Histologic Long-term Follow-up after Embolization with Polyvinyl Alcohol Particles

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Summary: A large facial vascular malformation was embolized with polyvinyl alcohol particles twice in 8 years. Resected tissue enabled long-term examination of this material, confirming its chemical inertness and revealing minimal tissue reaction to it apart from calcification. No particle migration, fragmentation, or absorption occurred. There was some recanalization of occluded vessels. Most vessels containing polyvinyl alcohol particles, and all of the larger vessels, were incompletely occluded, with particles becoming embedded in their walls.

Index terms: Interventional materials, particles and microspheres; Arteriovenous malformations, embolization

Polyvinyl alcohol was introduced as an embolic agent by Porstmann et al (1) in 1971. Studies of its effects on tissue and its behavior in the body are limited to animal studies and 2-year follow-up studies in humans (2–4). A case in which a large facial vascular malformation was embolized both 8 years and 6 days before resection provided a unique opportunity to examine short- and long-term effects of polyvinyl alcohol particles.

Case Report

A 33-year-old man had a large, severely disfiguring vascular malformation of the entire nose and some of the surrounding cheek and lip. Selective angiography in 1984 showed evidence of a previous ligation of the right external carotid artery at its origin. Supply toward a large maxillofacial arteriovenous malformation involving the nose, the right cheek, and the upper lip was noted from the left and right internal carotid arteries via their ophthalmic branches; from the facial, transverse facial, internal maxillary, and superficial temporal artery branches on the left side; and from the internal maxillary and facial artery branches indirectly via anastomoses from the vertebral, the deep, and the ascending cervical arteries on the right side. Embolization was then carried out with small particles of polyvinyl alcohol (150–250 μm; Ingenor) injected selectively through a 4F catheter (Ingenor, Paris, France) into the branches of the left external carotid system and then into the right ascending cervical artery until stagnation of flow occurred. Embolic material was demonstrated within the facial arteriovenous malformation on postembolization computed tomograms. Partial resection of a component involving the upper lip was then carried out without complication.

Complete surgical removal was contemplated in 1992, 8 years after the initial embolization. Angiography and embolization were carried out before surgery. Embolization was performed with medium-sized particles of polyvinyl alcohol (250–350 μm; Contour ITC, San Francisco, Calif) through a microcatheter (Tracker 18, Target Therapeutics, San Jose, Calif). In addition to the branches of the left external carotid artery, the right ascending cervical artery and the right ophthalmic artery distal to the retinal artery takeoff were also embolized.

No complications occurred after embolization, and 7 days after the procedure the entire nose and tissues containing the vascular malformation were surgically removed. All of the resected tissue was routinely processed by paraffin embedding and stained with standard hematoxylin-eosin and elastic–Martius scarlet blue stains. Unused particles of polyvinyl alcohol from the same manufacturer and of the same size range used in the embolizations were suspended in blood that was clotted and processed in the same way as the resected tissue. These unused particles were compared with those found in the resected tissue.

Histologic examination of the nose and surrounding facial tissue showed a diffuse arteriovenous lesion consisting of numerous malformed vessels throughout the tissue. These vessels had a highly irregular and constantly changing architecture, with varying thickness and caliber and patchy smooth muscle. Elastic was variably absent or present in diffuse strands or multiple layers. Only a few vessels contained polyvinyl alcohol particles from the previous embolizations.

Polyvinyl alcohol particles from the first embolization were the same size and had the same irregular "prickly sponge" shape as the unused particles did. With elastic

Received March 26, 1993; accepted after revision September 23.

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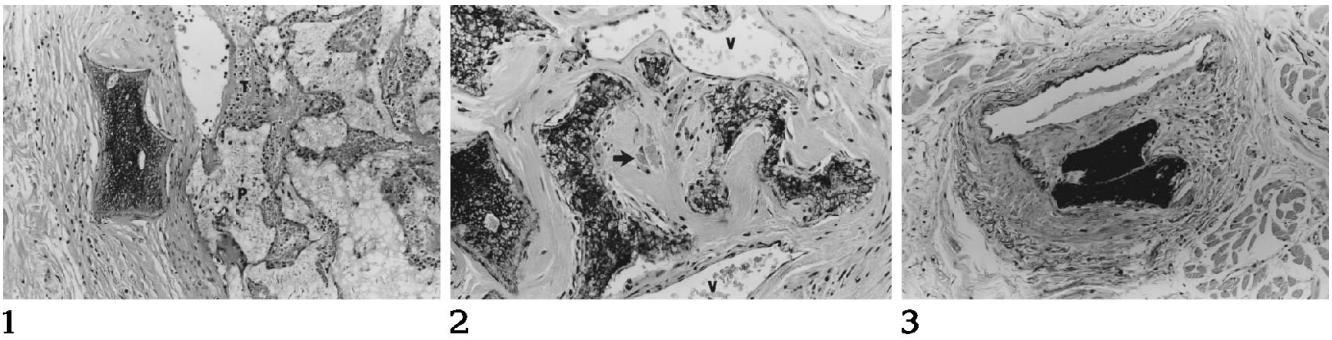
AJNR 16:843–846, Apr 1995 0195-6108/95/1604–0843



