Delayed venous occlusion following embolotherapy of vascular malformations in the brain.

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Delayed Venous Occlusion following Embolotherapy of Vascular Malformations in the Brain

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PURPOSE: To describe the nature and features of delayed venous thrombosis following embolization of arteriovenous fistulae. **METHODS:** Retrospective review of the available clinical history, details of embolization procedures, and results of follow-up angiography were carried out on all embolization procedures performed on high-flow vascular malformations of the brain done at our institution since 1987. **RESULTS:** Four patients were identified who had delayed (greater than 1 week) venous thrombosis/occlusion after embolization of the malformation associated with neurologic complications. Two patients had arteriovenous fistula and two had vein-of-Galen malformations. These patients had no untoward embolization of the venous outlet as a cause of the venous occlusion. **CONCLUSIONS:** It is postulated that thrombosis in the arteriovenous fistula group was induced by conversion (due to embolization) of a patulous high flow venous outlet into a slow flow system; in the vein-of-Galen group, the occlusion was thought to be due to high-flow venopathy.

Index terms: Thrombosis, venous; Arteriovenous malformations, cerebral; Arteriovenous malformations, complications

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Intracranial venous thrombosis has a variable clinical presentation and outcome. Venous thrombosis can occur in either or both the dural sinuses and cortical veins as well as deep draining veins (1). The symptoms may range from mild to severe, including death. The etiology of venous thrombosis is varied, including low-flow and hypercoagulable states, infection, dehydration, trauma, pregnancy and the puerperium, oral contraceptives, and long-term venous catheterization (2–4).

In embolotherapy of many types of vascular lesions, thrombosis is the goal of treatment. For instance, in aneurysms, materials are placed within the aneurysm lumen to promote thrombosis (5). In some dural arteriovenous fistula, the closure of fistulous communications is performed by directly occluding the venous outlet, thereby eliminating the arteriovenous gradient (6–8).

Cortical venous thrombosis and stenosis occurs as part of the natural history of brain arteriovenous malformations. The etiology is not entirely clear but may be related to high-flow states with turbulence and pressure changes (9, 10). We present four patients who had clinical complications related to delayed venous occlusion postembolization therapy. In two patients, the etiology of the delayed thrombosis was probably because the vascular malformation draining veins carried not only fistulous arterial blood, but also normal venous drainage from the brain. With reduction in flow from the arteriovenous fistula, a low-flow state was induced that led to thrombosis of the cortical veins and dural sinuses draining the brain with subsequent clinical neurologic deficit.

In the other two patients, who had vein-of-Galen malformations, the venous thrombosis was probably due to progressive occlusive venopathy, presumably caused by a persistent high-flow shunt.

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Subjects and Methods

A retrospective review of all brain vascular malformation embolization procedures since 1987 was performed. Four patients with neurologic complications presumably related to postembolization-delayed venous occlusion were identified and form the basis of this article. These patients were chosen after review of the clinical course, the embolization procedure, and follow-up cerebral angiography. Only those patients who had clinical and radiographic documentation of delayed venous thrombosis without venous embolization were included.

In thee patients, silicone detachable balloons (Interventional Therapeutics Corporation, South San Francisco, CA) attached to Tracker 18 microcatheters (Target Therapeutics Corporation, San Jose, CA) were guided to the fistula site, inflated, and detached resulting in complete elimination of the shunt flow. In the fourth case, microcoils (Cook Corporation, Bloomington, IN, and Target Therapeutics) were deposited via Tracker 18 microcatheters into the feeder vessels serving a vein-of-Galen malformation with partial obliteration of the fistula. In no case was there embolization of the venous outlet.

In all patients, the standard embolization procedure was to place a 4- to 8-F sheath into the femoral artery, followed by angiography using a 4- to 5.5-F diagnostic catheter (Balt Corporation, Montmorency, France, or Cook Corporation, Bloomington, IN). When detachable balloons were used, an 8-F thin wall catheter (Balt Corporation, or Ingenor Corporation, Paris, France) was placed into the appropriate vessel, and a Tracker 18 microcatheter mounted with a detachable silicone balloon was advanced to the fistula site, coaxially. The balloons were mounted onto the microcatheter by placing the stiff end of the guiding wire to the tip of the catheter, and inserting the catheter into the balloon without allowing the wire to perforate the balloon. When the balloon was at the site of the fistula, the balloon was inflated with dilute contrast, and detached with gentle traction. Angiography was then performed to assess the results of embolization.

