Atrial Septal Aneurysm: Association With Cerebrovascular and Peripheral Embolic Events

Robert N. Belkin, MD, Barrie J. Hurwitz, MB, MRCP, and Joseph Kisslo, MD

Patient records in 36 consecutively identified patients with typical echocardiographic findings of atrial septal aneurysm were reviewed. Ten of the 36 (28%) had cerebrovascular events. Of these 10, 5 had completed strokes of definite embolic origin on the basis of clinical, angiographic, and computed tomographic findings; 2 had transient ischemic attacks of probable embolic origin. One of the 36 patients had a definite peripheral vascular embolus. Thus, 6 of 36 consecutively identified patients (17%) had definite embolic events and 8 of 36 (22%) had definite or possible embolic events. The cause of the association between atrial septal aneurysm and emboli is unknown. While aneurysm-associated thrombus has been suggested, the high proportion (90%) of patients with interatrial shunting demonstrated by contrast echocardiography in this study suggests paradoxical embolization as a potential cause. Whatever its mechanism, the high prevalence of embolic events in this series strongly supports the premise that atrial septal aneurysm is a cardiac abnormality with embolic potential. (Stroke 1987; 18:856-862)

Atrial septal aneurysm (ASA) is an uncommonly recognized structure of uncertain clinical significance.1-14 It has been noted in infants with hypoplastic right heart syndrome and aortic atresia who lack obligatory interatrial shunts and has been thought to occur as a consequence of excessively high right or left atrial pressure.3-6 ASA has also been recognized in adults and has been the subject of many recent reports.1,2,3,5-15 The origin of this abnormality in adults remains obscure but does not appear to be related to excessive pressure differences between the atria.1,2,12 The presence of a congenital connective tissue defect, which over time leads to aneurysmal bulging of the fossa ovalis region, has been postulated.14

Since its earliest recognition in adults, scattered reports of cerebral or systemic embolization associated with ASA have appeared.15-20 The present report notes the clinical and echocardiographic characteristics of a series of patients encountered at Duke University Medical Center with a remarkably high prevalence of such events.

Subjects and Methods

Patients and Embolic Events

This study comprises a retrospective review of 36 consecutively identified patients with two-dimensional echocardiographic findings characteristic of ASA. These patients were studied over a 27-month period from November 1983 until January 1986. Patient charts were reviewed for clinical and/or laboratory evidence of peripheral or cerebral embolic events.

Cerebrovascular events were classified as definitely embolic only when the patient record indicated a completed stroke accompanied by strong corroborative angiographic and/or computed tomographic (CT) evidence. No patient with transient ischemic attacks (TIAs) was considered to have a definite embolic event. Nevertheless, when clinical and angiographic findings were otherwise strongly suggestive of embolus, these events were classified as probably embolic. Peripheral events were classified as embolic only when the patient record indicated a sudden vascular occlusion accompanied by supporting angiographic or surgical findings. All other events were classified as of uncertain etiology.

Echocardiographic Studies

Two-dimensional examinations were performed using a commercially available, focused, phased-array imaging system. Images were obtained in standard and selected intermediate planes to best visualize the atrial septum. ASA was defined as a thin, linear, localized segment of the atrial septum demonstrating an oscillating motion from one atrium to the other (Figure 1), or a less mobile bulge into one atrium throughout the cardiac cycle.12 Care was taken to differentiate these findings from a nonlocalized bulge of the entire septum13 or from atrial structures such as tumor, thrombus, Eustachian valve, or Chiari's net.7,11 Echo contrast studies were performed by injecting agitated paraben-preserved saline solution through a 20- or 18-gauge plastic catheter inserted into an ante-cubital vein.22 A shunt was defined as the appearance of contrast in the left atrium within 4 beats of its appearance in the right. Echocardiograms were reviewed by two observers blinded to the other's readings. Disagreements between the blinded observers as to the presence or absence of interatrial shunting were resolved by unblinded consensus review.
found in the aneurysm in 1 patient; multiple fenestrations were present in the other 3.

