Prevalence of Atrial Septal Aneurysm in Patients With Migraine: An Echocardiographic Study

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Objective.—To evaluate the prevalence of atrial septal aneurysm in patients with migraine.

Background.—Migraine has long been considered a risk factor for stroke. Atrial septal aneurysm is often observed in young patients with ischemic stroke and is frequently associated with other conditions potentially leading to embolism.

Methods.—We performed a transthoracic echocardiogram in 90 consecutive patients (65 women and 25 men; mean age, 35.3 years [standard deviation, 9]) with migraine but free from cerebral and cardiovascular disease and in 53 control subjects (37 women and 16 men; mean age, 34 years [standard deviation, 10]). The diagnosis of atrial septal aneurysm was performed according to Olivares-Reyes criteria. A transesophageal echocardiogram also was performed in 75 patients with migraine (83.3%).

Results.—The prevalence of isolated atrial septal aneurysm was higher in patients with migraine with aura (28.5%) than in patients with migraine without aura (3.6%) ($P < .005$) or in control subjects (1.9%) ($P < .005$).

Conclusions.—Our data suggest a role of atrial septal aneurysm in the genesis of aura in patients with migraine.

Key words: atrial septal aneurysm, echocardiography, migraine

Abbreviations: PFO patent foramen ovale, ASA atrial septal aneurysm

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Migraine has long been considered a risk factor for stroke since the 2 conditions share some pathogenetic mechanisms such as regional alterations in cerebral blood flow, platelet hyperaggregability, endothelial alterations, etc.[1] In addition, stroke may occur during a typical migraine attack, and headache similar to migraine manifests in 25% of patients with stroke.[2]

The recent improvement in image quality of 2-dimensional transthoracic echocardiography (TTE) and, more recently, the widespread use of transesophageal echocardiography (TEE) have made it possible to focus on the association between some cardiac abnormalities (eg, patent foramen ovale [PFO] or atrial septal aneurysm [ASA]) and cerebral ischemic events.[3]

Recent reports have pointed out a high prevalence of PFO in patients with migraine with aura,[4-5] but there is no evidence concerning the prevalence of isolated ASA in patients with migraine.

Atrial septal aneurysm is often observed in young patients with ischemic cerebral stroke and is frequently associated with other conditions potentially leading to embolism, such as PFO, mitral or tricuspid valve prolapse, atrial septal defect, endocranial vascular malformations, etc.[6-7]

The aim of the present study was to evaluate the prevalence of ASA in patients with migraine.

METHODS

Subjects.—We enrolled 90 consecutive patients (65 women and 25 men; mean age, 35.3 years [SD, 9]) with migraine but free from cerebral and cardiovascular disease, referred to the Headache Center,

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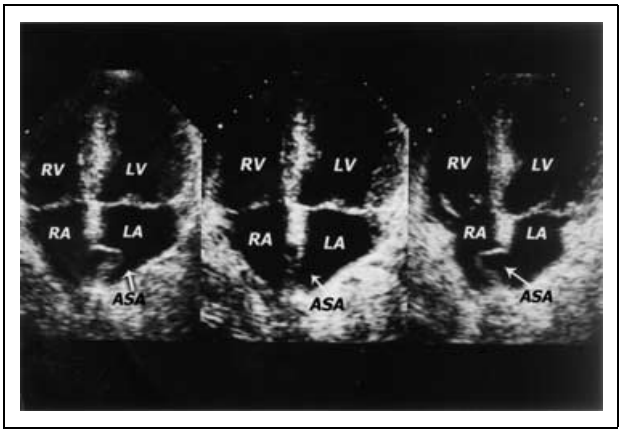
Department of Neurology, University of Messina, Italy from December 1999 to April 2001, and 53 control subjects (37 women and 16 men; mean age, 34 years [SD, 10]). Patients were divided into 2 groups: group A comprised 35 patients (10 men and 25 women; mean age, 33.2 years [SD, 8.1]) with migraine with aura, and group B consisted of 55 patients (15 men and 40 women; mean age, 36.6 years [SD, 9.1]) with migraine without aura. Group C included the 53 control subjects who had no history of migraine, neurologic defects, or cardiovascular disease.

The diagnosis of migraine was made according to the criteria of the International Headache Society classification.[8]

Investigations.—Subjects underwent a complete clinical examination including brain computed tomography (CT), ultrasonic study of the epi-aortic vessels, electroencephalogram, electrocardiogram, and echocardiogram. Information concerning current use of tobacco and oral contraceptives and a personal history of migraine was obtained (Table).

Transthoracic Echocardiogram.—Transthoracic echocardiogram (TTE) was performed by a GE System Five ultrasound machine (Orten, Norway), incorporating software for elaboration and analysis of the tissue harmonic signal. The latter technique provides high quality images, allowing a detailed analysis of the atrial septum.

