Cerebral Ischemic Attacks As A Complication Of Aortic And Mitral Valve Prolapse

G. A. Barletta, M.D.,* R. Gagliardi, M.D.,† L. Benvenuti, M.D.,†and F. Fantini, M.D.*

SUMMARY The high incidence of mitral valve prolapse (MVP) in patients with ischemic attacks is puzzling when compared with the very low incidence of cerebrovascular attacks observed in individuals known to have MVP. Our aim was to determine if it is possible to identify a patient subset with MVP at the highest risk of embolization on the basis of 2D-echocardiographic findings.

We compared the echocardiographic picture of a group of 39 patients with MVP and cerebral ischemic attacks (29 TIAs, 10 strokes) in the carotid territory, without any pathological lesions at angiography, with that of a control group of 111 patients with MVP without neurological complications. The two groups were not different for age or sex.

Patients with MVP and neurological complications showed a higher prevalence of aortic valve prolapse (62% vs 34%, p < 0.01), of an association between valvular diffuse thickening and aortic valve prolapse (54% vs 23%, p = 0.001), and of multiple valve prolapse with valvular diffuse thickening (26% vs 7%, p < 0.01) than those of the control group.

This study suggests that in young people cerebral ischemic events could be related to the presence of a combined valve prolapse and to an echocardiographic picture of valve diffuse thickening. These data suggest that in this selected group with multiple valve prolapse and valvar diffuse thickening prophylaxis against embolic events by pharmacological preventive measures should be considered.

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CEREBRAL ISCHEMIC EVENTS of cardiac origin, secondary to embolism or to hemodynamic alterations, have long been recognized. The association between embolism and bacterial endocarditis, myocardial infarction, cardiomyopathies, atrial fibrillation, and valvular prostheses have been documented by extensive experience. M-mode and two-dimensional echocardiography have aided the identification of heart disease previously overlooked as possible source of cerebral emboli, and to recognize intracardiac thrombi in patients with silent or manifest heart disease. In 1976 Barnett et al. described cerebral ischemic episodes as consequences of mitral valve prolapse (MVP). Since that initial report MVP has been diagnosed in numerous patients with transitory ischemic attacks (TIAs) or stroke. The high incidence of MVP in patients with cerebral ischemic attacks has been puzzling when compared with the very low incidence of cerebrovascular attacks observed in large groups of individuals known to have MVP. The available data report a very low percentage of TIAs or strokes, compared with other complications such as mitral regurgitation, arrhythmias or sudden death; some studies do not even mention neurological complications.

Two hypotheses could be made: 1) neurological complications have a very low risk evenly distributed among MVP population, 2) there are subsets of patients with a higher potential of embolization. The aim of this study was to ascertain if the echocardiographic examination gives any clues to the evaluation of the risk of thromboembolism by comparing the echocardiographic picture of patients with MVP and cerebral ischemic attacks with that of patients with MVP without neurological complications.

Patients and Methods

Ninety-four patients (63 male and 31 female, mean age 38 ± 14 yrs, ranging from 13 to 66 yrs) hospitalized in the Neurosurgical Department of Florence from
September 1981 to September 1983 with cerebral ischemic attacks in the carotid territory (63 TIs and 31 strokes), underwent M-mode and 2D echocardiographic examination in the Cardiologic Unit of the University of Florence. All patients had been submitted to an angiographic study of the carotid territories within a month of the echocardiographic examination (bilateral carotid angiography in 92%, carotid angiography to the ischemic event(s) in the remaining) as well as to a standard assessment of risk factors (such as hypertension, dyslipidemia, diabetes, coagulopathies, etc.). None of these patients showed vascular lesions (stenosis, plaque, or ulcer) that could account for the clinical symptoms, although in 10 cases an angiographic pattern suggestive of embolization of the distal branches of the intracranial cerebral circulation was found. The echocardiographic picture was normal in 33, showed MVP in 39 and other abnormalities in 22 (table 1). Patients with MVP and cerebral ischemic attacks were selected to form the study group (22 male, 17 female, aged from 13 to 68 yrs, mean age 31 ± 13 yrs). No patient showed atrial fibrillation or other obvious sources for embolization (valvular prosthesis, endocarditis, left ventricular thrombi, etc.) during hospitalization. None of these patients was suffering from or had a history of hypertension or diabetes; only 3 had a lipid profile abnormality. On admission 29 had TIAs and 10 had strokes. Seven of the patients with stroke had recently had prodromal symptoms (TIAs or amaurosis fugax).

