Tissue Response to Guglielmi Detachable Coils: Present Implications and Future Developments

Alex Berenstein

AJNR Am J Neuroradiol 1999, 20 (4) 533-534
http://www.ajnr.org/content/20/4/533

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Two articles presented in this issue of the *American Journal of Neuroradiology* describe the human tissue response in cerebral aneurysms after occlusion with present-design Guglielmi detachable coils (GDCs), and a third article illustrates the histologic tissue response to biologically altered GDCs in experimental animals.

The human studies analyze the histologic findings in three patients with cerebral aneurysms. Shimizu et al (page 546) report the histologic changes in a GDC-treated aneurysm in a 49-year-old woman who died 42 days after embolization because of the rupture of another untreated aneurysm. In the GDC-treated lesion, which was a wide-neck aneurysm embolized with loosely packed coils, there was no endothelization at the aneurysmal neck or orifice, although some inflammatory response at the peripheral portion (wall) of the aneurysm was noted. Molineaux et al described similar histologic findings in a giant aneurysm with a very wide orifice and neck that was also treated with loosely packed coils (1). Mizoi and colleagues also encountered similar findings in another large-neck aneurysm (2).

Castro et al (page 549) found ''significant'' fibrous connective tissue, most dense at the periphery of the sac, in both a carotid ophthalmic aneurysm and a middle cerebral aneurysm filled with GDCs. These coils were firmly attached to the aneurysmal wall. In the carotid ophthalmic lesion, in addition to the thick dense layer of collagenous tissue covering the neck, a single layer of endothelial cells was also noted. It is of interest to note that the capillary ingrowth in this small-neck aneurysm was continuous with the single layer of endothelial cells lining the surface of collagenous tissue that bridged the neck of this aneurysm. In 1997, Horowitz et al described similar findings in a small aneurysm with a narrow neck in which he noted fibrin-covered coils and new endothelium at the aneurysmal neck 4 weeks after embolization (3).

As we approach the end of the first decade since the introduction of the GDC, over 6000 people have been treated with this device. During the years immediately after their introduction, GDCs were reserved for treatment in ''non'' or poor surgical candidates. Presently, primarily in Europe and selected locations in North America, many patients with ''surgical'' aneurysms are being successfully treated with GDCs. The multicenter GDC study, which involved more than 1200 patients, showed a rebleed rate of less than 2% 6 months after embolization, even in incompletely treated aneurysms (4). These studies of histologic changes after GDC therapy show that the least endoluminal healing results at the level of the orifice when the aneurysmal neck is broad. This pattern of healing is similar to that found in other wounds in the human body. For example, sutures are necessary to approximate the edges or ''bridge'' the gap of a broad wound in the skin so that adequate scar formation occurs. Similarly, surgical clips placed extraluminally approximate the edges of an aneurysm, and lead to proper healing. Nonetheless, just as in a small superficial skin wound, healing can arise at the neck of an aneurysm without extraluminal approximation, if the orifice is small. Sufficient long-term follow-up and histologic evidence is accumulating to support the GDC treatment of small-neck (4-mm or less) aneurysms irrespective of their location, size, or presentation. Therefore, we believe the evidence permits us to conclude that GDC treatment should become the treatment of choice in small-neck, ''surgical'' aneurysms. Although present GDC treatment of broad-neck aneurysms is less than ideal, these aneurysms do develop some reinforcement of their walls after such therapy, which would explain the low rebleed rate in incompletely treated large-neck aneurysms. If the risk of microsurgery is acceptable, clipping is the preferred treatment in large-neck aneurysms, particularly if the patient is young. In treating difficult broad-neck lesions, there may be a role for partial clipping to approximate the edges of the aneurysm. When a suitable neck is formed, the surgery would be followed with GDC treatment.

