

BACTERIAL ENDOCARDITIS AS A COMPLICATION IN CALCIFIED MITRAL RING

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Abstract

Mitral annular calcification (MAC) is usually considered to be a benign, degenerative process. However, bacterial endocarditis developed on MAC is a complication that was formerly reported in autopsy series, but has been rarely described in vivo. This preliminary study reports our experience based on 6 cases of infective endocarditis (IE) on MAC (group 1) and 11 other cases with classical endocarditis on mitral leaflets (group 2), in which diagnosis was made by multiplane transesophageal echocardiography (TEE). In group 1 there was a higher occurrence of hypertension, diabetes mellitus, chronic renal insufficiency, malignant disorders and a higher mortality rate. *Staphylococcus* was the causative agent in 76% of group 1 whereas *Streptococcus* was more frequent in group 2 (58%). Degenerative lesions such as MAC could become an important underlying cause of endocarditis in elderly patients.

Key words

Bacterial endocarditis, Echocardiography, Heart, Mitral diseases, Mitral ring calcification, Sepsis

Abbreviations used

AML, anterior mitral leaflet; LA, left atrium; LV, left ventricle; MAC, mitral annular calcification; PML, posterior mitral leaflet; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; V, vegetation; IE, infective endocarditis

INTRODUCTION

Mitral annular calcification (MAC) is one of the most common cardiac abnormalities in elderly patients. It is found in about 8.5 to 12.5% of adult autopsies, almost all over 50 years of age, and with a preponderance of women (1, 2). It is, consequently, considered to be a result of degenerative processes within the cardiovascular fibrous skeleton. In younger patients, MAC can occur in association with factors that accelerate it, such as connective tissue disorders and metabolic disorders (3) or with conditions that increase mitral annular stress (4) such as chronic left ventricular overload as in hypertension or aortic stenosis. Today, MAC is still generally considered as a benign echocardiographic finding, with systolic murmurs as the only clinical consequence. Valvular functional

disturbance is usually mild; mitral regurgitation may be a consequence of distortion and atrial displacement of the posterior mitral leaflet (5). Some complicated pathological changes have been observed, e.g., ulceration and extrusion of calcium through a mitral cusp into the left atrium may account for a double risk of stroke, either by calcium embolisation or by thrombus formation and secondary migration (6, 7). Bacterial endocarditis involving a calcified mitral annulus fibrosus seems to be very uncommon. Although this complication has been described in several autopsy series (8), only a few isolated cases have been reported in vivo (9, 10).

MATERIALS AND METHODS

Between 1996 and 1998, 16 cases of infective endocarditis involving the mitral valve were diagnosed by means of multiplane transesophageal echocardiography (TEE) in the Department of Cardiology at Dijon.

Echocardiographic examinations were performed, using Hewlett-Packard Sonos 1500 and 2500 echographs. A 2-2.5 MHz transducer for trans-thoracic evaluation and a 3.7-5 MHz multiplane probe for transesophageal assessment were used.

Variance distribution and homogeneity in the two groups were assessed using Barlett's test. ANOVA and non-parametric Wilcoxon tests were used for statistical evaluation and a *P* value of 0.05 or less was considered to be statistically significant.

RESULTS

Among the 16 cases of infective endocarditis diagnosed, six were found to originate specifically from a calcified mitral annulus. Clinical, biological, echocardiographic and evolutive features of these cases (group 1) were compared to 11 other cases with classical mitral valve endocarditis with vegetations attached to the leaflets (group 2). Anamnestic, clinical and echocardiographic data of these two groups are shown in *Tables 1, 2, 3 and 4*.

In group 1 patients were slightly, but not significantly, older than in group 2 (mean age, 68 vs. 64 years). This group had a higher occurrence of cardiovascular risks due to the fact that 50% were hypertensives, 50% had diabetes mellitus, 16% had chronic renal insufficiency, 15% had pacemakers and 50% were diagnosed with active malignant diseases. Occurrence of cancer was significantly higher in group 1 than in group 2. Heart murmurs were absent in 50% of group 1 patients. In group 1, fever (higher than 38.0°C) was present in 100% of patients, as compared with 90% in group 2. Febrile coma or a clinical manifestation of meningoencephalitis associated with mental confusion was the initial clinical presentation in 66% of group 1 compared to 9% in group 2; this difference was statistically significant.

