Angiographic follow-up of large cerebral AVMs incompletely embolized with isobutyl-2-cyanoacrylate.

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Angiographic Follow-Up of Large Cerebral AVMs Incompletely Embolized with Isobutyl-2-Cyanoacrylate

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This study evaluated the long-term angiographic results in large cerebral arteriovenous malformations (AVMs) partially embolized with isobutyl-2-cyanoacrylate. Preembolization, immediate postembolization, and long-term follow-up angiograms were performed in 30 large, partially embolized brain AVMs. Particular attention was paid to the relative size of the residual AVM nidus and the embolized arterial feeders, to recruitment of new feeders, to the size of residual draining veins, and to the speed of arteriovenous shunt. Nine cases with less than 50% AVM nidus obliteration showed no significant morphologic changes. In 18 cases with 50–75% obliteration of the AVM nidus, 11 (61.1%) showed no significant changes, six (33.3%) showed enlargement of the AVM nidus, and one (5.5%) evolved to complete angiographic obliteration. In three cases with 75–99% AVM nidus obliteration, one remained unchanged, one showed an increase in the size of the AVM nidus, and one evolved to complete obliteration. Evaluation by plain film, CT, and cerebral angiography of the isobutyl-2-cyanoacrylate deposits showed that when the polymer was positioned predominantly in arterial feeders there was invariably reconstitution of the AVM nidus through leptomeningeal, deep medullary, and/or dural collaterals. This phenomenon did not occur when the isobutyl-2-cyanoacrylate was deposited mainly in the AVM nidus.

Progressive thrombosis of arteriovenous malformations (AVMs) partially embolized with isobutyl-2-cyanoacrylate (IBCA), leading to complete angiographic obliteration, has been observed previously [1]. The phenomenon of progressive postembolization thrombosis of a vascular lesion has also been described by Latchaw and Gold [2] and Tadavarthy et al. [3] after embolization with polyvinyl alcohol. The active thrombogenic effect of IBCA in partially embolized AVMs may be related to the substantial decrease in flow and pressure through the residual AVM nidus and the concomitant chronic reactive inflammation of occluded vessels and surrounding brain tissue that has been observed in histopathologic specimens [4, 5]. This progressive thrombosis may extend into the draining veins and result in a significant decrease in inflow and outflow to the residual nidus [1].

In 30 patients with large, partially embolized cerebral AVMs, preembolization, immediate postembolization, and long-term follow-up angiograms were compared to evaluate morphologic changes in the residual AVM nidus and embolized arterial feeders; recruitment of new leptomeningeal, deep medullary, and dural feeders; morphologic changes in the venous drainage of the AVM; and change in arteriovenous shunting time.

Materials and Methods

Of 100 patients with large cerebral AVMs who underwent endovascular embolization with IBCA, 30 cases, not surgically resected, have had proper long-term follow-up angiography and are the subject of this report. Twenty-one cases had complete surgical resection prior to embolization, demonstrated on postsurgical angiography, and the remaining 49 patients were lost to proper long-term follow-up.

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Twenty AVMs were in the left hemisphere and 10 were in the right. Twenty-six involved eloquent areas of the brain, such as speech (13 cases), motor-sensory (10 cases), and visual cortex (three cases). Four AVMs were in the frontal lobe, away from Rolando's area or the speech area. The decision to embolize these brain AVMs was taken by a neurosurgical-neuroradiologic team. It was decided that all brain AVMs that were of large size or eloquent topography carried a potentially high neurosurgical morbidity/mortality and should be embolized presurgically or treated by embolization alone. The aim of the endovascular embolization with IBCA was to totally obliterate the brain AVM nidus or to decrease its size, minimize operative blood loss, improve surgical manipulation, and decrease intraoperative time.

Twenty-two had a transfemoral approach, five had an intraoperative approach, and three had a combined approach (transfemoral and intraoperative embolization). A total of 120 arterial feeders were selectively catheterized and embolized with an average of four feeders per patient. All patients had immediate postembolization four-vessel angiograms performed by the transfemoral technique. In those cases that underwent intraoperative embolization, an immediate postembolization angiogram was performed 24–48 hr after surgery. One patient had a follow-up angiogram 1 week after embolization, and three patients had follow-up angiography 3–5 months after therapy. Twenty patients had a second angiogram 6–9 months after embolization, and six patients had a second postembolization angiogram 10–13 months after therapy. Comparison was made between preembolization angiograms and the two sets of postembolization angiograms.

