and the rest of the family were still in the Marquesas Islands and could not be examined.

Heparin treatment (Calciparine, Du Pont) associated with AT-III was administered on April 27. Despite anticoagulant therapy, pulmonary embolism occurred, resulting in an abortion and inferior vena cava occlusion. Currently, the patient is taking oral anticoagulants and has speech and gait defects.

One of two etiologies may account for our patient's manifestations. Sneddon's syndrome is a rare clinical entity prevalent in younger women. Approximately 60 cases have been reported to date. The neurological clinical picture includes recurrent transient or permanent ischemic cerebrovascular attacks, fits, and deterioration of intellect. Livedo reticularis may precede neurological manifestations for many years. Many cases have included the presence of phospholipid antibodies, leading to the hypothesis of Sneddon's syndrome as a phospholipid antibody disease. The association of Sneddon's syndrome and mitral heart disease, as observed in our case, was also recently reported, but because the pathophysiology of this entity remains unclear, no specific treatment strategy has been developed.

A second possible etiology is familial AT-III deficiency, an autosomal dominant disorder that causes a predisposition to recurrent venous thromboembolic disease and arterial occlusion. Thromboembolic disease is frequently encountered during pregnancy in association with Sneddon's syndrome or AT-III deficiency. To our knowledge, the association of Sneddon's syndrome and a familial deficiency of AT-III has never been reported. The combination of livedo reticularis, mitral valve prolapse, and AT-III deficiency observed in our patient probably accounts for the multiple arterial and venous thrombi and the failure of anticoagulant therapy.

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References

Risk of Stroke in Idiopathic Hypertrophic Subaortic Stenosis

To the Editor:
The association between idiopathic hypertrophic subaortic stenosis (IHSS), more recently defined as hypertrophic cardiomyopathy, and cerebral ischemia has only rarely been appreciated, and IHSS has never been considered a high-risk disease for stroke.

Russell et al.1 have recently reported in Stroke an extremely high incidence of cerebral ischemic events (22%) in a large series of patients with IHSS followed for 6.5 years. In five patients, stroke was the presenting manifestation of IHSS. The authors conclude that patients with IHSS are at high risk for ischemic cerebrovascular complications. These new, interesting data are apparently in contrast with current neurological opinion. Who is right?

In dealing with patients with cardiac disease and stroke, it is crucial to establish a cause-and-effect relationship between cardiac disease and cerebral ischemia. Besides presumptive clinical neurological criteria, the absence of atherosclerotic vascular disease based on cerebral angiography or carotid echotomography is an essential requisite for the diagnosis of cardiogenic cerebral embolism.4 It is likely that, following these criteria, a presumably cardioembolic etiology of cerebral ischemia was consequently established in only nine patients in the series of Russell et al.3 Considering only these cases, the incidence of cerebral ischemic events approximates the figures reported in the literature.1,5–11 (Table 1). In the remaining patients with atheroembolic, atherothrombotic, or lacunar stroke, IHSS can represent only a coincidental finding. An advanced age at stroke and an extremely high prevalence of hypertension may represent the major risk factors for cerebral ischemia rather than IHSS itself. Moreover, in the presence of long-standing hypertension, whose prevalence in the series of Russell et al was as high as 69%, the diagnosis of IHSS may be complicated by a differential diagnosis of hypertensive heart disease.

But even considering only those nine patients with cardioembolic stroke or transient ischemic attack, the data reported by Russell et al.1 are noteworthy, confirming our previous observations derived by a different approach to the problem. In a series of 380 consecutive patients (mean age 53.6 years) with cerebral ischemia who were referred to the Neurosurgical Department, embologenic cardiac lesions were documented by two-dimensional echocardiography in 27 patients (7%); among these cases, six patients with IHSS were identified. In five cases, associated factors responsible for embolism were identified: paroxysmal atrial fibrillation in three patients, infective endocarditis with mitral valve vegetation in one, and evolution of IHSS into a dilatative form with intraventricular thrombus in one. In all cases, cerebral angiography or carotid echotomography excluded the presence of atherosclerotic vascular lesions.12

A careful analysis of larger series of IHSS reported in the literature demonstrates that the risk of cerebral embolism in IHSS is not negligible, occurring in 2–15% of patients, with an estimated incidence of embolism of 0.4–2.4% yearly. Nevertheless, the stratification of the embolic risk has not received much attention up to the present time. Russell et al.1 deserve credit for stressing this aspect.