Five additional patients, generally without clinical and laboratory evidence of ostium secundum atrial septal defects, underwent catheterization. None of these patients showed hemodynamically significant shunting, though green dye curves were positive for right-to-left shunting in 2 presenting with hypoxemia. None of the remaining patients with positive echo contrast studies demonstrated increased pulmonary vasculature or echocardiographic evidence of right-sided volume overload. Thus, though atrial level communications were present in the majority of patients, they were generally not of hemodynamic consequence.

Cerebrovascular and Peripheral Embolic Events

Ten of 36 patients (28%) had cerebrovascular events (Table 4); 1 had a peripheral vascular embolus. All of the 11 had positive echo contrast studies. In all, 6 of 36 patients (17%) had definite embolic events and 8 of 36 (22%) had definite or possible embolic events.

In 5 patients with stroke, an embolic etiology was considered definite. Clinical details are shown in Table 4. Patient 1 was a 68-year-old woman who presented with left-sided weakness and dysarthria. She had a history of hypertension, but no diabetes mellitus. Cerebral angiography demonstrated a distal occlusion of the right middle cerebral artery (MCA). Patient 2 was a 55-year-old woman who developed sudden left homonymous hemianopsia and left-sided weakness. She too had a history of hypertension. Abrupt occlusion of the right posterior cerebral artery was documented on cerebral angiography. CT scan in Patient 2 showed a hemorrhagic right parieto-occipital infarct. In Patient 3, embolic stroke was diagnosed on the basis of history, physical examination, and the occurrence of multiple new infarcts. Patient 3 was a 63-year-old man...
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Table 2. Primary Indications for Echocardiography

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrovascular event</td>
<td>8</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>4</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>3</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>3</td>
</tr>
<tr>
<td>Murmur</td>
<td>3</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>3</td>
</tr>
<tr>
<td>Aortic valve disease</td>
<td>3</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>3</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>2</td>
</tr>
<tr>
<td>Left ventricular function</td>
<td>2</td>
</tr>
<tr>
<td>Anomalous pulmonary veins</td>
<td>1</td>
</tr>
<tr>
<td>Source of peripheral embolus</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>36</strong></td>
</tr>
</tbody>
</table>

Table 3. Echocardiographic Findings

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial septal aneurysm</td>
<td>36</td>
</tr>
<tr>
<td>Oscillating</td>
<td>33</td>
</tr>
<tr>
<td>Fixed left atrium</td>
<td>2</td>
</tr>
<tr>
<td>Fixed right atrium</td>
<td>1</td>
</tr>
<tr>
<td>Positive atrial shunting by contrast</td>
<td>28/31 (90%)</td>
</tr>
<tr>
<td>Other echocardiographic findings</td>
<td></td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>6</td>
</tr>
<tr>
<td>Right ventricular enlargement</td>
<td>8</td>
</tr>
<tr>
<td>Mitral annular calcification</td>
<td>2</td>
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<tr>
<td>Left ventricular hypertrophy</td>
<td>5</td>
</tr>
<tr>
<td>Right ventricular hypertrophy</td>
<td>1</td>
</tr>
<tr>
<td>Left ventricular dilatation</td>
<td>2</td>
</tr>
<tr>
<td>Focal left ventricular abnormality</td>
<td>2</td>
</tr>
<tr>
<td>Anomalous pulmonary veins</td>
<td>1</td>
</tr>
<tr>
<td>Mild Ebstein’s anomaly</td>
<td>1</td>
</tr>
<tr>
<td>Doppler findings</td>
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<tr>
<td>Aortic regurgitation</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonic regurgitation</td>
<td>1</td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td>2</td>
</tr>
</tbody>
</table>

Results

Patients

Patients' ages varied from 31 to 83 years. Sixteen patients were men, 20 women. Associated cardiac conditions were present in 23 of the 36 patients (Table 1). The indications for echocardiography were diverse (Table 2).

