficit (4). DSA gives physiologic information about flow contribution from the injected artery. This physiologic effect is sometimes a disadvantage, because slow-flow vessels distal to a stenosis may be poorly filled with contrast material and thus poorly visualized. Multiple arteries often need to be injected to show collateral blood flow. For posterior circulation stenosis, both vertebral arteries generally need to be evaluated. For those of us who work in referral centers where complex patients whose symptoms are refractory to medical therapy are referred, angioplasty or bypass surgery is sometimes offered. These patients will all have conventional angiography as part of their preintervention evaluation.

As Bash et al have shown, CTA can give excellent anatomic visualization of intracranial atherosclerosis. The use of CT angiography does not avoid the use of contrast material or ionizing radiation, but these offer trivial risks in most patients relative to the potential risks associated with symptomatic intracranial atherosclerosis. Spatial resolution may occasionally limit our ability to distinguish very severe stenosis from occlusion compared with DSA. Calcium might also occasionally cause overestimation of a stenosis, as was described for CTA of the cervical carotid artery (5).

But perhaps we cannot quite handle the truth yet. There is certainly confusion about the best medical therapy for intracranial atherosclerosis. The latest results of WASID (Warfarin versus Aspirin Symptomatic Intracranial Disease) indicate that coumadin offers no benefit over aspirin (6). Newer antiplatelet agents such as clopidogrel have not yet been subjected to rigorous testing for efficacy in the treatment of intracranial atherosclerotic disease. Patients with ischemic symptoms may get the same antiplatelet therapy regardless of the appearance of intracranial arteries on imaging. Nevertheless, we should strive to keep the art of diagnostic imaging ahead of the art of therapy. Treatments targeted to a patient's specific disease can be developed only if we can reliably diagnose that disease.

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