When microcoils were used, a 4-F catheter (Balt Corporation) was used as the guiding catheter, and a Tracker 18 microcatheter was placed coaxially into the feeding vessels, and microcoils (Cook Corporation and Target Therapeutics) were deposited. The coils were advanced in the catheter using a coil pusher (Target Therapeutics). All patients had the coaxial system flushed with heparinized saline (5000 U in 1000 mL of normal saline for adults, and 2500 U in 1000 mL of normal saline for pediatric cases).

These cases were specifically chosen because the embolic material could unequivocally be localized and untoward venous embolization could confidently be excluded. In two cases embolized with balloons, the vascular lesion was an arteriovenous fistula. In the other two cases, the lesions were vein-of-Galen malformations.

Results

Four patients were identified whose embolization procedure, clinical history, and follow-up angiography confirmed progressive or complete delayed venous occlusion as a cause of their clinical neurologic deficit. Follow-up angiography at the time of neurologic deterioration demonstrated absence, narrowing, or stagnation of flow in veins, confirming the presence of venous thrombosis or occlusion. Case summaries are listed below.

Case 1

A 19-year-old man presented with severe headaches and right inferior quadrantanopia. On computed tomography (CT) scan, a subarachnoid, intraventricular, and intraparenchymal hemorrhage from a left occipital vascular malformation was identified. Subsequent cerebral angiography showed a left posterior cerebral artery arteriovenous fistula (Figs. 1A and 1B). Venous drainage was complex through a network of dilated veins that eventually emptied into the sagittal sinus via pial veins, and into the left transverse sinus via pial veins and the vein of Labbé. After the patient recovered from the hemorrhage with only a residual visual field cut, detachable microballoons were deposited into the fistula. A total of three balloons were used. Postembolization angiography showed occlusion of the fistula and sluggish flow in the draining veins (Figs. 1C–1E). The immediate postprocedure course was uneventful. Eleven days later, the patient developed acutely increased headache, meningismus, and hemianopia. A CT performed at that time demonstrated an intracerebral hematoma with intraventricular and subarachnoid extension in the same distribution as the preprocedure hemorrhage. Follow-up angiography revealed no arteriovenous fistula, but nonfilling of the previously dilated occipital veins that had been present and utilized by the brain on the immediate postembolization study (Fig. 1F compared to Fig. 1E). The arterial pedicle (left posterior cerebral artery) was unchanged from the postembolization study indicating that the hemorrhage was not due to an arterial cause. The patient recovered with only a residual hemianopia.

Case 2

An 8-year-old boy presented with night terrors and headache. Cerebral angiography showed a right posterior temporal arteriovenous fistula fed primarily by the posterior cerebral artery, but additionally from a branch of the middle cerebral artery (Figs. 2A and 2B). The arterial feeders

