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David F. Kallmes

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Device-Mediated Effect versus the Healing Response in Interventional Neuroradiology

The case report by Blanc et al. in this issue of *AJNR* is important in several respects. First, the report presents a rare but devastating complication that may occur with Hunterian occlusion for treatment of giant aneurysms. Second, the management of the case can be used as a model for other practitioners who encounter similar complications. Third, and perhaps most relevant, the report serves as a reminder that the physiologic response of the patient to an embolic agent may be of as much importance as the mechanical characteristics of the embolic agent itself.

Most literature on interventional procedures focuses primarily on aspects of the implanted device, including technique of implantation and therapeutic end point. However, in the case of occlusion devices, thrombus induced by the procedure often represents the primary therapeutic "device." For instance, endosaccular occlusion of aneurysms by use of platinum coils, even in the most skilled hands, results in <30% of aneurysm volume occupied by coils. The long-term outcome of platinum coil embolization of aneurysms therefore probably depends to a greater extent on the body's own processing of the coil-induced thrombus than on the coils themselves. Furthermore, polyvinyl alcohol embolization of vascular malformations and tumors results in reliable tissue devascularization. Much or most of the treatment effect represents propagation of thrombus within the embolized tumor bed, with only a minority of the vessels occluded with the polyvinyl alcohol particles themselves. Last, although balloon occlusion of the carotid artery seems to be a simple device-mediated occlusion technique, much of the permanent vessel occlusion is effected by organization of thrombus induced by the balloon rather than by the balloon itself. Each of these examples emphasizes the paramount importance of the body's own healing mechanism in determining outcome of the interventional procedure.

The case report by Blanc et al. represents an important example of the natural healing mechanism gone wrong. Permanent carotid artery occlusion is a highly efficacious technique for obliteration of large and giant aneurysms at the skull base. As noted above, occlusion of these aneurysms is effected through organization of balloon- or coil-induced thrombus in the parent artery and aneurysm cavity. In most cases, the thrombosis of the aneurysm is relatively controlled. Over months and years, the thrombosed aneurysm retracts and be-

comes small and permanently occluded. However, organizing thrombus is an extraordinarily "biologically active" tissue. Cytokines released from cellular elements within the thrombus, including platelets, neutrophils, monocytes, and macrophages, promote angiogenesis, tissue ingrowth, and matrix production. Fibrin and fibrin degradation products are also important substrates for the process of thrombus organization. In experimental aneurysms, we note that extensive neovascularity is present throughout aneurysm cavities within the first few weeks after coil embolization. Increased capillary permeability of these neovessels within the evolving thrombus likely promotes transient enlargement of the aneurysm cavity. It is well known that permanent occlusion of giant aneurysms around the skull base can cause transient increased symptoms of cranial neuropathy. In the current case, it seems that such processes have been promoted to the point of occlusion of the ipsilateral middle cerebral artery.

Many research labs, including our own, have focused substantial efforts on improving efficacy of aneurysm embolization by increasing the "biological activity" of coils. Such research has been stimulated by the widely held position that platinum is biologically inert and, to improve intra-aneurysmal healing, other agents need to be added to coils. Perhaps this line of reasoning is flawed. As shown by the behavior of the giant aneurysm in the current case, blood clot is extraordinarily "biologically active." Perhaps we could harness the physiology of a thrombus-filled aneurysm to effect permanent aneurysm occlusion, without need for coil modification techniques. One area to which we might turn for guidance is the cardiology literature, which is replete with important advances such as glycoprotein IIb/IIIa inhibitors and local radiation therapy that rely on modification of the body's response to the implanted devices to improve therapeutic efficacy.

The current case reminds us of the importance of the medical management of cases, including nonsteroidal anti-inflammatory agents, and potentially steroid therapy, to improve outcome. Perhaps more importantly, it reminds us that as therapists, we are only tipping the balance against the pathologic process and, in the end, relying on Mother Nature to cure the pathologic abnormality.

DAVID F. KALLMES, MD
University of Virginia Health Services