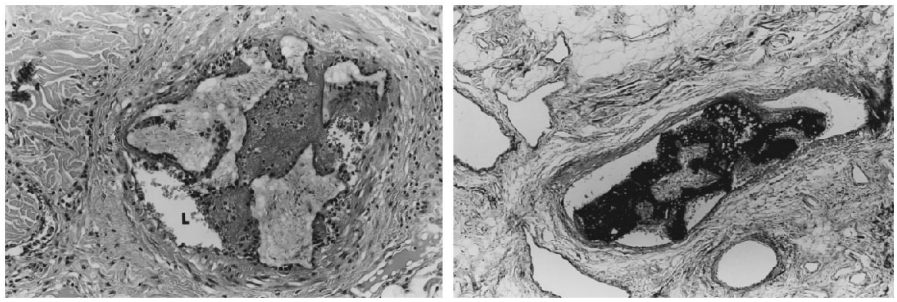


Fig 1. Photomicrograph (hematoxylin-eosin stain) of histologic section. On the left, a calcified black particle of polyvinyl alcohol several years old is embedded in old organized thrombus on the wall of a blood vessel. On the right, grayish, slightly foamy new polyvinyl alcohol particles (*P*) lie in the vessel lumen, with the intervening spaces filled with recent thrombus (*T*).

Fig 2. Photomicrograph (hematoxylin-eosin stain) shows calcified black particles of old polyvinyl alcohol embedded in an old organized thrombus filling a vessel lumen. Occasional macrophages are filled with contrast material from the time of first embolization (*arrow*). Recanalization has produced small new vessels (*V*).

Fig 3. Photomicrograph (elastic–Martius scarlet blue stain) shows black particles of polyvinyl alcohol have become embedded in collagen on the wall of a vessel by the process of thrombus organization, leaving only a small lumen above. The (incomplete) elastic lamina of the vessel is the thick wavy black line surrounding the remaining lumen and part of the mass of polyvinyl alcohol and collagen.

Fig 4. Photomicrograph (hematoxylin-eosin stain) shows a small vessel almost totally occluded by gray particles of polyvinyl alcohol and fresh thrombus. A small lumen (*L*) remains visible. Most vessels were incompletely occluded.

Fig 5. Photomicrograph (elastic–Martius scarlet blue stain) of oblique section of a blood vessel shows a black-staining particle of polyvinyl alcohol covered with thrombus adherent to the vessel wall but not completely occluding it. Flow is clearly reduced.

stains, both unused particles and those from the resected specimen were a uniform black. With hematoxylin-eosin, unused particles of polyvinyl alcohol were faintly blue, whereas those in the resected specimen were calcified and therefore purple, with the spaces in the sponge filled with amorphous material, contrast material, and some cellular debris (Fig 1). No inflammation associated with the particles from the first embolization was found, except for occasional multinucleate giant cells next to a few of the particles. No cellular atypia suggestive of premalignant change was seen. Rare hemosiderin deposits around occasional vessels indicated very little remote hemorrhage.

Polyvinyl alcohol particles from the first embolization were present in medium to large vessels. Some medium-sized vessels had been totally occluded: the original lumen was partly occupied by particles of polyvinyl alcohol, and the remaining space was taken up by old thrombus organized into dense collagen. All of these vessels showed some degree of recanalization by vascular spaces lined by endothelial cells and had no smooth muscle or other vascular components (Fig 2). Many medium-sized vessels and all of the larger ones contained polyvinyl alcohol particles as marginal deposits. These deposits often protruded into the lumen and were covered by dense collagen and sometimes by smooth muscle cells as well (Fig 3). Their appearance suggested that particles adhered to the walls of vessels, were covered with thrombus, and then were organized into collagenous masses, without stasis and thrombosis of the rest of the vascular lumen. Macrophages containing contrast material were seen in some of the vessels containing particles.