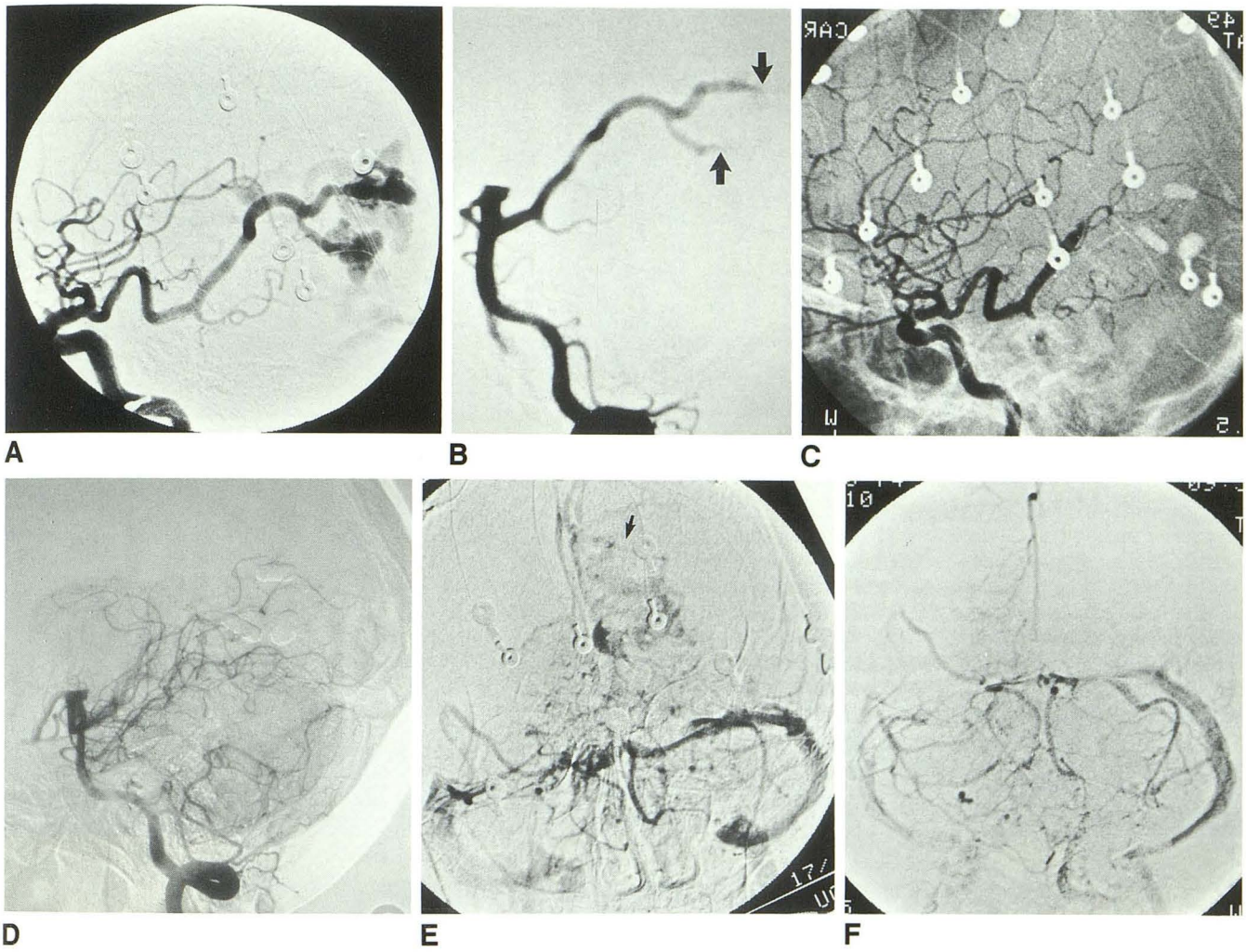

Fig. 1. *A*, Left internal carotid injection, lateral view. The posterior communicating artery fills the left posterior cerebral artery which supplies a fistula and empties into a complex venous outlet.

B, Very early arterial phase left vertebral angiogram, lateral view, demonstrates the occipital arteriovenous fistulous connections to the venous drainage (*arrows*), without an associated arteriovenous malformation nidus.

C, Postembolization, lateral, left internal carotid angiogram shows the detachable balloons in place with elimination of the fistula.

D, Postembolization, lateral, left vertebral angiogram shows the detachable balloons in place with elimination of the fistula.

E, Postembolization AP left vertebral artery injection showed sluggish flow through patent, normal occipital draining veins (*arrow*) as well as patulous veins now draining the brain which had previously also drained the fistula.

F, Venous phase of the Townes projection vertebral angiogram at the time of the second hemorrhage shows absence of the draining veins serving the occipital lobe, which had been patent on the immediate postembolization angiogram. (compare to *E* and see text).

connected to a varix that had two draining veins; the smaller one entering the sagittal sinus, the larger one emptying into the right transverse sinus (Figs. 2B and 2C). The patient underwent balloon embolization using two detachable silicone microballoons that resulted in obliteration of the fistula (Fig. 2D). The immediate postprocedure course was uneventful. Sixteen days after the procedure, the patient had acute decline in mental status. A head CT was performed that demonstrated a small subdural hematoma in the right middle cranial fossa with severe temporal lobe edema. A cerebral angiogram showed occlusion of the arteriovenous fistula and nonfilling of the occipital, right transverse, and right sigmoid sinuses consistent with venous sinus thrombosis (Figs. 2E–2H). Note that, in Figure 2E, the right posterior cerebral artery is still open, confirming that arterial ischemia is not the cause of the edema. The subdural hematoma was evacuated and the patient slowly recovered without neurologic deficit.

Case 3

A female neonate presented in the first day of life with congestive heart failure. CT scanning and transcranial ultrasound examination demon-