The diagnosis of ASA was performed according to Olivares-Reyes criteria.[6] The 5 possible types of ASA movements, described in this classification, are: (1) type 1R: the ASA protrudes from the midline of the atrial septum to the right atrium throughout the cardiorespiratory cycle, (2) type 2L: the ASA protrudes from the midline of the atrial septum to the left atrium throughout the cardiorespiratory cycle, (3) type 3RL: the maximal excursion of the ASA is toward the right atrium with a lesser excursion toward the left atrium, (4) type 4LR: the maximal excursion of the ASA is toward the left atrium with a lesser excursion toward the right atrium, and (5) type 5: the ASA movement is bidirectional and equidistant to the right as well as to the left atrium during the cardiorespiratory cycle (Figure). In any case, the excursion of the atrial septum must be at least 10 mm, with an amplitude, measured at the base of the aneurysm of at least 15 mm.



Atrial septal aneurysm (ASA), type 5, characterized by equal displacement to the right and to the left. RV indicates right ventricle; RA, right atrium; LV, left ventricle; LA, left atrium.

To improve the definition of atrial septum during TTE, a bolus of agitated saline solution was injected into a peripheral vein while recording an apical 4-chamber view: as soon as the contrast agent filled the right atrium, the subject was requested to perform a Valsalva maneuver. To define the presence of right-to-left shunting due to PFO, we used the criteria proposed by Kühl et al,[9] namely detection of at least 5 contrast bubbles in the left atrium within the first 3 cardiac cycles after contrast appearance in the right atrium, either spontaneously or during Valsalva maneuver. The direction and movement of ASA were carefully studied in parasternal short-axis, apical 4-chamber, and subcostal views.

Transesophageal Echocardiogram.—Transesophageal echocardiogram was performed in 30 patients (85.7%) of group A and in 45 patients (81.8%) of group B; all gave informed consent. Echocardiographic images were recorded on SVHS videotapes and analyzed by 2 independent observers who were unaware of the type of migraine (with or without aura) experienced by the patient.

Statistical Analysis.—Statistical analysis was performed by an analysis of variance test and by the Fisher exact test.

RESULTS

Groups A and B did not differ from each other regarding age, gender, and migraine characteristics such as history, attack duration, and therapy. The only

Characteristics of Study Participants*

Feature	Group A (n = 35)	Group B (n = 55)	Group C (n = 53)	*P* Values		
				Group A Versus B	Group A Versus C	Group B Versus C
Age, mean (SD), y	33.2 (8.1)	36.6 (9.1)	34 (10)	NS	NS	NS
Sex						
Male	27	28.5	30	NS	NS	NS
Female	73	71.5	70	NS	NS	NS
Migraine history, y						
≤10	67	57	—	NS	—	—
>10	33	43	—	NS	—	—
Attack duration, h						
≤24	51	48.5	—	NS	—	—
>24	49	51.5	—	NS	—	—
Migraine frequency/mo						
≤1	9	37	—	.006	—	—
>1	91	63	—	.003	—	—
Tobacco use						
Yes	27.3	23	25	NS	NS	NS
No	73	77	75	NS	NS	NS
Oral contraceptive use						
Yes	23	31	28	NS	NS	NS
No	77	69	72	NS	NS	NS

*Values are percentages unless otherwise indicated. NS indicates not significant.

difference concerned the attack frequency; it was significantly higher in the patients in group A (Table). The control subjects did not show any difference, with respect to groups A and B, concerning age and gender.

Atrial septal aneurysm was detected in 12 (13.3%) of 90 patients with migraine (group A plus group B) and in only 1 (1.9%) of 53 control subjects ($P < .05$). When the 2 groups of patients with migraine were analyzed separately, ASA was observed in 10 (28.5%) of 35 patients of group A and in 2 (3.6%) of 55 patients of group B ($P < .005$). The difference between group A and group C was statistically significant ($P < .005$); whereas no difference was observed between groups B and C ($P = .9$). In group A, the ASA was associated with PFO in 3 cases (30%); while in group B, both patients with ASA also had PFO. In group C, PFO was present in the unique patient with ASA.

The TEE examination, when performed, did not provide additional information with respect to that obtained by TTE with tissue harmonic imaging. We also evaluated a possible relationship between ASA morphology and type of migraine, but none of the different morphologies of ASA were significantly associated with the occurrence of aura.

COMMENTS

The prevalence of ASA is significantly higher in patients with migraine with aura compared with patients with migraine without aura and with control subjects. Most patients had an isolated ASA without any other detectable abnormality; this could suggest a direct involvement of ASA in the genesis of aura.

An association between ASA and cryptogenic stroke has recently been reported.[10-16] Several pathogenetic mechanisms concerning the relationship between ASA and cerebral ischemia have been hypothesized: clot formation near to the aneurysmatic surface which is often riddled with microscopic holes, paradoxical embolization through a coexistent PFO or atrial septal defect, association with other cardiac abnormalities potentially responsible for embolism (eg, mitral valve prolapse).[3,6]

Migraine, particularly migraine with aura, has been suggested as a possible risk factor for cryptogenic stroke.[17-19] The high prevalence of ASA in patients with migraine with aura could further contribute to clarify the relationship between migraine and cryptogenic stroke.

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