Comparative analysis of postembolization angiograms (immediate and follow-up) included relative sizes of embolized and unembolized feeders; recruitment of new feeders (leptomeningeal, medullary, and dural); relative size of the residual AVM nidus; morphologic changes in the venous drainage; and relative speed of arteriovenous shunting. This assessment was subjective and approximate based on a comparison of the nidus from pre- and postembolization angiograms. This method was consistent and useful for comparative purposes. All angiographic criteria and their consistency were verified by separate evaluation by two authors (F.V. and A.J.F.) in every case.

The protocol of angiographic interpretation included evaluation of the vascular territory involving the AVM and a detailed analysis of all ipsilateral and contralateral potential sources of collateral feeders to the AVM. This approach was essential for evaluation of the true morphologic results of embolization in AVMs at or near vascular watershed areas.

Evaluation on plain film, CT, and cerebral angiography of the location of the IBCA deposits in relation to the IBCA nidus was done in all cases. The IBCA was easily identified on noncontrast CT scan by its very high CT numbers (in the hundreds). It was possible to identify venous from arterial IBCA by comparing the plain film and CT findings with the morphologic and topographic information on the preembolization angiogram.

Results

Changes observed in the size of the AVM nidus were classified into four groups according to the proportion of AVM that had been blocked. Group 1, less than 25% obliteration; group 2, 25–50% obliteration; group 3, 50–75% obliteration; group 4, 75–99% obliteration (Table 1).

In group 1 (less than 25% obliteration initially—eight cases) and group 2 (25–50% obliteration initially—one case) there was no significant change in nidus size at the time of late follow-up angiography, and all cases remained in the same group (Table 1). This was not surprising because the embolization failed to achieve significant anatomic or dynamic changes.

TABLE 1: **Angiographic Evaluation**

Immediate Angiograms		Follow-up Angiograms	
Group	Number	Group	Number
1 <25%*	8	1	8
2 25–50%*	1	2	1
3 50–75%*	18	Complete	1
		3	11
		2	4
		1	2
4 75–99%*	3	Complete	1
		4	1
		2	1

* Percent of nidus obliteration.

In group 3 (50–75% obliteration initially—18 cases), 11 cases (61.1%) remained in the same group on late follow-up angiograms, one case (5.5%) evolved to complete AVM occlusion, and six cases (33.3%) showed increase in nidus size (Table 1).

In group 4 (75–99% obliteration initially—three cases), one case remained in the same group, one evolved into complete obliteration, and one showed an increase in nidus size on late follow-up (Fig. 1).

The angiographic patterns in the 14 cases of group 3 and group 4, which showed no change or reduction in the relative size of the nidus on late follow-up, are described in Table 2.

The angiographic findings in groups 3 and 4 showing an increase in size of the nidus on follow-up angiograms (seven cases) are described in Table 3. In these two tables, one can see development of a collateral network to the AVM nidus (four of 14 cases in Table 2 and six of seven cases in Table 3) and an increase in size of nonembolized pial feeders (six of 13 cases in Table 2 and six of seven in Table 3) (Fig. 1). Development of new dural feeders was seen in four of 14 cases in Table 2 and one of seven cases in Table 3. Development of new transdural anastomoses in groups 3 and 4 was observed in cortically located AVMs with proximally occluded pial feeders. In five of the eight intraoperative embolizations, this transdural anastomosis appeared to be enhanced by the presence of a craniotomy.

Discussion

Analysis of the immediate postembolization and long-term follow-up angiograms on the 30 patients show that final morphologic results are related to the relative success or failure of embolization and occlusion of the AVM nidus. In those cases in which plain film, CT, and angiography showed