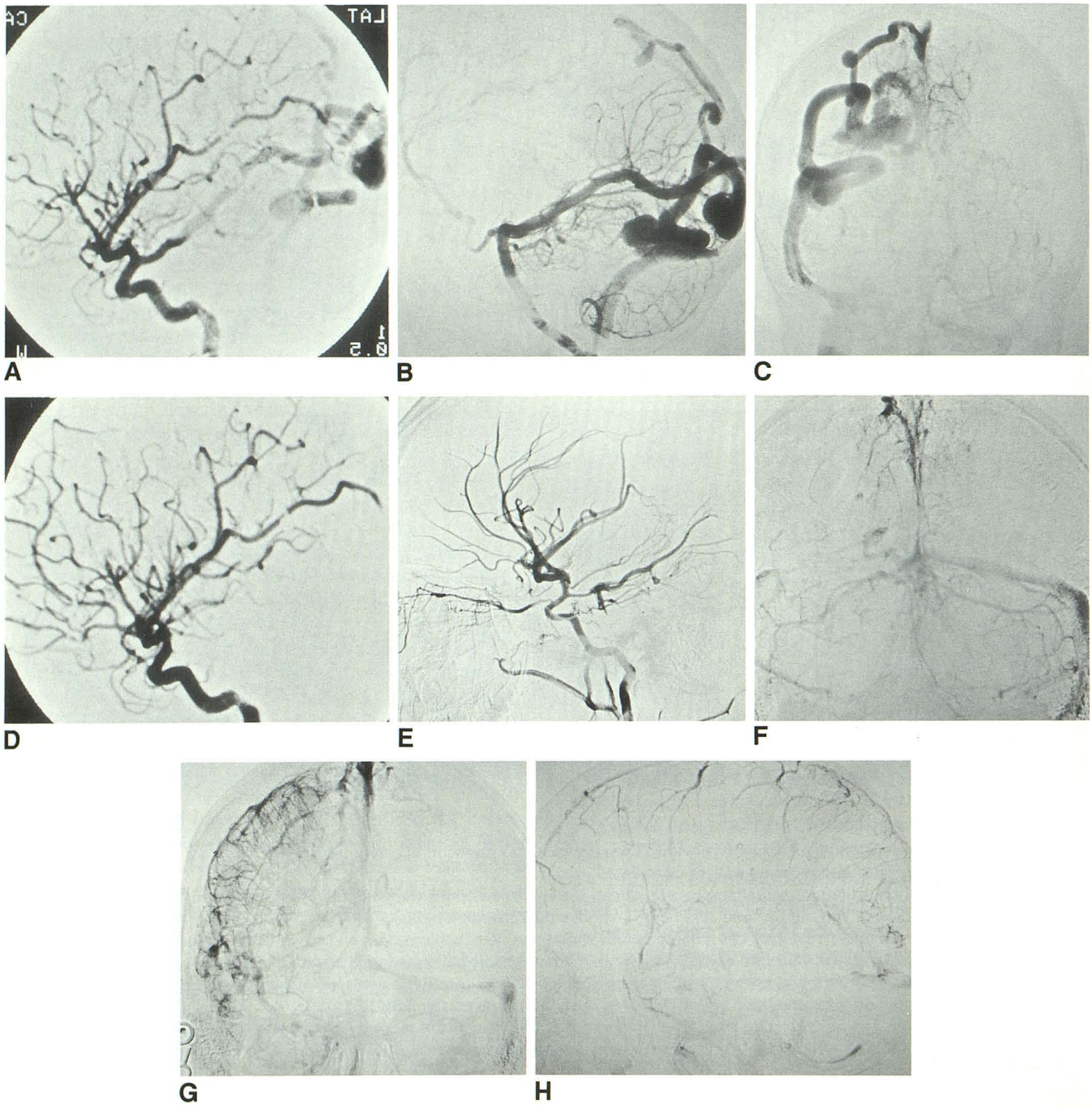

Fig. 2. *A*, Preembolization, lateral, right internal carotid angiogram shows a right posterior temporal arteriovenous fistula.

B, Left vertebral angiogram, lateral projection, shows the right posterior cerebral artery filling the fistula and venous drainage into the superior sagittal sinus and right transverse/sigmoid sinus.

C, AP view of the left vertebral injection confirms the venous drainage pattern.

D, Postembolization right internal carotid arteriogram, lateral projection, shows balloon occlusion of the fistula.

E, Right common carotid angiogram, lateral projection, at the time of clinical symptoms 16 days after embolization. Note that the posterior cerebral artery still fills, but the fistula does not.

F, Townes projection left vertebral angiogram in the venous phase shows nonfilling of the transverse and sigmoid sinuses.

G, Right internal carotid injection, AP view, venous phase, also confirms occlusion of the right transverse and sigmoid sinuses. There is drainage into the cavernous sinus on the right and, via the superior sagittal sinus, the left transverse sinus.

H, Lateral view, venous phase right internal carotid angiogram confirms occlusion of the transverse/sigmoid sinuses on the right and accessory drainage into the cavernous sinus.

