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
treatment, 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 manifesta-
tions. 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 cerebral vascular attacks, fits, and deterio-
ration of intellect. Livedo reticularis may precede neurological
manifestations for many years.1 Many cases have included the
presence of phospholipid antibodies,2 leading to the hypothesis of
Sneddon’s syndrome as a phospholipid antibody disease.3 The
association of Sneddon’s syndrome and mitral heart disease, as
observed in our case, was also recently reported,2 but because the
pathophysiology of this entity remains unclear, no specific treat-
ment 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.4
Thromboembolic disease is frequently encountered during preg-
nancy in association with Sneddon’s syndrome or AT-III deficien-
cy.5 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 anticoag-
ulant therapy.

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Risk of Stroke in Idiopathic Hypertrophic
Subaortic Stenosis
To the Editor:
The association between idiopathic hypertrophic subaortic ste-
nosis (IHSS), more recently defined as hypertrophic cardiomyop-
athy, and cerebral ischemia has only rarely been appreciated,1,2
and IHSS has never been considered a high-risk disease for stroke.

Russell et al 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 cerebrovas-
cular 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
requirement for the diagnosis of cardiogenic cerebral embolism.4

It is likely that, following these criteria, a presumably cardioem-
boletic 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 approxi-
mates the figures reported in the literature1-5 (Table 1). In the
remaining patients with atheroembolic, atherothrombotic, or lacu-
nar 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 cardioem-
boletic stroke or transient ischemic attack, the data reported by
Russell et al 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,
embolagic 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 fibril-
ation in three patients, infective endocarditis with mitral valve
vegetations 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 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.5,13
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 de-
velops 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 risk factor in the natural history of IHSS. Among the risk factors for stroke, 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.

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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, 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

Stroke. 1992;23:612-614
doi: 10.1161/01.STR.23.4.612

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/23/4/612.citation

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