Tamatani et al (page 541), with type I collagen-coated platinum microcoil delivery, address the next generation of endovascular tools for the treatment of cerebral aneurysms: biologically active devices. In addition to the mechanical protection already produced by ordinary coils, these devices actually elicit a biological response from the human body that results in a better, more durable occlusion. In 1996, Dowson reported delivery of collagen-primed coils with interlocking detachable coils in experimental aneurysms (5). Although collagen-primed coils may represent progress in the development of improved embolic devices, some problems need to be resolved before their clinical trials. Although it has been noted that endothelial cells can grow directly on the collagen-primed coils, proper distribution of collagen remains a challenge. In addition to priming coils with collagen, ion implantation for protein-coating of GDCs, as described by Murayama, will increase further the variety of bioactive material that can be added to endovascular devices (6). Because type I collagen-primed coils seem to have a longer lasting result than conventional coils, they could be used to treat broad-based aneurysms by creating a matrix of coated coils resulting in fibrosis of the lumen and wall, and a supplementary neoendothelization of the orifice. Although there is concern regarding the po-

tential of distal emboli with biologically active coils, devices used to protect the aneurysmal neck (i.e. neck bridges) are concurrently being developed to reduce this possibility.

The delivery of coated or biologically altered coils into the aneurysmal lumen seems to be a promising method for producing intravascular scars, and may represent a revolution in the management of presently unmanageable lesions. In the future, GDCs may serve as a delivery vehicle for biologically or chemically active substances. These works demonstrate the great potential of minimally invasive techniques for becoming the primary method of treatment of cerebral aneurysms.

ALEX BERENSTEIN, M.D.
Beth Israel Medical Center
New York, NY

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Imaging Intractable Epilepsy: How Many Tests Are Enough?

The challenge faced when choosing the best diagnostic studies for the evaluation of patients with intractable epilepsy reminds me of playing Monopoly. As beginners, we have less experience and tend to ''buy'' all properties (or studies as is the case here). As we become better players, we choose only those options that yield the highest return. In the imaging of epilepsy, there are many studies from which we can choose including CT, MR imaging, proton MR spectroscopy (MRS), functional MR (fMR), T2 relaxometry, single photon emission tomography (SPECT), positron emission tomography (PET), and Wada testing. As seasoned players, neuroradiologists are expected to narrow down the number of examinations obtained in the seizure patient if we are to remain in control of the practice of neuroimaging. Otherwise we risk depleting the ''Community Chest,'' and are forced to pay more ''luxury taxes.''

When evaluating potential surgical candidates, the neuroradiologist should 1) confirm lateralization (left- vs. right-side disease), particularly when this cannot be done clinically, 2) identify focal lesions that may be amenable to tailored resections, and 3) establish the relationship between seizure foci and eloquent brain regions. Most of our imaging tests accomplish the first two objectives, whereas the evaluation of eloquent brain regions still depends on the Wada test (fMR, however, is being increasingly used for this purpose, but has yet to replace the Wada test). Multitechnique imaging studies are considered critical for evaluating patients in whom electroencephalography (EEG) and MR imaging findings are discordant (about 40% of them). How do all of these techniques compare?

In the evaluation of intractable lobe epilepsy, MR imaging has a sensitivity of 85–98% in the detection of an abnormal hippocampus (1). MR is easy to perform, and is readily accessible, but requires high-resolution sequences to image the hippocampus adequately. SPECT, using ^{99m}Tc-HMPAO, is available in most hospitals, and has a sensitivity in lateralizing that is greater than 90% if the radiotracer is injected intraictally or periictally (2). PET with fluorodeoxyglucose, when given interictally, has a sensitivity of 84% (2). Recent studies regarding proton MR spectroscopy report this technique can lateralize an abnormal temporal lobe in over 90% of cases (3). From these data it is obvious that we have become proficient in the multitechnique imaging of patients with intractable epilepsy. Nonetheless, we now need to decide which of these tools is best for ''buying or selling''; which ones should we build on, and which ones bypass?

In this issue of the *AJNR*, Won et al (page 593) compared results of MR imaging, PET, and SPECT in 118 patients with intractable epilepsy, using pathologic diagnoses as their standard of reference. Several aspects of their investigation are important. When these three most widely used imaging techniques were compared to each other, MR imaging findings had a greater concordance with PET than with SPECT. When compared with histologic findings, MR imaging correctly lateralized the epileptogenic foci in 72% of patients (very similar to their results with SPECT), whereas PET lateralized the focus in 85% of patients. In my opinion, the results of MR imaging in this series are disappointing, and in my experience, MR performs much better than portrayed in this article. The MR techniques the authors used are not significantly different from what we routinely use at our institution. Our protocol includes coronal 3-mm sec-