Results of bacteriological examination revealed that *Staphylococcus* was the causative organism in 76% of group 1 whereas *Streptococcus* was predominant in group 2 (58%). Transthoracic echocardiography showed moderate to severe MAC in group 1. Transoesophageal echocardiography revealed a number of features

Table 1

Characteristics of the two groups of patients studied

| Patient characteristics | Group 1 (n=6) | Group 2 (n=11) | <i>P</i> value |
|--------------------------|------------------|-------------------|-------------------|
| Mean age | 68.2 ± 6.7 | 64.4 ± 9.7 | NS |
| Sex ratio | 1.5M / 1F | 2.9M / 1F | NS |
| Coronary heart disease | 33.3% | 36.3% | NS |
| Hypertension | 50% | 36.3% | NS |
| Diabetes mellitus | 50% | 18.2% | < 0.04 |
| Hypercholesterolemia | 16.7% | 18.2.1% | NS |
| Pacemaker | 16.7% | none | NS |
| Congestive heart failure | 16.7% | 9.1% | NS |
| Chronic renal failure | 16.7% | 9.1% | NS |
| Malignant disorders | 50% | 18.2% | < 0.05 |

Table 2

Clinical data in both groups

| Clinical data on admission | Group 1 (n=6) | Group 2 (n=11) | <i>P</i> value |
|----------------------------|------------------|-------------------|-------------------|
| Fever | 100% | 90% | NS |
| Mean temperature | 39.3 ± 0.65 | 38.1 ± 0.87 | NS |
| Coma or mental confusion | 66% | 9% | < 0.001 |
| Heart murmur | 50% | 67.8% | NS |

Table 3

Bacteriological analysis of blood cultures in both groups

| Results of blood Cultures | Group 1 (n=6) | Group 2 (n=11) | P value |
|---------------------------|---------------|----------------|---------|
| <i>Staphylococcus</i> | 76.6% | 26.4% | 0.05 |
| <i>Streptococcus</i> | 23.4% | 58.1% | 0.04 |
| Other germs | 0 | 18.5% | – |

Table 4

Echocardiographic findings in both groups

| Finding | Group 1 (n=6) | Group 2 (n=11) | P value |
|-----------------------------|---------------|----------------|---------|
| Vegetations mean width (mm) | 10.6±6.9 | 5.9±1.8 | < 0.05 |
| mean length (mm) | 15.7±9.1 | 12.6±4.5 | NS |
| Calcifications | 80% | 8.6% | < 0.01 |

specific to IE on MAC; this was significantly different from group 2 (*Figs 1 and 2*). A unique, large-sized vegetation attached to the posterior part of the annulus was frequently observed (*Fig.2*).

Four patients in group 1 died from incontrollable sepsis despite antibiotic therapy and from multi-organ failure during hospitalisation. This group had a very high in-hospital mortality rate of 66%, as compared with 36% in group 2; however, the difference was not significant.