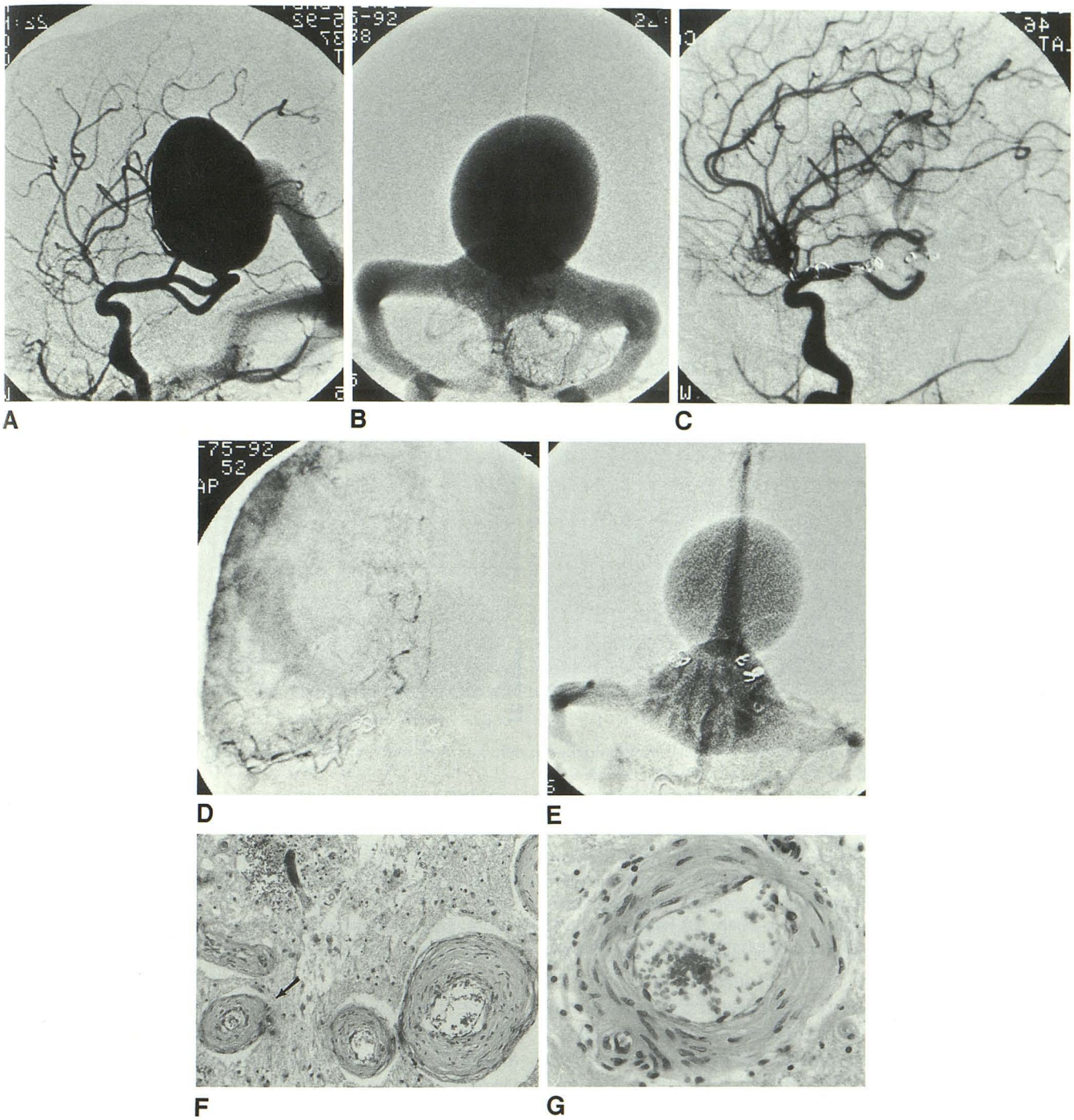

Fig. 3. *A*, Preembolization left lateral common carotid angiogram demonstrates the vein-of-Galen malformation.

B, Preembolization venous phase AP left vertebral angiogram shows very large transverse/sigmoid sinuses. The superior sagittal sinus has already been cleared of contrast.

C, Postembolization angiogram demonstrates reduced flow into the vein of Galen, with improved circulation of the anterior cerebral territory.

D, AP right internal carotid angiogram, 12 months postembolization shows severely delayed contrast washout with intense capillary staining.

E, Late venous phase of the AP left vertebral injection shows progressive stenosis of the transverse and sigmoid sinuses. This frame is 5 seconds later than the corresponding frame (*B*) on the initial angiogram (see text for explanation).

F, Microscopic section of the gray/white matter junction showing encephalomalacia of the brain tissue with microcystic change. The vessels seen are all veins with extensive smooth muscle cell hyperplasia. Some vessels are almost totally occluded as a result of wall thickening (*arrow*). Magnification ×205.