A control group, composed of 111 patients (55 female and 56 male, aged 10 to 74 yrs, mean age 37 ± 19 yrs) with idiopathic MVP, was collected in the same period of time. These patients had been seen in the Cardiologic Unit of the University of Florence for cardiovascular symptoms, although they did not present neurological disturbances and on examination were found to have an idiopathic MVP. Two patients had aortic prosthesis, four showed aortic insufficiency, five mitral insufficiency, four a clinical history of endocarditis.

Echocardiographic examination was performed by commercially available scanners (ATL Mark III with a 3 MHz transducer and a Diasonic 3400 R with a 2.25 MHz transducer). The diagnosis of MVP was made using the criteria proposed by Morganroth et al and supplemented by a further criterion obtained from the apical four chamber view. Idiopathic MVP was diagnosed by excluding MVP associated with atrial septal defect, rheumatic valvular disease or coronary artery disease. Aortic and tricuspid prolapse was identified using the criteria proposed by Morganroth et al and Ogawa et al. For utilizing the grading criteria for MVP we identified three degrees of aortic valve prolapse. The diagnosis of myxomatous degeneration was considered only when the valve thickening was diffuse and uniform both in the longitudinal and in the transversal bidimensional sections (figs. 1, 2). All the echocardiograms were evaluated by two experienced observers who were aware of the neurological diagnosis.

Results

In patients with MVP and cerebrovascular attacks the echocardiographic examination showed a mild prolapse in seven, a moderate prolapse in 24 and a severe prolapse in eight. Aortic valve prolapse was found in 24 (62%): mild in 6, moderate in 14 and severe in 4. Eight were female, 16 male. Twelve (31%) showed a tricuspid valve prolapse (4 female, 8 male). An echocardiographic pattern suggesting a valvular myxomatous degeneration was present in 25 patients (12 female and 13 male; 64%). The association between myxomatous degeneration and aortic valve prolapse was observed in 21 patients (54%), 13 male. Multiple valve prolapse (tricuspid, aortic, mitral valve) and myxomatous degeneration were both present in 10 patients (26%), eight male. Four patients (10%), two male, showed an enlargement of the aortic root.

The control group showed in 34 cases a mild MVP, in 54 a moderate MVP, in 23 a severe MVP. Thirty-eight patients (34%), 19 male, showed aortic valve prolapse (18 mild, 14 moderate, 6 severe). Twenty-seven (24%), 16 male, had a tricuspid valve prolapse. Fifty-one (46%), 26 male, showed an echocardiographic pattern suggesting a valvular myxomatous degeneration. The association between aortic valve prolapse and myxomatous degeneration was present in 26 patients (23%), 13 male. Multiple prolapse and myxomatous degeneration were both present in 8 patients (7%), 5 male. A dilatation of the aortic root was present in 31 patients (28%), 16 male. The patients with aortic root enlargement were older than the patients without (43.6 ± 20.4 years vs 33.9 ± 17.4 years, p < 0.025) (table 2).

The neurological and control group differed in the prevalence of aortic valve prolapse (62% vs 34%, chi-square test p < 0.01). The association between myxomatous degeneration and aortic valve prolapse showed a higher incidence in patients with neurological complications than in patients without (54% vs 23%, chi-square test p < 0.001). Multiple valve prolapse and myxomatous degeneration were more frequent in patients with cerebral ischemic attacks (26% vs 7%, chi-square test p < 0.01). No other significant difference was found between the two groups (severity of MVP or aortic valve prolapse, presence of tricuspid

| Table 1 | Echocardiographic Findings in Neurological Patients
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<tr>
<td>No. of Patients</td>
<td>Mitral valve prolapse</td>
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<tr>
<td></td>
<td>Normal pattern</td>
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<td>Enlargement of aortic root</td>
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<td></td>
<td>Left atrial myxoma</td>
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<td>Bicuspid aorta</td>
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valve prolapse, valve myxomatous degeneration) (fig. 3). The two groups did not differ for age or sex (fig. 4). No significant differences in age or sex were found in any of the subsets considered.