Polyvinyl alcohol particles from the recent embolization were identical in size, shape, and staining characteristics to similar unused particles. Embolized vessels contained polyvinyl alcohol particles mixed with fresh thrombus. Some were completely occluded, but most were subtotally blocked and had small lumen remaining (Figs 4 and 5). Inflammatory cells were seen in only a few vessels, as a peripheral sprinkling in the "adventitia." Patchy angionecrosis was seen in a few vessels, with death of some smooth muscle cells but no rupture. No necrosis was seen in any of the adjacent tissue.

Discussion

Polyvinyl alcohol particles are used domestically as synthetic sponge and have been in clinical use since 1952. The substance was introduced as an embolic material in 1971, and was

chosen for its biocompatibility and inertness (4–13). It is used to reduce blood flow in vascular malformations and some tumors, making subsequent surgical resection easier (4, 14). Observations of its effects on tissues are limited to short-term animal experiments and one study in humans up to 2 years after embolization (2, 3, 7, 15). Our case provided an opportunity to examine the fate of particles used for embolization 8 years after their use.

The acute reaction to polyvinyl alcohol particles is thrombosis with subsequent collagenous organization of the thrombus. Previous studies reported temporary acute inflammation, sometimes with giant cells, and some acute vasculitis or angionecrosis, although this varied greatly in severity. Proposed mechanisms for the vasculitis include ischemia, direct toxicity of polyvinyl alcohol, and an allergic reaction (2, 4, 6, 7, 16, 17). In our case, only a few embolized vessels showed mild acute inflammation and necrosis of some cells in the vessel wall. Although hemorrhage might be expected to occur as a result of vessel necrosis, bleeding has rarely been reported as a complication of embolization with polyvinyl alcohol (4). Our specimen showed no sign of recent or remote hemorrhage, and the few vessels with necrotic cells showed no sign of rupture.

Observation of the particles used in the first embolization procedure confirmed claims of this material's chemical inertness. Particles of polyvinyl alcohol retained their size and shape, and no small fragments or lysosomal digestion were seen to suggest remote or ongoing degradation. The only alteration after 8 years in the body was slight calcification. Polyvinyl alcohol particles are believed not to fragment in use (17, 18), and no small fragments were seen in our case, although small pieces formed at the time of the procedure might have passed through the malformation and gone to the lungs. Our findings agreed with previous studies showing little chronic irritation by polyvinyl alcohol particles (2, 6, 7), with no chronic inflammation in our specimen and only rare foreign body giant cells. Foreign body giant cells are a nonspecific reaction to many foreign materials and do not by themselves indicate toxicity (19).

Contradicting some claims (6, 7, 20–22) and agreeing with others (3, 4), recanalization of embolized vessels did occur. Tiny tortuous capillary-type vessels traversed old thrombi containing particles of polyvinyl alcohol. The cross-sectional area of available lumen in these vessels was greatly reduced, so the restored flow should have been small. Recanalization is a slow process occurring over weeks and months and should not pose a clinical problem, because current techniques use polyvinyl alcohol embolization to reduce blood flow hours or days before surgery.

In larger vessels and many medium-sized ones, the first embolization procedure did not occlude the lumen totally, and the particles of polyvinyl alcohol became buried in a collagenous nodule at the edge of the vessel. In the more recent embolization procedure, smaller vessels were embolized, but most of these showed incomplete occlusion, with some vascular lumen remaining. This suggests that polyvinyl alcohol acts more by particle adherence to vascular walls, slowing blood flow, than by direct plugging vessels with secondary thrombosis. This mode of action of polyvinyl alcohol (reducing flow but not completely plugging the vessel) has been reported (17). It is consistent with other published histologic observations (17, 23) and is supported by experimental work suggesting polyvinyl alcohol works mainly by adhering to vessel walls and not by plugging them shut.

Polyvinyl alcohol and methacrylate have been reported to migrate out of vessels, and a mechanism for this has been proposed (3, 24). No migration was seen in our case, but collagenization of marginal deposits in incompletely occluded vessels, so prominent in this case, might produce an appearance suggestive of extravasation and might explain previous reports of embolic material "leaving" the blood vessels.

In summary, examination of a vascular malformation embolized with polyvinyl alcohol particles just before resection as well as 8 years earlier confirmed the stability and biocompatibility of this material and suggested that it acts by adhering to vessel walls, temporarily reducing blood flow. In the long term it is incorporated into vessel walls, and blood flow is partly restored by revascularization through old thrombi.

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