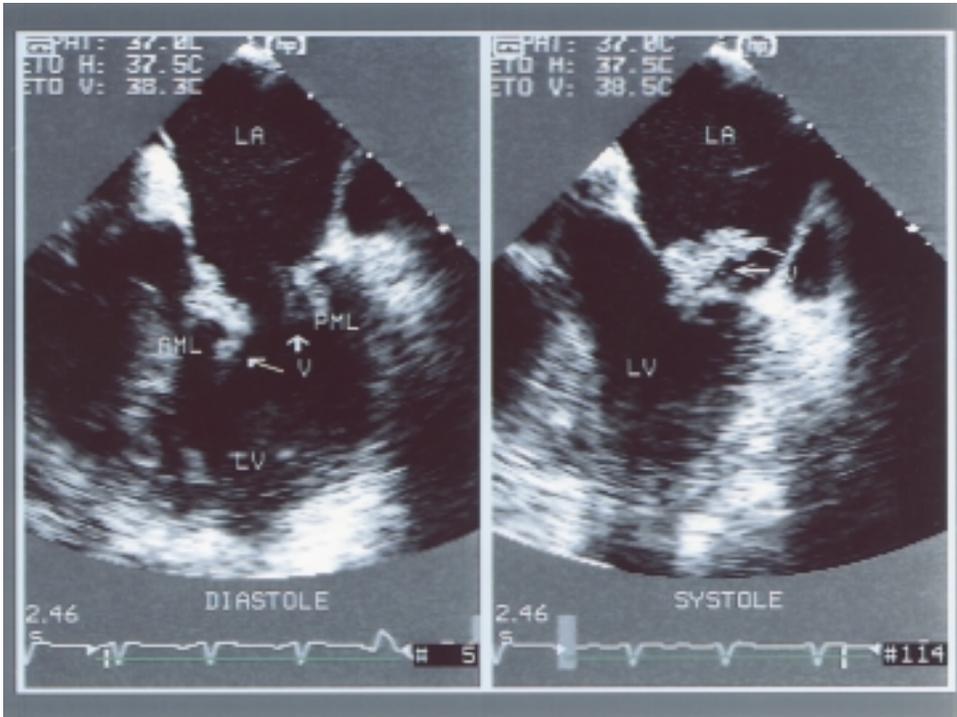


Fig. 1
Typical appearance of mitral endocarditis localised on the leaflets.

DISCUSSION

Bacterial endocarditis usually occurs on valves previously damaged by other disease processes (for example, rheumatic heart disease or mitral valve prolapse), but also some congenital heart diseases may present a risk factor for cardiac sepsis.

The spectrum of diseases predisposing to bacterial endocarditis also includes degenerative lesions, the incidence of which is increasing in the aging population (11). Valvular abnormalities induce stenotic or regurgitant lesions with high velocity jets. These traumatise endothelium and the ensuing endocardial erosions are locations of possible infections. Patients with mitral insufficiency typically develop vegetations on the atrial surface of the mitral leaflets.

All these stages of the infective process can be applied to the calcified mitral annulus fibrosus. Clinical series concerning endocarditis and MAC are rare. *Fulkerson et al. (4)*, reviewing the clinical features of 80 patients with MAC,

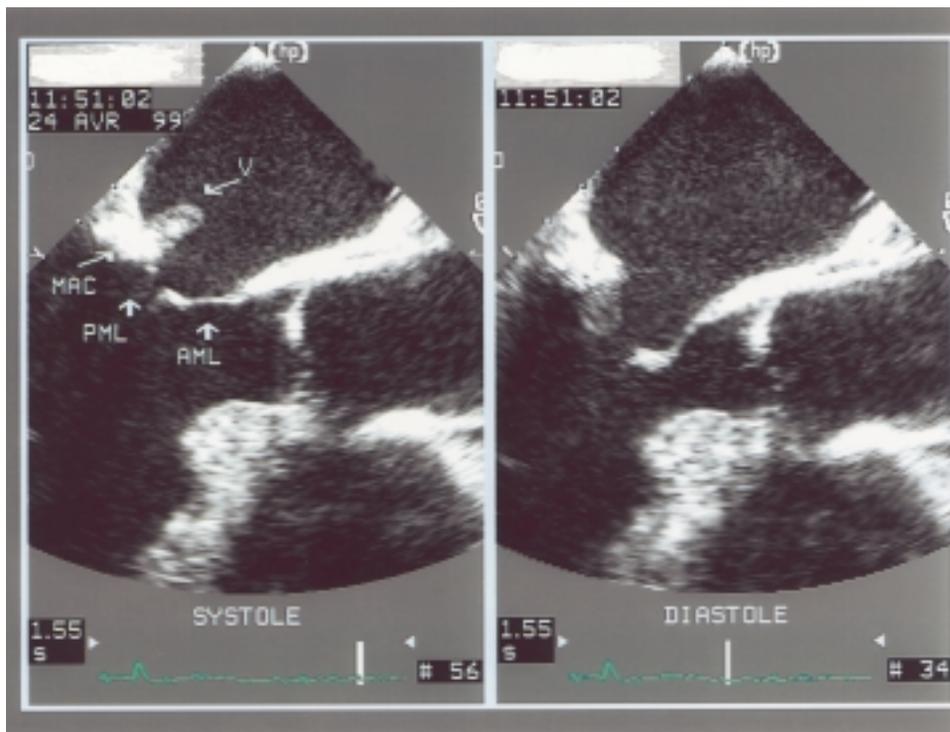


Fig. 2
Example of endocarditis with a single vegetation on a calcified mitral ring.