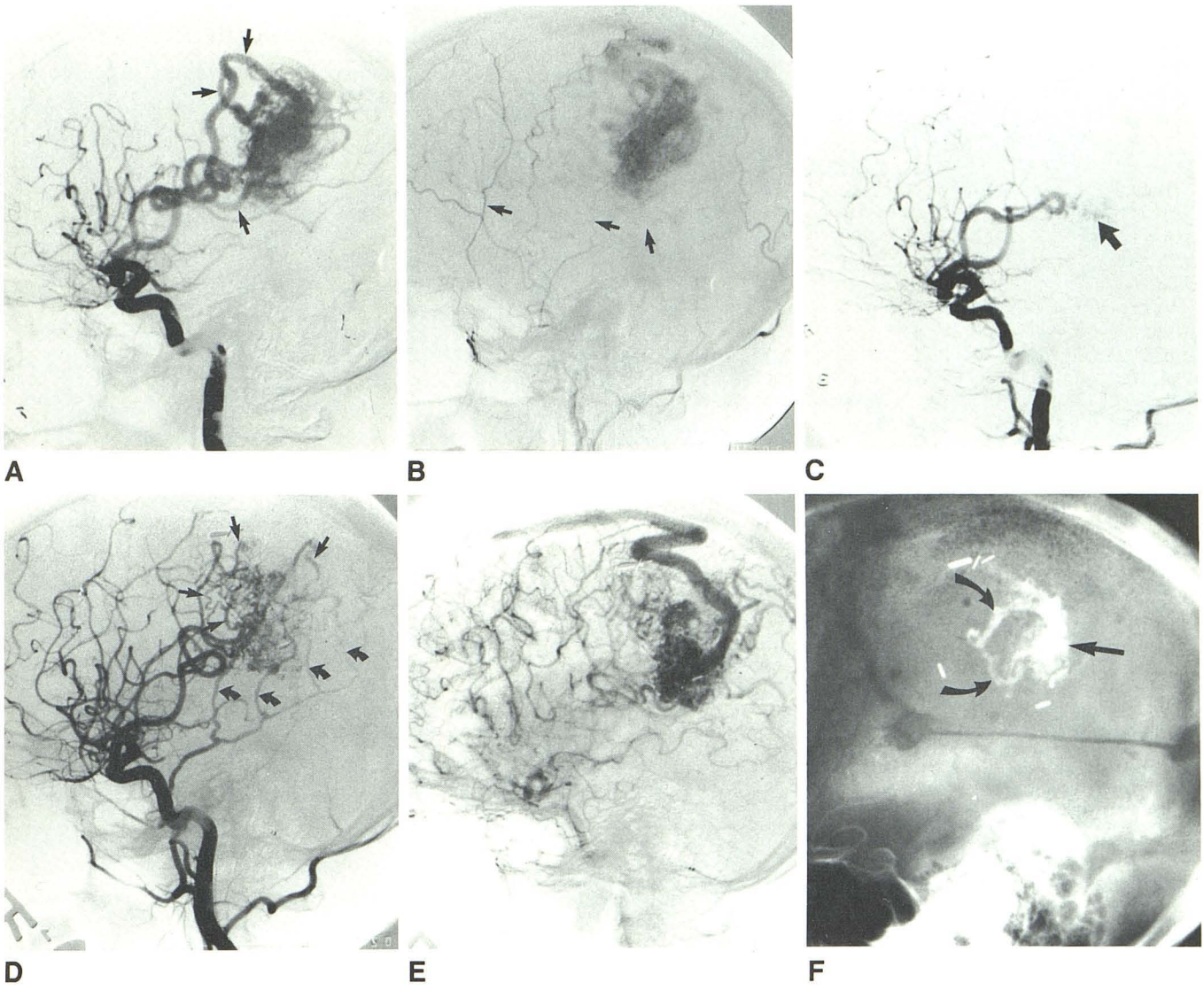

Fig. 1.—**A**, Lateral right internal carotid angiogram shows large right anteror parietal AVM supplied by several enlarged middle cerebral artery feeders. Intraoperative embolization of three feeders (*arrows*) was performed. **B**, Lateral right external carotid angiogram shows size of middle meningeal artery (*arrows*) before embolization. Reflux of contrast material in internal carotid artery enabled visualization of brain AVM. **C**, Immediate postembolization angiogram shows nonvisualization of most of the AVM nidus and a small residual AVM in its most inferior aspect (*arrow*). Early (**D**) and late (**E**) arterial phases of follow-up angiograms 6 months after embolization show a profuse leptomeningeal (*straight arrows*) and dural (*curved arrows*) network reconstituting an enlarged residual AVM. The arteriovenous transit time was markedly increased and the dominant draining vein recovered its preembolization size. **F**, Postoperative lateral plain skull film shows isobutyl-2-cyanoacrylate in the AVM nidus (*straight arrow*) and in two AVM feeders (*curved arrows*). A craniotomy was performed to do an intraoperative embolization. This case moved from group 4 to group 2 after evaluation of follow-up angiograms.