G, Magnification ×525 detail view of one hyperplastic vein.

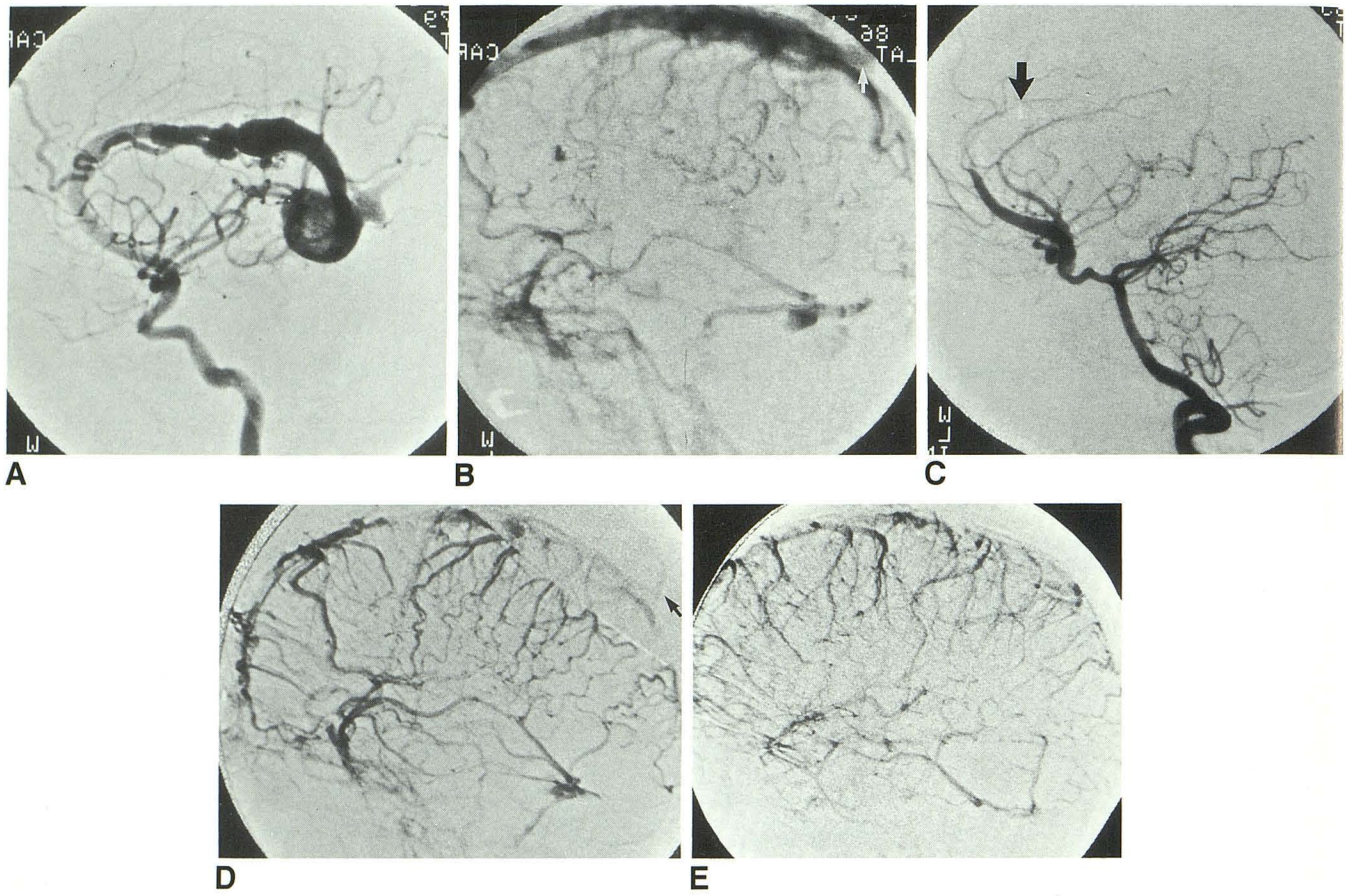

Fig. 4. *A*, Preembolization right lateral internal carotid angiogram demonstrates the vein-of-Galen fistula supplied by the pericallosal artery.

B, Venous phase shows obliteration of the sigmoid and transverse sinuses with primary drainage via the sagittal sinus into emmissary veins (*arrows*), with additional flow through the pterygoid plexus. Note the filling of the superior sagittal sinus as compared to figure *D* and *E*.

C, Postembolization lateral vertebral angiogram shows occlusion of the pericallosal feeder by the balloon (*arrow*).