reported an incidence of endocarditis of 3.7%. In a prospective study, *Aaronow et al.* (12) demonstrated a higher incidence of bacterial endocarditis in elderly patients with MAC at 39 months follow-up. Echocardiographic findings of bacterial endocarditis and mitral annular calcification reported in the literature are limited to 5 isolated cases, one detected by TTE (13) and four by TEE (9, 10, 14, 15). The scarcity of such reports contrasts with autopsy series in which these diagnoses account for 14% of 63 endocarditis restricted to the mitral valve in the study of *Fernicola et al.* (16), 25% of 20 fatal endocarditis in the report by *Mambo et al.* (17) and 42% of 12 staphylococcal mitral endocarditis in *Watanakunakorn's* series (18). These results confirm that the frequency of IE on MAC is undoubtedly underestimated. The difficulty of confirming the diagnosis, either clinically or echocardiographically, probably accounts for this discrepancy.

Our preliminary report permits an outline of the clinical picture of this disease. Traditionally, elderly patients and patients on haemodialysis are at greater risk of

developing severe MAC (16, 17). Our findings suggest that diabetes mellitus and neoplastic disorders may be additional risk factors. In regard to the initial clinical presentation, mental confusion or coma were the main features in our patients (66%) as well as in previously published reports (13, 18, 19). These clinical features (mental confusion and coma) could have been related to a high frequency of emboli, which is in agreement with the frequency of cerebral and peripheral emboli found at autopsy in most reported studies.

Echocardiographic diagnosis may also prove to be difficult. Sensitivity of TTE for the diagnosis of infective endocarditis has been reported to be decreased to 45% in patients older than 70 years, as compared with 75% in patients younger than 55 years (15). In our patients, TTE usually showed moderate to severe annular calcification.

Annular abscesses are a well-known complication of aortic valve endocarditis. In our experience, no abscess is ever seen on the mitral ring except in association with MAC (66% of the patients in group 1). In this case, infection develops primarily within the annulus and, moreover, calcification itself could represent a risk factor of abscess formation in relation to poor diffusion of antibiotics. Infective endocarditis remains a severe disease, as evidenced by the 36% mortality in group 2, which is similar to the findings in larger studies in the same age range (12, 20).

It is concluded that degenerative lesions due to calcification, particularly MAC, are common in elderly persons and are becoming one of the most frequent risk factors for infective endocarditis.

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BAKTERIÁLNÍ ENDOKARDITIDA JAKO KOMPLIKACE KALCIFIKOVANÉHO MITRÁLNÍHO PRSTENCE

S o u h r n

Kalcifikace mitrálního prstence je běžně považována za benigní degenerativní proces. Bakteriální endokarditida, vzniklá na kalcifikovaném mitrálním prstenci, je však komplikací, popisovanou spíše v sekčních nálezech než v diagnózách *in vivo*. Tato předběžná studie přináší zpracované výsledky u 6 případů bakteriální endokarditidy na kalcifikovaném mitrálním prstenci (skupina 1) a u 11 případů mitrální endokarditidy s klasickým postižením mitrálních cípů (skupina 2). Diagnostickým nástrojem byla ve všech případech transesofageální echokardiografie. U pacientů skupiny 1 byl zaznamenán značný výskyt hypertenze, diabetu, chronické renální insuficience a malignit společně s vysokou mortalitou. Ve skupině 1 byl hlavním kauzálním činitelem stafylokok (76%), zatímco ve skupině 2 byl ve většině případů diagnostikován streptokok (58%). Degenerativní léze včetně kalcifikovaného mitrálního prstence mohou mít značný význam u starších pacientů.

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