TABLE 2: **Follow-up Angiograms Showing No Increase in Size of AVM Nidus (n = 14)**

	No Change	Decrease	Increase
Pial feeders	1	7	6
Collateral network	10	0	4
Dural feeders	10	0	4
A/V shunting	2	9	3
Venous drainage	5 (smaller than preemb.)	6	3 (smaller than preemb.)

TABLE 3: **Follow-up Angiograms Showing Increase in Size of AVM Nidus (n = 7)**

	No Change	Decrease	Increase
Pial feeders	1	0	6
Collateral network	1	0	6
Dural feeders	6	0	1
A/V shunting	1	0	6
Venous drainage	3	0	4

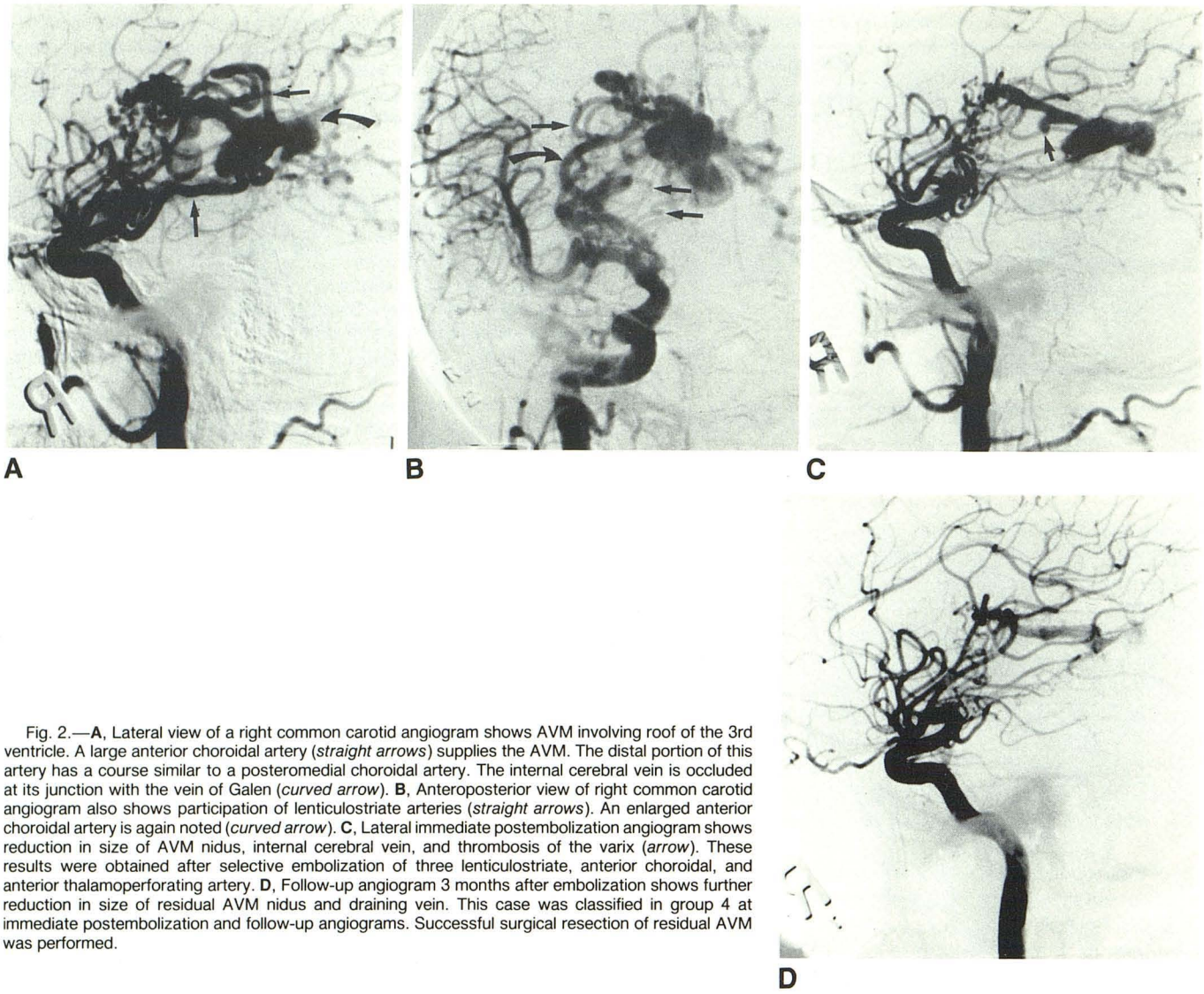

Fig. 2.—**A**, Lateral view of a right common carotid angiogram shows AVM involving roof of the 3rd ventricle. A large anterior choroidal artery (*straight arrows*) supplies the AVM. The distal portion of this artery has a course similar to a posteromedial choroidal artery. The internal cerebral vein is occluded at its junction with the vein of Galen (*curved arrow*). **B**, Anteroposterior view of right common carotid angiogram also shows participation of lenticulostriate arteries (*straight arrows*). An enlarged anterior choroidal artery is again noted (*curved arrow*). **C**, Lateral immediate postembolization angiogram shows reduction in size of AVM nidus, internal cerebral vein, and thrombosis of the varix (*arrow*). These results were obtained after selective embolization of three lenticulostriate, anterior choroidal, and anterior thalamoperforating artery. **D**, Follow-up angiogram 3 months after embolization shows further reduction in size of residual AVM nidus and draining vein. This case was classified in group 4 at immediate postembolization and follow-up angiograms. Successful surgical resection of residual AVM was performed.

an important IBCA deposit in the AVM nidus, the long-term angiographic results offered no evidence of nidus enlargement. No significant long-term morphologic changes in the AVM nidus were observed in cases where less than 50% of the nidus was initially obliterated (groups 1 and 2). In groups 3 and 4 (21 cases), seven cases showed a late increase in size of the residual AVM (Fig. 1). In some cases the residual nidus remained smaller than the preembolization nidus. This partial reduction in nidus size was sometimes accompanied by a concomitant reduction in size of the arterial feeders and draining veins, and reduction in speed of the arteriovenous shunting.

An analysis of the location of the IBCA deposits in groups 1 and 2 showed that most of the IBCA was deposited in arterial feeders, with only a small amount seen in the nidus. These unsuccessful results are comparable to the long-term results observed with bead embolization or surgical ligation of arterial feeders without removal of the nidus.

Groups 3 and 4 comprise 21 patients. The immediate postembolization angiogram in 18 patients showed nonvisualization of 50–75% of the nidus (group 3). Three patients were included in group 4, and their angiograms showed 75–99% nonvisualization of the AVM nidus (Fig. 2). The long-term follow-up angiograms in groups 3 and 4 (21 patients) show three different angiographic patterns (Tables 2 and 3). In 12 patients the residual AVMs remained essentially unchanged in size. In seven of these 12 patients a significant decrease in arteriovenous shunting and size of the draining veins was seen. In five cases arteriovenous shunting was accelerated on late angiography despite observation of a decrease in size of the corresponding draining vein. In two cases progressive thrombosis led to complete angiographic obliteration of the residual AVM. These two cases share common, immediate postembolization angiographic findings; that is, marked reduction of the nidus with no more than one or two small residual arterial feeders. These two cases were