Echocardiographic Findings

ASA was identified in all 36 patients, and echocardiographic findings are summarized in Table 3. ASAs were hypermobile in 33 patients (Figure 2), rapidly oscillating from the left atrium in early systole to the midposition or right atrium in late systole and diastole. ASA was confined to the left atrium in 2 patients and the right atrium in 1 (Figure 3), and showed more restricted mobility in these 3 cases. In no case was thrombus observed within the aneurysm. Six of the 36 patients demonstrated mitral valve prolapse.

Atrial Shunting

Adequate contrast studies were possible in 31 patients. Of these, 28 (90%) had evidence for interatrial shunting. Identification of the presence or absence of shunt by the blinded observers differed in only 2 cases and were later agreed upon by consensus. Four of these 28 patients had clinical, laboratory, and catheterization evidence for ostium secundum atrial septal defect. Each underwent surgical repair and under direct visualization displayed aneurymal bulging of the fossa ovalis (Figure 4). A single atrial septal defect was

![Figure 1. Schematic diagram showing hypermobile interatrial septum characteristic of atrial septal aneurysm. For details, see text.](image-url)
with hypertension who developed sudden left hemiparesis followed by left homonymous hemianopsia. CT scan revealed 2 recent infarcts, in the right parietal and occipital lobes. Carotid ultrasound showed a smooth plaque of minimal size (<30% narrowing) in the bulb of the left internal carotid artery (ICA) and intimal thickening of the right ICA without plaque or flow disturbance. Patient 4 was a 42-year-old woman with no cerebrovascular risk factors who developed right hemisphere disturbance. Patient 5 was a 69-year-old woman with a history of diabetes mellitus and hypertension who developed sudden left hemiparesis and left lower extremity paresthesias. Neurologic examination and brain CT scan were normal. Though the patient had a history of diabetes mellitus and hypertension, cerebral arteriography showed only minimal irregularity with no ulceration or luminal narrowing of the left common carotid artery at the bifurcation, indicating no significant atherosclerotic disease. Patient 7 had no history of migraine headache or hematologic or inflammatory disease. Patient 8 was a 55-year-old man without cerebrovascular risk factors. He presented with a single 5-minute episode of right amaurosis fugax and right upper extremity weakness associated with headache, though he did not otherwise have a history suggestive of migraine. On other occasions, he experienced recurrent brief episodes of vertigo, diplopia, and dysarthria. CT scan was normal. Arteriography showed total occlusion of the left vertebral artery and a 70% stenosis of the right vertebral artery. The amaurosis fugax was unexplained by the arteriographic findings as only nonsignificant changes were present in the right carotid circulation without ulceration or significant intraluminal narrowing. Patient 8 also had no history of migraine or hematologic or inflammatory disease.

One of these 8 patients with embolic events (Patient 1) had echo findings consistent with cardiomyopathy though no ventricular thrombus was noted. None of the other 7 had any structural cardiac disease except their ASA. None of the 8 patients had evidence of sustained supraventricular or ventricular arrhythmias on routine or continuous electrocardiographic recordings.

In Patients 9, 10, and 11, etiologies for cerebrovascular events could not be firmly established. None were classified as embolic for the purposes of this study. Patient 9 was a 74-year-old woman with diabetes mellitus and hypertension. She experienced episodic and transient left-sided weakness over 2 years. She was finally admitted to the hospital with lethargy and persistent left-sided weakness and dysarthria. CT scan demonstrated an infarction in the right MCA distribution and an old infarction in the right occipital lobe. Neither carotid ultrasound nor cerebral arteriography were performed. Patient 11 was a 74-year-old white man with hypertension. In 1977 he presented with 2 brief episodes of dysarthria, left tongue numbness, and headache. He was readmitted 8 years later with episodic dysarthria, left-sided weakness and numbness, and left facial weakness. Echocardiography was first ordered on this occasion. CT scan showed old basal ganglia infarcts bilaterally. Carotid ultrasound and cerebral arteriography were not performed. Patient 10 was a 71-year-old woman without cerebrovascular risk factors. She reported the abrupt onset of an episode of dizziness and gait unsteadiness while hospitalized for...
chronic obstructive lung disease. A subsequent detailed neurologic examination was negative, with the exception of difficulty on tandem walking. She displayed no significant postural changes in blood pressure or heart rate. Due to its sudden onset with no other identifiable cause, the episode was felt to be consistent with a small infarct in the distribution of the posterior circulation. Again, neither carotid ultrasound nor arteriography were performed.