D, Three-year follow-up, late venous phase right lateral internal carotid angiogram. Thrombosis/occlusion has progressed in the sagittal sinus and flow through the emissary vein is reduced (*arrow*).

E, Three-year follow-up, late venous phase left internal carotid angiogram. This confirms reduced filling of the superior sagittal sinus and rerouting of venous drainage through medullary veins since *B*.

strated a vein-of-Galen vascular malformation. Posterior choroidal, pericallosal, and thalamoperforators fed the malformation (Figs. 3A and 3B). The patient's congestive heart failure was controlled after two transarterial embolization procedures using a combination of microcoils (Fig. 3C). Follow-up of this patient was performed over a period of the next 15 months. In the first 9 months, the patient had normal neurologic development without congestive heart failure. However, subsequently the patient began to lose developmental milestones. Follow-up angiography performed at 12 months of age showed progressive venous occlusion involving the transverse and sigmoid sinuses. This probably led to the patient's demise. On the angiogram at 12 months of age, there was an intense cerebral parenchymal blush and delayed venous sinus filling (Figs. 3D and 3E). When this anteroposterior (AP) view of the transverse and sigmoid sinuses is compared to the initial preembolization venous phase (Fig. 3B), the degree of occlusive venopathy can be appreciated. The size of the transverse and sigmoid sinuses were significantly reduced in the interim. This was especially notable in the sigmoid/jugular bulb. Also, the superior sagittal sinus was seen in the same frame as the transverse sinus/jugular bulb in the follow-up study, whereas contrast in the superior sagittal sinus had washed out by the time the jugular was seen on the preembolization study. This indicates tremendously delayed venous drainage due to stenosis

of the venous outlet with secondary stagnation in the superior sagittal sinus. Additionally, the frame in Figure 3E is 5 seconds later than the corresponding frame seen in Figure 3B. Figures 3F and 3G are representative microscopic sections of the gray/white matter, which show smooth muscle cell hyperplasia of the veins with some veins nearly completely occluded, presumably secondary to the high-flow arteriovenous shunt and sinus outlet stenosis. Pathologic analysis of the dural sinuses revealed similar findings, with occasional mural thrombi.

Case 4

A 9-year-old boy presented with decreased intellectual function, as well as ataxia. Head CT revealed a vein-of-Galen vascular malformation fed by the pericallosal artery. The straight sinus and transverse sinuses were occluded. Egress of blood from the brain was from emissary veins of the cranial vault and pterygoid and clival plexi. (Figs. 4A and 4B) A detachable microballoon was deposited in the pericallosal artery with elimination of the vein-of-Galen fistula (Fig. 4C). Follow-up angiography 3 years later demonstrated progressive thrombosis or occlusion of the venous outlet, with prolonged contrast transit time (Figs. 4D and 4E). Note that the superior sagittal sinus did not fill as fully from either the right or left internal carotid injections on the most recent study as compared to the study performed 3 years previously. There also was progression of medullary vein recruitment. Also note that the emissary veins had decreased in size over the interim. The patient had continued decrease in intellectual function and worsening of the ataxia.

Discussion

Inadvertent embolization and sudden occlusion of the draining veins of a cerebral vascular malformation may, in some cases, lead to disastrous complications. With continued inflow into the malformation, but impaired venous outflow, risk of rupture may increase (7). However, delayed venous thrombosis without direct venous embolization is an unusual complication of embolization therapy of a brain vascular malformation. This can occur at a significant time after embolization and the consequences may be unpredictable. In this article, the patients selected were only those in whom it could unequivocally be determined that there was no untoward venous embolization. The use of balloons and coils allowed for exact determination of the site of embolization, and exclusion of migration of embolic material. In this way, it was felt that spontaneous postembolization venous thrombosis could be isolated. This is not to say that this mechanism does not occur in other patients after embolization of their high-flow vascular malformations. However, in arteriovenous malformations embolized with particulate agents or acrylic glues, it may be that partial venous embolization with induced venous thrombosis may occur, but the inadvertent venous embolization is unrecognized. Since this mechanism of venous thrombosis cannot be excluded with certainty, such patients were excluded from this evaluation.

In the first two cases of arteriovenous fistula, it is presumed that with elimination of the high-flow state in the patulous and ectatic draining veins, thrombosis was induced. Since these abnormally dilated veins also serve the normal brain parenchyma, there can be neurologic deficits generated by venous outlet impairment. In the cases presented, the changes in the venous drainage have been documented on the pre-, post-, and/or delayed angiograms. It is interesting to note that these two patients had delayed complications at 11 and 16 days posttreatment, respectively. The time course of the complication may indicate the etiology of the problem. Inadvertent embolization of the venous outlet might cause an immediate or early postprocedure complication.

