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Polyvinyl Alcohol Foam–Gelfoam for Therapeutic Embolization: A Synergistic Mixture

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Gelfoam and polyvinyl alcohol foam particles each have advantages and disadvantages for therapeutic embolization. It was theorized and confirmed that a mixture of the two retains the advantages and eliminates the disadvantages of each. Two mixtures were prepared, tested in animals, and used successfully in 14 patients. It was found that the mixtures of Gelfoam and polyvinyl alcohol foam particles fulfilled the expectations and needs for particulate embolic materials.

Gelfoam is preeminent among materials currently in use for particulate therapeutic embolization. It is easy to use since it slides smoothly through most catheters when the particles are suspended in contrast material or other aqueous fluids. It is not an ideal agent: it is fairly quickly degraded by the body’s proteolytic pathways and therefore permits rapid recanalization of embolized vessels. Polyvinyl alcohol (PVA) foam is not perfect either. It takes months to years for PVA to be absorbed by the body [1], and is thus effectively permanent. Its high coefficient of friction causes its particles to roll within the embolization catheter resulting in "logjams." Although this can be overcome by simply increasing the force of injection, it cannot usually be done with maintenance of the physiologic "slow-flow" technique [2]. We needed a permanent, easy-to-use material for therapeutic embolization. For us, the mixture of Gelfoam and PVA foam fulfilled this pair of requirements. We report here its preparation, technique of use, and results.

Theory

Figure 1A shows how Gelfoam particles pass easily through a delivery catheter. Since Gelfoam has little frictional drag, the particles flow smoothly and with little rotation.

PVA particle passage is more complex. Having a much higher coefficient of friction, PVA particles tend to tumble (fig. 1B). So long as all PVA particles are the same size and shape and, most importantly, are very widely spaced, they move almost as easily as Gelfoam. But they suspend much less well than do Gelfoam particles, shape is irregular, and the particles tend to jam with great frequency when used in usual concentrations [3, 4].

Two PVA–Gelfoam mixtures can be utilized. Embolization of abnormalities proximal to capillary beds (e.g., vascular tumors) can be accomplished with a mixture of PVA particles and Gelfoam powder suspended in contrast material. High-flow lesions (e.g., arteriovenous malformations), which do not provide the protective filtering action of capillary beds, require larger Gelfoam particles mixed with smaller ones of PVA. Each of these combinations should have the advantages of both facile use and relative permanence. Figure 2 illustrates the motions for each combination.
Materials and Methods

Preparation of the Mixtures

PVA particles/Gelfoam powder. One gram of Gelfoam powder (Upjohn, Kalamazoo, MI) is placed into a small stainless steel basin containing about 25 ml of contrast material. Stirring this gently and slowly with a flat object (e.g., the handle of a scalpel) reduces it from a fine aerated dust to a wet semisuspension with an appearance similar to that of small-curd cottage cheese. At this point, further stirring helps very little. To smooth the dispersion, about 5 ml of the mixture are transferred to a 20 or 30 ml syringe. As much air as possible is expelled with the syringe pointed upward. The operator's index finger is placed over the orifice of the syringe and the plunger is pulled back as far as can be held stably, usually to about the 16–20 ml mark for a 20 ml syringe. This creates a partial vacuum, which in turn causes even very small bubbles in the Gelfoam "curds" to swell. The syringe is shaken to free the Gelfoam of bubbles. Pressure is then slowly released, permitting contrast material to seep into the Gelfoam. Performing this procedure two or three times yields a smooth, thick slurry of Gelfoam powder, about the consistency of mucilage [5]. The above suspension is diluted with contrast material to the desired consistency and combined with PVA particles of the desired size [6]. Available particle sizes are 0.5–1, 1–1.4, 1.4–1.7, and 1.7–2 mm (Pittsburgh Medical Supplies, Pittsburgh, PA). Cumbersome as the technique sounds, a small amount of practice enables the operator to prepare the mixture in 3–4 min.

PVA microparticles/Gelfoam particles. As in the first mixture, the Gelfoam particles are suspended first. They can be cut during the procedure using a sterile scalpel or scissors or they can be cut at a prior time, placed into a 20 ml glass syringe, and autoclaved. Autoclaving makes the Gelfoam appear intractable, but resuspending the particles as one would the powder yields an easily manageable mixture. To this mixture are added PVA particles, 250–590 μm in size (Unipoint Ind., High Point, NC) to the desired concentration. The operator should slowly increase the concentration of PVA particles until a slurry is made that still moves easily through the catheter. It is important not to attempt to sterilize Gelfoam with ethylene oxide since this will react with the Gelfoam and may alter its biochemical properties. It is further recommended that both
mixtures be made and experimented with using the same size catheters which one expects to use for the embolization itself.

**Application**

We selected four healthy mongrel dogs with dual blood supplies to at least one kidney. We then embolized one blood supply with Gelfoam powder slurry, the other with PVA particles suspended in the Gelfoam powder slurry. The second untouched kidney permitted the animal to remain eunephric and provided the luxury of a chronic preparation. The animals were sacrificed after 6–8 weeks, their kidneys were removed, and gross and microscopic examinations were performed.