**Prevalence Data**

During the 27-month study period, a total of 6,979 echocardiograms were performed; 36 of 6,979 echo studies (0.5%) displayed an ASA. During this same period, 442 of 6,979 patients (6.3%) were referred for echocardiography because of a stroke, TIA, or peripheral embolus.

Of the 11 ASA patients with embolic cerebrovascular events, unclassified cerebrovascular events, or peripheral embolic events, 9 were referred for echocardiography to exclude an intracardiac cause. Thus, 9 of 442 patients (2.0%) undergoing echocardiography for this purpose had an ASA.

**Discussion**

**Relation of ASA With Embolic Events**

These data demonstrate the highest prevalence of definite or probable embolic events in a consecutively studied series of patients with ASA reported to date (22%) and further confirm the previously suggested association of ASA with such events. Isolated reports of 1 or 2 patients with ASA and cerebrovascular events have appeared. A more recent series has reported cerebrovascular events in 16 of 80 patients with ASA (20%). Such events were considered possibly embolic in 5%.

Case reports of embolic events to other arterial circulations, including coronary and pulmonary, have appeared. While conclusive proof of a causal relation between ASA and embolic events is lacking, the frequency of such events in our patients with ASA remains striking.

**Diagnosis of Embolic Events**

Suggested criteria for the diagnosis of embolic stroke have recently been published. In each of these, the diagnosis of definite embolic stroke requires the presence of a recognized, likely source of embolus. Thus, any report of an association between a previously unrecognized potential embolic source and stroke cannot hope to fulfill these criteria. Nevertheless, the diagnoses of embolic stroke made in this report conform to these and other published criteria in other respects.

First, the presence of an abrupt branch occlusion of the involved circulation on cerebral arteriography in the absence of other occlusive disease is a recognized criterion for embolic stroke, and for practical purposes is diagnostic of it. Such occlusions were demonstrated in Patients 1, 2, and 4 in this study. Patient 4 was unusual in that an abrupt occlusion of the ICA above the bifurcation was demonstrated. While occlusion in such a location may be less common than in a smaller branch vessel, occlusion of a larger vessel such as this is nevertheless a well-recognized finding in certain cases of embolic stroke. In Patient 2, a hemorrhagic infarct was present on CT scan, supplying additional corroborative laboratory evidence for embolic stroke. In addition, symptoms in Patient 2 were of abrupt onset, another hallmark of an embolic event. Because historical data in this study were obtained from chart review, a clear description of the temporal characteristics of stroke in Patients 1 and 4 was not available.

Cerebral arteriography was not performed in Patient 3. Nevertheless, his presentation was considered diagnostic for cerebral embolism. His neurologic deficits were of abrupt onset. In addition, CT scan demonstrated recent infarcts in different locations. The occurrence of multiple infarcts in close temporal proximity is generally considered characteristic of embolism, though it is not included in two recent lists of suggested criteria. The absence of significant atherosclerotic disease on carotid ultrasound provided corroborative laboratory information.

