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melanoma, and squamous cell carcinoma spread along nerves, in our experience and in the current study, adenoid cystic carcinoma is the most common traveler along the perineural pathway. These tumors arise in salivary glands both major and minor as well as in the lacrimal glands. Neural connections from these areas are of obvious importance. The foramen ovale and the stylomastoid foramen are the key transit points from the parotid. The highest concentration of minor salivary glands in the body is in the posterior roof of the mouth, and adenoid cystic carcinoma frequently originates in this location. The pterygopalatine fossa becomes an extremely important landmark as shown in the current article.

The anatomy of the head and neck is indeed complex. Following neural pathways through the region can be an arduous task. Demonstration of an enlarged foramen, an enhancing nerve, or an enlarged cavernous sinus is indeed ominous. The fat planes adjacent to the skull base are equally important and deserve the same understanding and scrutiny. Indeed, when searching for perineural tumor spread, as in many situations in head and neck imaging, fat is truly a friend.

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No Drug Is Benign

Despite the excellent safety record of gadolinium-based compounds for enhanced MR imaging, the potential neurotoxic effects of these drugs are not completely understood. Normally, the blood-brain barrier protects cerebral tissue from foreign chemicals and the overaccumulation of native ones. A variety of pathogenic processes are known to heighten the permeability of the blood-brain barrier, however, allowing a significant increase in the local concentration of a given pharmacologic compound. Creating reproducible and consistent models for the study of the compromised blood-brain barrier remains challenging. Obviously, histologic analysis of cerebral tissue after administration of contrast medium must be performed in an experimental animal rather than a human subject. Examination of animal tissue with an intact blood-brain barrier does not provide insight into gadolinium-induced toxicity, and the results of induced blood-brain barrier compromise are often inconsistent and nonquantitative.

Ray et al in this issue of the *American Journal of Neuroradiology* (page 1455) describe the use of the intraventricular injection model as a reproducible and consistent way of studying the effects of the local accumulation of a compound that may diffuse into the cerebral parenchyma after injection. This type of testing has always been performed for drugs, such as myelographic compounds, intended for intrathecal and intraventricular space injection. While the gadolinium-based agents were initially developed for intravenous injection, other methods of administration are well known. Ray et al do not cite the results of any tests initiated by pharmaceutical developers that examined the effects of gadolinium-based compounds after intrathecal or intraventricular injection in the experimental animal. These tests may have been carried out previously; the manufacturer of the contrast material administered in the present study was interested enough in this line of investigation to fund the project.

The results obtained by Ray et al. indicate that, although the effects of gadopentetate dimeglumine and gadodiamide are similar, they produce pathologic effects that vary in character and location. This variance can, in part, be attributed to differences in chemical composition: one is ionic, the other nonionic. Striking pathologic manifestations were reported after high-dose intraventricular administration of both gadolinium compounds, however; indicating that the acute excitatory effects were not agent-specific.

The authors admit that when these drugs are injected intravenously with the typical doses prescribed for conventional MR imaging, it would not be likely that tissue concentrations would produce changes of the severity reported in their study. We should nevertheless be careful with these drugs. A broken blood-brain barrier may allow a drug to reach unusually high concentrations in the cerebral parenchyma; it would be important to know the threshold of accumulation that would allow lesser, but significant, pathologic changes. It is worthwhile to remember that there is always individual variation among tissues and subjects.

There is a tendency for physicians to maximize the amount of, or even overuse, a drug: if a little is good, a lot may be better. The recent protocols for "triple-dose gadolinium" are a good example. While these protocols have not been associated with any higher rate of occurrence of overt neurologic complications, we do not really know about the potential pathologic changes that may be induced from such doses, especially when the blood-brain barrier is broken. Although we radiologists always want to see more, we must remember that there is a risk-benefit ratio to any compound.

There has been the question of injecting gadolinium-based compounds into the intrathecal space for cisternography to diagnose, for example, subtle leakage of cerebrospinal fluid. Other indications for intrathecal and intraventricular gadolinium injection

can be contemplated, but when disease has weakened the blood-brain barrier, high-dose administration of gadolinium compounds should not be approached with impunity until more experimental work has demonstrated the safety and efficacy of this procedure. The article by Ray et al gives us the appropriate model and a baseline of information from which to proceed.

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Intracranial Angioplasty: A Little Science Enters into the Mix

Since the publication in 1980 of the first report of successful balloon angioplasty for symptomatic basilar artery atherosclerotic stenotic disease in two patients (1), several articles have appeared in the literature providing additional reports of the successes, limitations, and pitfalls of this evolving technique. All of the articles have had severe limitations in their study design, including small numbers of patients, loosely defined inclusion and exclusion criteria, lack of randomization, and retrospective analysis. The most encouraging results of any of the studies published to date suggest that balloon angioplasty for symptomatic intracranial atherosclerotic disease is probably the highest risk procedure with the least certain long-term clinical benefits in the therapeutic armamentarium of the interventional neuroradiolgist. Despite this fact, the busy practicing interventional neuroradiologist is frequently referred for consideration for balloon angioplasty the desperate patient with symptomatic intracranial atherosclerotic disease, who has not responded to "maximal medical therapy," and is not considered a viable candidate for extracranial-intracranial bypass surgery. With everybody's personal experience with the procedure being relatively small, and the existing literature being confusing and somewhat conflicting, it is difficult for the interventional neuroradiologist to provide wise counsel to the patient and referring clinician.

In this issue of the *American Journal of Neuroradiology* (page 1525), Mori et al provide the readership useful information regarding angiographic characterization of intracranial atherosclerotic stenotic lesions. Using angiographic lesion characteristics described in the coronary artery angioplasty literature, the authors retrospectively sorted treated intracranial lesions into three categories and found significant differences in clinical success rates and the primary end points of death, ipsilateral stroke, or ipsilateral bypass surgery among the three categories. Forty-two patients were examined retrospectively, making this the largest published intracranial balloon angioplasty series. The authors are to be commended for providing the readership with guidelines regarding which lesions may be amenable, with acceptable risk, to balloon angioplasty.

Mori et al are careful to point out the many limitations of their study design. One addition potential source of confusion deserves further comment. One of the inclusion criteria for balloon angiogplasty was for the patients to be "unresponsive to maximal medical therapy." Unfortunately, what constituted maximal medical therapy was not defined. Were patients unresponsive to aspirin or warfarin antiocoagulation or a combination of both? If patients were on warfarin anticoagulation, were they at therapeutic levels of anticoagulation at the time of failure? This is theoretically important, given the data we have from the warfarin-aspirin symptomatic intracranial disease study (2), another retrospective study that demonstrated a significantly lower percentage of major vascular events in patients treated with warfarin compared with patients treated with aspirin. In this study, of 88 patients treated with warfarin for a median duration of 14.7 months, six patients (7%) had an ischemic stroke (five nonfatal, one fatal).

Mori et al conclude their discussion by calling for a randomized trial comparing balloon angioplasty with medical therapy for the treatment of type A intracranial atherosclerotic lesions. This is certainly laudable, but in reality has little chance of being accomplished in the foreseeable future. The relative rarity of the proposed disease to be studied with nearly equivalent event rate of stroke expected between the two study groups will make it difficult to enroll enough patients to test the primary study hypothesis with sufficient power. Continuing advancements in catheter technology and the eventual introduction of stents capable of being deployed intracranially will make it increasingly tempting to treat patients with intracranial atherosclerotic disease endovascularly. We must remain cognizant, however, that warfarin anticoagulation at therapeutic levels remains an effective form of therapy for the majority of patients with this disease.

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