Discussion

Patients with ischemic cerebral events in the carotid territory and with normal carotid arteriograms showed a high incidence (41%) of MVP. Our study underlines the clinical relevance of the association between cerebral ischemic attacks, probably due to embolization, and MVP. Patients with MVP and cerebrovascular attacks, on blind echocardiographic examination, showed a higher incidence of combined aortic and/or tricuspid prolapse than patients with uncomplicated MVP. The incidence of aortic valve prolapse and tricuspid valve prolapse in the control group was similar to that found by other investigators. Slight differences could depend on more restrictive criteria for MVP.

Multiple valve prolapse is probably a picture linked to mucinous degeneration. The myxomatous degeneration is a pathological diagnosis. Considerable confusion surrounds the concept of myxomatous degeneration of cardiac valves and its relation to various disease states. The most severe degrees of myxomatous degeneration are typical of the "floppy valve," but its presence in other diseases suggests that there could be a spectrum of valvular abnormalities related to different causes. Numerous conditions, including ageing, rheumatic heart disease and Marfan’s syndrome, have been associated with some degrees of valvular myxomatous degeneration. We have suggested that the diffuse and uniform thickening of the valves could indicate the myxomatous degeneration. The significance and the specificity and sensitivity of this echocardiographic pattern need more experience. Recently Shah suggested that it could be a hallmark of the "true" MVP. A higher incidence of cardiac complications has been observed in patients with MVP and thickened leaflets.

Figure 1. In the same patient: top left, severe mitral valve prolapse (indicated by the arrow), on the right moderate aortic valve prolapse (indicated by arrow); bottom left, diffuse thickening of aortic cusps suggesting myxomatous degeneration (arrows); right tricuspid prolapse (indicated by the arrow). Abbreviations: LV = left ventricle; Ao = aorta; LA = left atrium; RV = right ventricle.

Figure 2. Short axis parasternal left ventricular view at mitral level. The diffuse thickening of the mitral leaflets is evident.
TABLE 2. Echocardiographic Findings in Patients with Mitral Valve Prolapse

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<thead>
<tr>
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<th>Neurological</th>
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<tr>
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<td>Enlargement of aortic root</td>
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Echocardiographic alterations suggesting myxomatous degeneration of cardiac valves were found more frequently in patients with cerebral ischemic attacks and MVP (64% vs 46% in the control group). This difference was not statistically significant ($p = 0.06$), whilst the incidence of combined myxomatous degeneration and aortic and/or tricuspid valve prolapse in patients with cerebral ischemic attacks was highly significant. Taking into account our results, we hypothesized that myxomatous degeneration could be even more frequent and severe in patients with MVP and cerebral ischemic attacks, because we consider myxomatous degeneration to be responsible for multiple prolapse even if the echocardiographic criteria are absent.

Areas of fibrin deposition on the cusps or on the mitral leaflets and chordae without evidence of inflammation are reported. In several studies, collection of fibrin-platelet thrombi and red cells loosely adherent to valve surface similar to those described by Pomerance were observed. By echocardiographic examination some authors described thrombi adherent to the mitral leaflets in patients with MVP. We observed some images analogous to that picture but we did not diagnose thrombi because, in our opinion, the resolution of bidimensional echocardiography is not good enough to permit the differential diagnosis either with myxomatous degeneration or with some "normal" variants. In fact some localized enlargement of mitral valve echoes is often seen in healthy people.

This study suggests that in young people cerebral ischemia could be related to the presence of a combined valve prolapse and echocardiographic picture of myxomatous valvular degeneration. Clearly, no prophylactic treatment to prevent stroke in asymptomatic people with MVP is warranted. However, if a subset of patients with a higher risk of embolization could be identified (and the echocardiographic picture of multiple valve prolapse and diffuse and uniform thickening of valves in our study is four times more frequent in patients with cerebral ischemic attacks) then prevention of embolic events could be taken into account. Future studies are needed to evaluate the natural history of this subset of MVP and the cost and risk of prophylactic therapy.

**References**

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