No disadvantages or contraindications to the use of the mixture being apparent from the canine work, we used the mixtures to embolize two dural arteriovenous malformations (AVMs), one dural/orbital AVM, one pial AVM, one facial AVM, one facial hemangioma, one renal AVM, four hypernephromas, one hyperfunctioning pheochromocytoma, one juvenile aggressive vascular fibroma of the left arm (deltoid region), and one subclavian artery to pulmonary artery fistula. The five kidneys, the pheochromocytoma, and the aggressive fibroma were subsequently removed. Close follow-up of the patients with dural, pial, and facial AVMs was possible; we have not succeeded in getting follow-up on the patient with the subclavian–pulmonary artery fistula.

**Results**

**Canine**

Figure 3 shows a gross section and specimen radiograph of a representative pair of kidneys from an autopsied dog. Barium-impregnated PVA particles are evident within the upper pole of the experimental kidney; Gelfoam alone was used in the lower pole. Complete obliteration of the upper pole renal cortex is shown microscopically in figure 4A; the lower pole cortex, while thinned, still demonstrated intact although abnormal nephrons. All embolized kidneys showed erosion of PVA particles through the internal elastic lamina (fig. 4B). Occasional giant cells were noted. Presacrifice arteriography confirmed the predictable renal arterial revascularization. All animals showed similar changes.

**Human**

AVMs. External carotid arterial supply to both dural AVMs remained occluded. This permitted cures in both cases (figs. 5 and 6), although the vertebral artery supply to the AVM shown in figure 6 closed slowly, but completely, over 1 year.

The mixed dural and orbital AVM was treated in several stages. Isobutyl-2-cyanoacrylate occluded a large part of the malformation permitting a surgical removal of the orbital component. Residual dural malformation was treated with the PVA–Gelfoam mixture.

The patient with the mixed pial/dural AVM was likewise treated in two stages. At the first sitting, PVA-Gelfoam was used to occlude the occipital and internal maxillary branches of the external carotid artery. Later the internal carotid artery supply was treated by embolization with PVA.

Gelfoam alone was used for the first treatment of the patient with a facial hemangioma involving maxilla and mandible. Upon return, no change from his preembolization study was manifest. PVA–Gelfoam permitted facile occlusion of the bulk of the malformation. Not yet restudied, he
has remained clinically stable since the second embolization.

Pheochromocytoma. Considerable necrosis and hemorrhage within the pheochromocytoma was noted pathologically. Following embolization serum catecholamine levels were reduced to 8% of the preembolization values.

Kidney. Renal cells from embolized kidneys were shown to be effectively devitalized by failure of both trypan blue exclusion and growth in tissue culture. Blood loss at nephrectomy has averaged 100 ml. Surgery was further simplified since total thrombosis of the renal vascular pedicle made its mobilization unnecessary: transection of the renal artery and renal vein was rendered bloodless.

Extremity. Only about 100 ml of blood loss attended resection of the aggressive fibroma despite the fact that surgery was necessarily performed too proximally to permit use of a tourniquet. Dissection of the mass from surrounding tissue was reported by the orthopedic surgeons to have been facilitated by devascularization of the tumor.

Chest. Although the patient with systemic to pulmonary arterial fistula had been lost to follow-up, his bruit and murmur disappeared after embolization. We cannot comment upon the permanence of the occlusion.

Discussion

Therapeutic particulate embolization can be a facile and, for practical purposes, permanent treatment. Used as a definitive approach (e.g., as an alternative to surgery for AVM), it affords a high margin of safety. As a preoperative adjunct to surgery, PVA-Gelfoam permits the luxury of a planned stabilization interval between embolization and surgery without concern that the occlusion and additional thrombosis will be resorbed.

Is PVA embolization permanent? This depends on the definition of “permanent.” That PVA emboli remain in place for a long time has been shown by us, Castaneda-Zuniga et al. [7], Porstman et al. [8] and White et al. [9]. We have shown that recanalization can take place even adjacent to PVA particles after they have been “wrapped” in retracting clot/scar. Thus, although permanent endovascular occlusion with PVA is unreliable, solid occlusion does persist long enough to kill tissue (fig. 4B). Disruption of the internal elastic lamina is a constant finding. Only occasional giant cells are seen.

Our experience with the endovascular effects of PVA is similar to that of Castaneda-Zuniga et al. White et al. did not demonstrate disruption of the internal elastic lamina. This may be due to their using less PVA per vessel than did we or Castaneda-Zuniga et al. We would suggest that the endothelial disruption is the result of a local pressure effect of impacted Ivalon on the endothelium, remembering that Ivalon is sponglike and, therefore, if compressed, tends to exert a restoring force in an attempt to resume its pre-compression size and shape.

Both our preliminary laboratory and practical experience recommend this mixture for trial by the therapist. We found that it combined the advantages of both Gelfoam and PVA, but was encumbered by none of the disadvantages of either material alone. The only cost was the additional time needed to prepare the combination, but that time was more than repaid by the ease of its introduction and use.

REFERENCES

Fig. 6.—Dural AVM before and after unsuccessful embolization. A and B, Occipital arteriograms, frontal view. Opacification of left transverse sinus (arrows) during early arterial phase confirms arteriovenous nature of malformation. C, Lateral view of internal maxillary arteriogram shows supply via posterior division of middle meningeal artery. Early opacification of transverse sinus (arrows). D, Lateral view after external carotid embolization. Nonfilling of AVM. E, Left vertebral arteriogram demonstrates reason for persistence of AVM: posterior muscular/meningeal artery (short arrows) could not be catheterized deeply enough for safe embolization. Early opacification of transverse sinus (long arrows). F, 18 month follow-up study shows marked diminution of feeder (arrows). Clot propagation within malformation nidus has closed it completely.