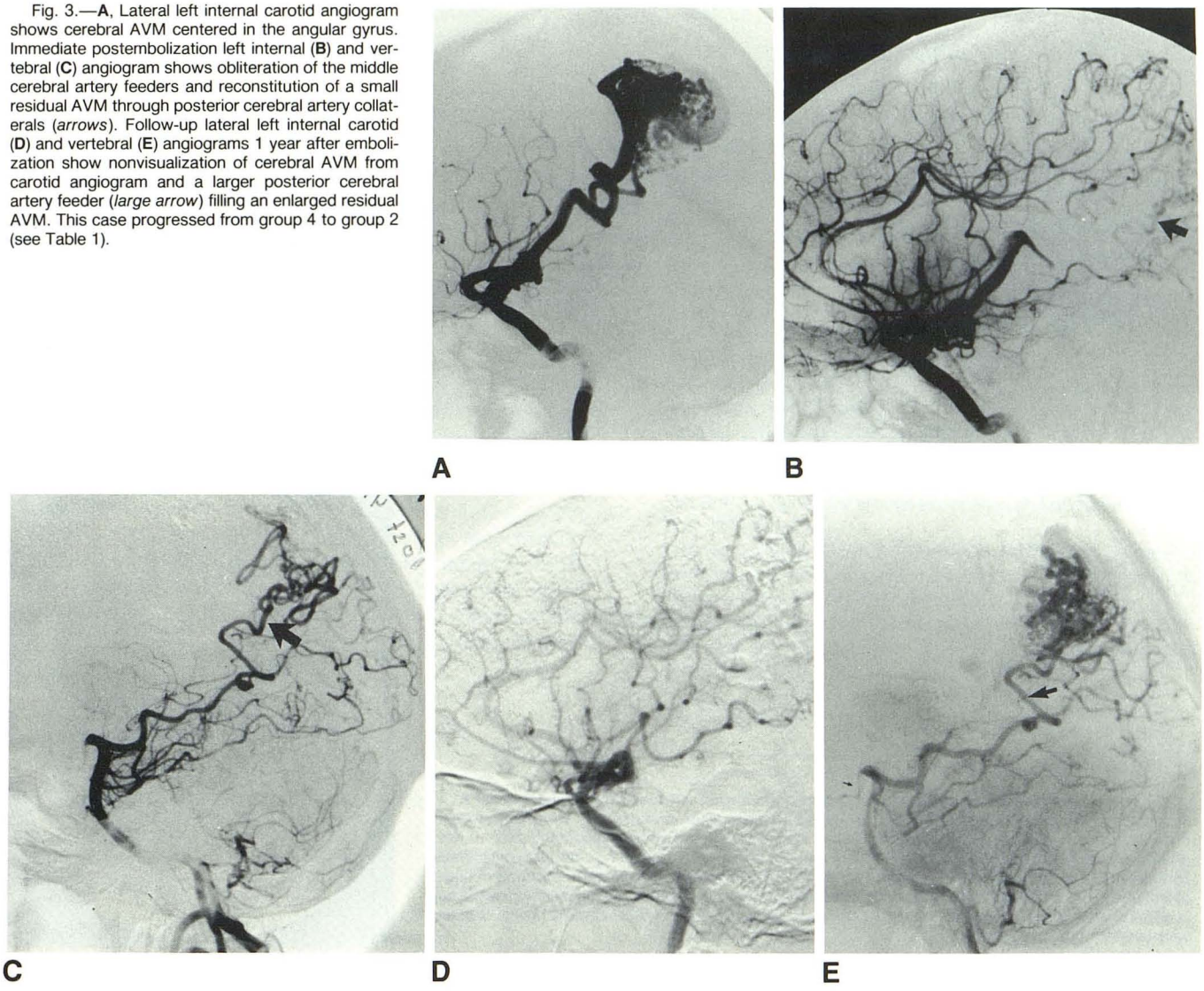

Fig. 3.—**A**, Lateral left internal carotid angiogram shows cerebral AVM centered in the angular gyrus. Immediate postembolization left internal (**B**) and vertebral (**C**) angiogram shows obliteration of the middle cerebral artery feeders and reconstitution of a small residual AVM through posterior cerebral artery collaterals (*arrows*). Follow-up lateral left internal carotid (**D**) and vertebral (**E**) angiograms 1 year after embolization show nonvisualization of cerebral AVM from carotid angiogram and a larger posterior cerebral artery feeder (*large arrow*) filling an enlarged residual AVM. This case progressed from group 4 to group 2 (see Table 1).

reviewed in a previous report [1]. Six patients in group 3 and one patient in group 4 showed an increase in size of the AVM nidus on long-term angiographic follow-up. In three cases the nidus enlarged to its preembolization size, and in four cases to slightly less than its preembolization size (Fig. 3). Six of these seven cases showed marked increase in speed of arteriovenous shunting, and four showed an increase in number and size of the draining veins.