Patient 5 was also classified as having an embolic stroke. The onset of her symptoms was abrupt; angiography showed no embolic occlusion, but it was performed 1 week after the stroke. Such a finding is not unexpected in embolic stroke. In fact, while embolic fragments are found angiographically in >75% of clinical embolic events within 48 hours of the onset of symptoms, they are present in only 11% when angiography is repeated beyond this time, presumably representing dissolution and fragmentation of the embolic material over time. While the presence of a potential intracardiac embolic source alone cannot be invoked to support the diagnosis of cerebral embolism for the purposes of this study, we believe the sudden occurrence of a left MCA stroke in the absence of significant atherosclerotic changes on arteriography is sufficient to make the diagnosis in Patient 5. A small infarct was noted in the left corpus callosum on CT scan, though her clinical presentation was not consistent with any recognized lacunar syndrome and she was not hypertensive.

Two patients with TIAs were identified in this study. While these events have conventionally been considered most commonly thrombotic in origin, it is now generally believed that TIAs are usually embolic (either artery-to-artery or heart-to-artery) in origin. Repeated TIAs involving the same vascular distribution are usually explained by the tendency of embolic material to follow the same path on each occasion as a result of laminar flow, and in such cases proximal artery-to-artery embolism may be more likely than heart-to-artery. This, however, may not always be true. It is now recognized that many cardiac conditions, including arrhythmias, valve disease, atrial myxoma, and cardiomyopathy, may produce TIAs. Arteriography in a recent series of 260 patients with well-defined retinal and cerebral TIAs revealed normal
proximal vessels in 18–27% of cases, again raising the question of a possible cardiac source in these patients.

Therefore, we believe that TIAs may be cardiac in origin, particularly if their characteristics suggest different arterial locations and when no source other than a cardiac one can be identified. Both Patients 7 and 8 fulfill the above criteria and are included as being of probable cardiac embolic origin. Patient 7 had no atherosclerotic cerebrovascular risk factors, she had symptoms in multiple vascular distributions, and only minimal irregularity was present on cerebral arteriography (and in the contralateral carotid circulation), making a thrombotic event or artery-to-artery embolus very unlikely. Patient 8 experienced an episode of true amaurosis fugax associated with right upper extremity weakness; cerebral arteriography revealed only insignificant changes in the carotid circulation, again making a thrombotic event or artery-to-artery embolic event unlikely. However, this patient also had vertebrobasilar TIAs and significant atherosclerotic changes in his vertebral arteries.

The cerebrovascular events in Patients 9–11 were of uncertain etiology because of either multiple possible causes or insufficient laboratory data to suggest a direct heart-to-brain relation.

### Possible Mechanisms for Emboli

This study has not demonstrated a causal relation between ASA and embolic events. Nevertheless, certain mechanisms linking the two phenomena can be postulated. Earlier reports describing fewer patients with ASA and embolic events have hypothesized that thrombus arising from the ASA is responsible. Based on the visualization of clot within the ASA after surgical resection in 1 patient with stroke and on the frequent identification of thrombus at the base of the aneurysm in a necropsy series, echocardiographic identification of aneurysm-associated thrombus has not been reported.

Another potential mechanism is paradoxical embolization through an interatrial communication. An association of ASA with patent foramen ovale or atrial septal defect in the absence of significant hemodynamic shunting may even constitute an indication for surgical closure. None of our patients had clinical evidence of deep venous thrombosis. This does not exclude a venous source of emboli, however, since venous thrombosis is also inapparent in many patients with documented pulmonary embolism.

### Clinical Implications

Our subjects represent a highly selected group of patients. All were hospitalized and referred for echocardiography at a tertiary medical center. The disproportionately high prevalence of embolic events noted in these individuals may not represent the frequency of such events in less highly selected individuals with ASA. Nevertheless, this study lends support to the premise that ASA be considered a cardiac abnormality with embolic potential.

The widespread use of two-dimensional echocardiography has led to increasingly frequent recognition of ASA. The identification of such a structure in a patient with embolic cerebrovascular or peripheral arterial events warrants contrast echocardiography. The presence of ASA in a patient with such events may be an indication for chronic anticoagulation or even surgical closure if a shunt is demonstrated.

### References


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**KEY WORDS** stroke • atrial septal aneurysm • intracardiac shunting
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