Although arterial hemorrhage is a possibility in case 1, it is unlikely since the hemorrhagic zone directly corresponded to the previous hematoma. It is presumed that the venous side ruptured. Since both hemorrhages occurred in the same location, presumably they were both venous hemorrhages. In addition, there was no interval change in the arterial pedicle between the post-embolization angiogram and the angiogram at the time of the hemorrhage. These facts, combined with confirmation of the persistent occlusion of the fistula, make it extremely unlikely that there was an arterial cause for the hemorrhage (either occlusion or rupture). In fact, the only change in the angiograms performed after the embolization and at the time of second hemorrhage was the absence of the occipital veins. These veins were patulous with sluggish flow after the embolization. It is likely that they subsequently thrombosed, leading to a hemorrhagic venous infarction.

In case 2 the tremendous amount of edema of the temporal lobe, with only a small subdural

hematoma, points towards a veno-occlusive phenomenon. A significant change in the venous outlet pattern corresponding to the clinical complication was well documented, with nonfilling of the transverse and sigmoid sinuses on the side of the previous fistula, and redirection of flow into accessory channels (middle cerebral vein/cavernous sinus complex and contralateral transverse sinus). Again, an arterial cause is eliminated, since the arterial pedicle was unchanged (other than some diameter reduction) in the interim.

The venous obstructive pattern in vein-of-Galen fistulae is different. Instead of a delayed but abrupt veno-occlusive event, there is a progressive occlusion of the dural sinuses, resulting in diversion of flow into medullary veins with hypertrophy of these venules. The sinus occlusion is due to underlying hyperplasia of the vessel wall elements, presumably secondary to shear forces related to the turbulent high-flow fistula. This has been described pathologically in animals by both Stehbens and Pile-Spellman et al (11, 12). The changes described include vessel wall thickening, primarily of the intima, but also with some degree of elastica and smooth muscle thickening. Also, Stehbens describes some splitting of the intima with thrombus formation and attempts at reendothelialization, presumably due to shear stress on the venous wall (12). Mawad et al described progressive occlusive phenomenon in arteries serving arteriovenous malformations, and postulated a similar mechanism (13). The pathologic examination in case 3 supports this hypothesis. The primary pathologic changes in this case was smooth muscle cell hyperplasia. The changes in the blood vessel wall, once triggered, may be inevitable and may not be forestalled by embolization therapy. However, in case 3, there was some residual fistula left. Perhaps aggressive embolization is necessary to completely eliminate the fistula so that no further shear stress is applied to the outlet venous system (superior sagittal-transverse-sigmoid sinuses and jugular bulb) by the continued abnormal flow through the vein of Galen. It is possible that this would be the only way to prevent the extensive dural sinus venopathy.

Venous occlusion has also been seen in other arteriovenous malformations. Viñuela et al described a similar pattern of deep venous thrombosis in deep seated arteriovenous malformations (9). This pattern of deep venous occlusion with development of alternate venous drainage is similar to what was observed in case 4. By age 9, the sigmoid-transverse sinuses had occluded, presumably due to the same mechanism as seen in case 3. However, this patient was able to develop enough collateral flow to survive. However, there may have been further progression of thrombosis/occlusion leading to the progression of symptoms. Subsequently, this process continued even with embolization of the residual fistula. In fact, it is probable that flow was so reduced by the embolization that thrombosis was induced. In this case, the recruited channels (emmisary veins, cavernous sinus, and ophthalmic/ethmoidal veins) had been converted to sluggish flow that led to further thrombosis/occlusion and continued neurologic deterioration. This does not mean that embolization was unwise in this case, because the venous outlet that remained was draining both the brain and the fistula. This competition places the brain at risk. However, it may have been useful to place the patient on additional therapy to prevent thrombus induction.

Prospective prediction and prevention of these venous complications is problematic. Aspirin or heparin may be useful after embolization treatment to forestall an abrupt venous occlusion in cases of non-galenic arteriovenous fistula, but this is purely conjecture. This appears to be an unusual complication, and since cases 1 and 2 had symptoms approximately 2 weeks postembolization, an extended course of heparin would have been required.

With vein-of-Galen malformations, the impetus for venous stenosis may have already developed prior to birth, in which case there may not be a reasonable method for its prevention. If, however, the degree of stenosis is related to duration or volume of fistulous flow through the veins, a more aggressive early attempt to eliminate the fistula may be important.

In any case, greater attention to the venous side of vascular malformations is necessary to further elucidate the role of veins in the genesis of complications and outcome of embolization therapy.

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