Idiopathic hypertrophic subaortic stenosis per se is not an embolic cardiac condition; the rapid flow and lack of opportunity for stasis do not predispose the patient to the formation of left ventricular thrombi. The risk of embolism is almost always related to the occurrence of atrial fibrillation, which occurs in 5–10% of patients with IHSS, usually late in the course of the disease.9,13 Similar findings resulted from the series of Russell et al (seven of nine patients). Infective endocarditis or evolution toward dilation with systolic dysfunction and congestive heart failure, which develops in about 10% of patients with IHSS, represent other major events predisposing patients to embolism. Left atrial enlargement, mitral annulus calcification, and low cardiac output can be invoked as contributing mechanisms. In Table 1 the incidence of atrial fibrillation, infective endocarditis, and embolism in larger series of IHSS is reported. The risk factors for embolism are specified in the last column.
Physicians should be aware of the possibility of cerebral ischemic events in patients with IHSS. Management implications regarding the prevention of cerebral embolic risk in IHSS are long-term anticoagulation treatment in patients with stable or paroxysmal atrial fibrillation and antibiotic prophylaxis of infective endocarditis. The concomitance of left atrial enlargement, mitral annulus calcification, or decrease in cardiac output seems to be a determining element for anticoagulation. In conclusion, besides paroxysmal atrial fibrillation and antibiotic prophylaxis of infective endocarditis, atrial fibrillation plays the most important role. An awareness of this substantial embolic risk and its role in IHSS does not seem to be widespread among cardiologists.

<table>
<thead>
<tr>
<th>Series</th>
<th>Cases (n)</th>
<th>Follow-up (yr)</th>
<th>Infective endocarditis (%)</th>
<th>Atrial fibrillation (%)</th>
<th>Embolic events (%)</th>
<th>Embolic risk (%/yr)</th>
<th>Type of embolism and associated factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frank and Braunwald, 1968</td>
<td>126</td>
<td>12</td>
<td>6 (4.8)</td>
<td>10 (7.9)</td>
<td>...</td>
<td>...</td>
<td>Systemic or pulmonary embolism (three cerebral); three with stable AF, one with probable paroxysmal AF, three with probable WPW.</td>
</tr>
<tr>
<td>Swan et al, 1971</td>
<td>85</td>
<td>4</td>
<td>4 (4.7)</td>
<td>4 (4.7)</td>
<td>...</td>
<td>...</td>
<td>All cerebral embolism; four with AF, one with AF+MAC, two with LA enlargement without AF.</td>
</tr>
<tr>
<td>Hardarson et al, 1973</td>
<td>119</td>
<td>4.6</td>
<td>4 (3.4)</td>
<td>10 (8.4)</td>
<td>11 (9.2)</td>
<td>2</td>
<td>Six cerebral, two peripheral, one splenic; six with AF and severe LA enlargement.</td>
</tr>
<tr>
<td>Shah et al, 1974</td>
<td>190</td>
<td>5.2</td>
<td>2 (1)</td>
<td>13 (6.8)</td>
<td>11 (7)</td>
<td>1.3</td>
<td>All cerebral embolism; four with AF, one with AF+MAC, two with LA enlargement without AF.</td>
</tr>
<tr>
<td>Furlan et al, 1984</td>
<td>136</td>
<td>5.5</td>
<td>...</td>
<td>7 (4.6)</td>
<td>3 (2.2)</td>
<td>0.4</td>
<td>Four cerebral, one femoral; all with AF (one paroxysmal), one with CHF.</td>
</tr>
<tr>
<td>Koga et al, 1984</td>
<td>66</td>
<td>3.7</td>
<td>...</td>
<td>15 (22.7)</td>
<td>6 (9)</td>
<td>2.4</td>
<td>All cerebral embolism; two with persistent AF, one with paroxysmal AF.</td>
</tr>
<tr>
<td>Kogure et al, 1986</td>
<td>60</td>
<td>6.3</td>
<td>1 (1.6)</td>
<td>11 (18)</td>
<td>9 (15)</td>
<td>2.4</td>
<td>All cerebral embolism; seven with AF (two paroxysmal), four with MAC, two with LA enlargement without AF.</td>
</tr>
<tr>
<td>Cohen et al, 1986</td>
<td>60</td>
<td>6.5</td>
<td>...</td>
<td>22 (18)</td>
<td>9 (7.5)</td>
<td>1.1</td>
<td>All cerebral embolism; seven with AF (two paroxysmal), four with MAC, two with LA enlargement without AF.</td>
</tr>
<tr>
<td>Russell et al, 1991</td>
<td>119</td>
<td>6.5</td>
<td>...</td>
<td>22 (18)</td>
<td>9 (7.5)</td>
<td>1.1</td>
<td>All cerebral embolism; seven with AF (two paroxysmal), four with MAC, two with LA enlargement without AF.</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; WPW, Wolff-Parkinson-White syndrome; MAC, mitral annulus calcification; CHF, congestive heart failure; LA, left atrial.

References


The following is in response:

To the Editor:

We would like to thank Dr. Di Pasquale and colleagues for their comments on our study and review of their experience with idiopathic hypertrophic subaortic stenosis (IHSS) and stroke. Although the prevalence of hypertension in our series was high, we do not believe this adequately explains the high incidence of recorded cerebral ischemic events (22%). In patients with presumed noncardioembolic strokes, based on the Harvard criteria,1 eight cerebral angiograms were available for review. Four of these were normal or showed minimal irregularity of extracranial and no atherosclerosis of the intracranial vessels. An additional three
Risk of stroke in idiopathic hypertrophic subaortic stenosis.
G Di Pasquale, S Urbinati, G Pinelli and A Andreoli

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