Specific angiographic findings are demonstrated in this special group of cases from groups 3 and 4, which showed an increase in size of the AVM nidus. These cases all showed no evidence of reconstitution of previously embolized arteriovenous feeders, an increase in size of nonembolized feeders, and development of a prominent collateral network around the AVM nidus with participation of leptomeningeal, deep medullary, and transdural collaterals. The development of new dural collaterals was enhanced by the presence of a craniotomy, observed in five postoperative patients. This collateral pattern was sometimes difficult to differentiate angiographically from the original AVM nidus. At first glance it may seem that the AVM nidus had extended to surrounding territories previously uninvolved, but careful angiographic assessment of the early and middle arterial phases showed that filling of this collateral network is not accompanied by arteriovenous shunting and visualization of early draining veins. This network may reach the AVM nidus or it may reconstitute a primary feeder that was occluded proximal to the AVM nidus.

Careful evaluation of the angiograms is important for understanding hemodynamic differences observed in partially embolized AVMs. This assists the endovascular therapist and neurosurgeon in evaluating the true size of the residual AVM. Intraoperatively, it is practically impossible to separate this "functional network" from the AVM nidus. It is imperative to preserve this collateral network because it may supply functional brain tissue and it would be a mistake to embolize or resect these vessels in the belief that they belong to an

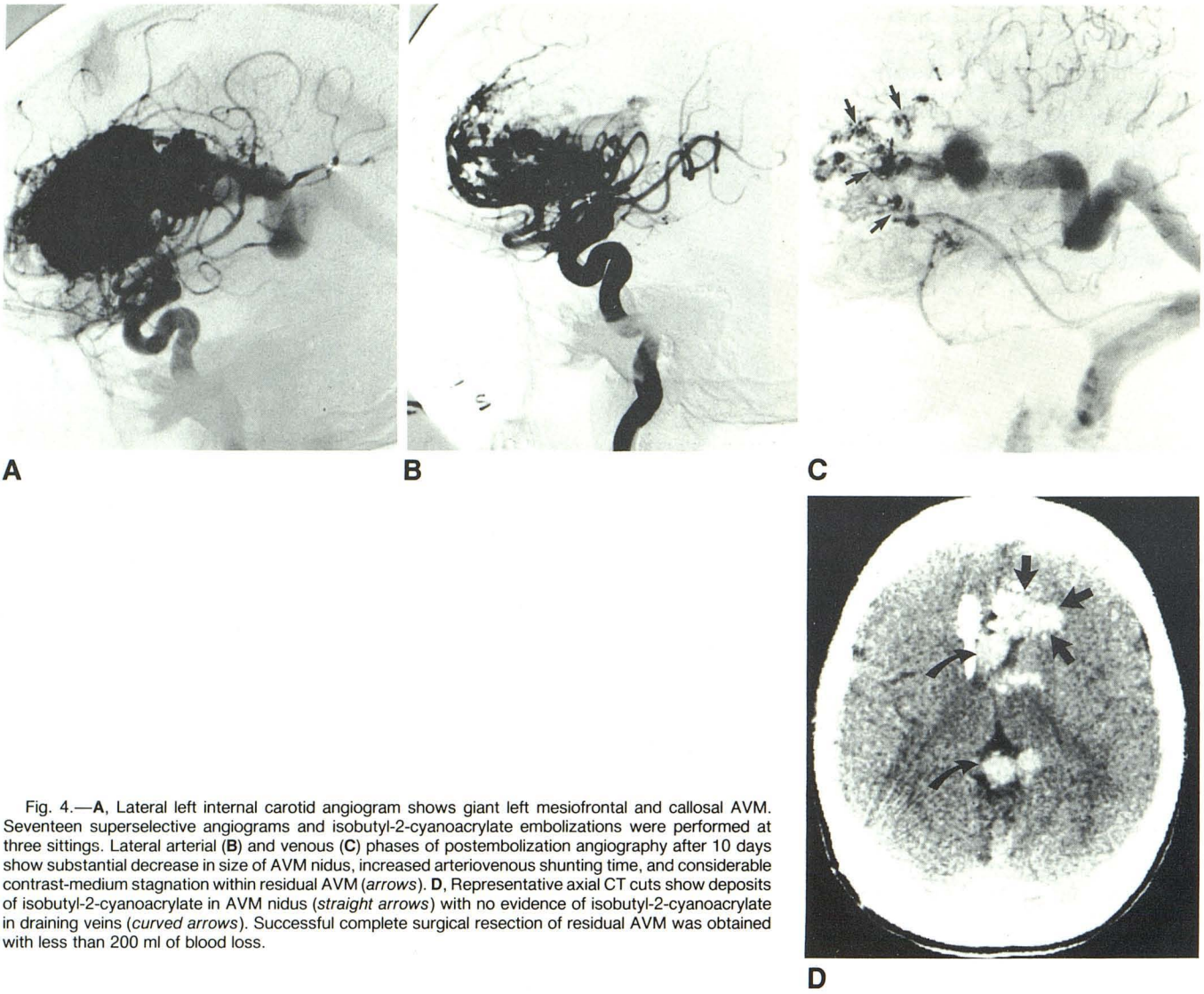

Fig. 4.—**A**, Lateral left internal carotid angiogram shows giant left mesiofrontal and callosal AVM. Seventeen superselective angiograms and isobutyl-2-cyanoacrylate embolizations were performed at three sittings. Lateral arterial (**B**) and venous (**C**) phases of postembolization angiography after 10 days show substantial decrease in size of AVM nidus, increased arteriovenous shunting time, and considerable contrast-medium stagnation within residual AVM (*arrows*). **D**, Representative axial CT cuts show deposits of isobutyl-2-cyanoacrylate in AVM nidus (*straight arrows*) with no evidence of isobutyl-2-cyanoacrylate in draining veins (*curved arrows*). Successful complete surgical resection of residual AVM was obtained with less than 200 ml of blood loss.

"enlarging AVM nidus."

The overall disappointing results of these 30 cases should force endovascular therapists to critically review all the technical aspects of endovascular therapy with IBCA. The main technical problem is related to inaccurate delivery of IBCA into the nidus of the AVM. In the great majority, if not all, of the less than adequate results there was proximal deposition of IBCA into arterial feeders with failure to reach the core of the nidus.

Two technical variations to the original technique described by Kerber et al. (6) and Debrun et al. [7] have been developed. A new mixture of IBCA, tantalum powder, iophendylate, and glacial acetic acid was used. Laboratory and animal work done by Spiegel et al. [8] demonstrates that this mixture has a more consistent polymerization time and less viscosity. It is easier to inject through the calibrated-leak balloon. No more than 0.1–0.2 ml of this mixture needs to be delivered each time, followed by rapid deflation of the calibrated-leak balloon. This technical variation has improved the final angiographic results. The relatively fast injection speed and the different biological behavior of this mixture has decreased the proximal deposition of IBCA into arterial feeders and increased deposition in the AVM nidus. The proportions used in the mixture are 30–40 μl of glacial acetic acid, 1 g of tantalum powder, 0.3 ml of iophendylate, and 1 ml of IBCA. This technique also enables the endovascular therapist to use a single arterial feeder more than once because it remains open until its distal territory has been completely blocked.

Three giant and two large cerebral AVMs have been embolized with this new embolization mixture in recent months. An average of 10 embolizations was performed in each case using these technical variations. Each embolization was performed with a different calibrated-leak balloon. We do not use the same balloon for a second embolization because of the

probability of a change in the balloon's size if tantalum powder and/or IBCA is deposited in the tip of the balloon. Postembolization angiograms in these five cases revealed that more than 80% of the nidus was obliterated. CT scans showed that the great majority of the IBCA was deposited into the nidus of the AVM with little or no IBCA deposited in arterial feeders, draining veins, or intracranial sinuses (Fig. 4). Chest radiographs failed to demonstrate significant IBCA embolization of the lungs. Surgical resection of the residual AVM was performed in these three cases. Surgical resection was clearly facilitated by embolization. Despite the large size of the original AVMs, none of the three cases needed blood-volume replacement. Histopathologic specimens demonstrated massive occlusion of AVM vessels with IBCA.

In summary, a critical review of long-term angiographic results of 30 cases of partially embolized large cerebral AVMs shows that deposition of IBCA solely into arterial feeders is systematically followed by enlargement of remaining primary feeders; development of profuse collateral networks (leptomeningeal, medullary, and dural); and reconstitution of the AVM nidus. Morphologic and clinical results of embolization in our last five large cerebral AVMs, using adjusted IBCA techniques, are encouraging. Repetitive delivery of small amounts of this new IBCA mixture, pushed with dextrose into individual arterial feeders, leads to a more accurate embolization of the core of the AVM.

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