Echocardiographic features of *Candida* species endocarditis: 12 cases and a review of published reports

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Abstract

Objective—To describe the specific echocardiographic features of *Candida* species endocarditis.

Design—Retrospective review of the case records of patients with confirmed candida endocarditis.

Setting—Cases referred to three French university centres over an eight year period were studied.

Design—12 patients with confirmed *Candida* species endocarditis infection were identified. The transthoracic (n = 12) and transoesophageal (n = 12) echocardiographic appearances were compared with the surgical findings (n = 10).

Results—Large dense heterogeneous vegetations were found in 11/12 cases. A hyperechogenic heterogeneous myocardial texture, observed in seven of the 12 patients, was associated with extensive myocardial damage at surgery. While it was possible to diagnose candidal cardiac infection in all patients by transthoracic echocardiography, transoesophageal echocardiography was useful for optimal assessment of the valvar and paravalvar structures.

Conclusions—In the setting of endocarditis, the detection of myocardial involvement, which is characterised by a heterogeneous myocardial texture, is an argument in favour of *Candida* species endocarditis and may warrant early surgical intervention.

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Keywords: echocardiography; *Candida* species; endocarditis

Echocardiography is an extremely effective tool for the diagnosis of endocarditis. *Candida* species endocarditis is a rare form of the condition, in which coexisting myocardial involvement is not uncommon. It has a particularly poor prognosis. In this report we present 12 new cases of cardiac infection with *Candida* species. We describe the unusual appearances of vegetations in this particular form of endocarditis and report abnormalities in the texture of the myocardium on echocardiography—shown at surgery to represent myocardial involvement—which we feel have important implications when planning surgical intervention.

In this rare condition, echocardiography is helpful both in making a diagnosis and in guiding the treatment strategy. Some investigators consider that the size of the vegetations is of paramount importance in the decision to undertake surgical intervention.¹ While this is a major factor, we provide evidence suggesting that the echocardiographic texture of the infected cardiac tissue is also important and may be an argument in favour of early surgical intervention.

Methods

PATIENTS

From the records of the echocardiography departments of three French University Hospitals (Hôpital Bichat-Paris, Angers, and Poitiers), we identified 12 patients, who, between October 1991 and September 1999, underwent echocardiography for suspected endocarditis and subsequently had *Candida* species endocarditis confirmed, either on

repeated blood cultures (10 cases) or on culture of valve tissue removed at surgery (two cases).

The mean age of the patients was 41 years (range 21–81 years). Eight were men. Four were intravenous drug users, two of whom were HIV positive. Two patients had mechanical cardiac valves, one a permanent cardiac pacemaker, and one an indwelling venous catheter. All patients were classified in the category of definite endocarditis according to the Duke criteria.²

ECHOCARDIOGRAPHY

All 12 patients underwent both transthoracic and transoesophageal echocardiography, the diagnosis of endocarditis being made exclusively on the transthoracic examination (table 1). Transoesophageal echocardiography was carried out in order to obtain more detailed information on the size and location of the vegetations, the degree of involvement of valvar or paravalvar structures, the presence of abscess formation, and so on.

Results

ECHOCARDIOGRAPHIC FINDINGS

Left ventricular function was normal in all patients. Two had small pericardial effusions. Aortic valve involvement was present in six patients, mitral valve involvement in three, and tricuspid valve involvement in three; multiple valves were affected in two patients. Of the three patients with tricuspid endocarditis, one was an intravenous drug user, one had an infected pacemaker (infected thrombus in the

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Table 1 Characteristics of study patients and their echocardiographic and surgical findings

Patient	Sex/age (years)	Valve(s)	Echocardiographic description of the vegetation	Left ventricular function	Pericardial effusion	Surgical findings
1	F/67	Mitral	Two voluminous hyperechogenic vegetations on the anterior and posterior valve with major regurgitation (TTE) and echogenic appearance of the perivalvar tissue (TOE)	Normal	No	Patient died before surgery
2	F/75	Mitral	Heterogeneous and voluminous mass on a thick anterior mitral valve; important regurgitation (TTE and TOE)	Normal	Minor	Patient died before surgery
3	M/39	Aortic	Voluminous, dense vegetation (TTE), without valvar destruction. Valvar regurgitation grade 2, no abscess (TOE)	Normal	No	Voluminous, dense vegetation "hook to" the posterior cusp
4	M/32	Aortic	Enormous (>20 mm), dense, vegetation; little valvar regurgitation (TTE and TOE)	Excellent	Minor	Very large vegetation with destruction of the tissue surrounding the aortic valve
5	F/60	Tricuspid (central venous catheter)	Voluminous hyperechogenic vegetation (TTE confirmed by TOE)	Conserved	No	Voluminous tumour invading almost the entire right atrium; some abscesses found in the interatrial septum
6	M/37	Pacemaker and pericardiac structure infection	Hyperechogenic, dense vegetations (> 20 mm); no important tricuspid regurgitation (TTE and TOE)	Conserved	No	Voluminous mass fixed on the pacemaker probe and on the narrowing tissue
7	M/81	Aortic (bioprosthesis)	Enormous vegetation (TTE); hyperechogenic, extremely mobile and obstructive (TOE)	Myocardial hypertrophy; some reduction in left ventricular function	No	Voluminous mass (>20 mm) clinging to aortic cusps
8	M/56	Tricuspid	Large dense voluminous vegetation (TTE) (11×13 mm and 8×13 mm) with perivalvar hyperechogenic appearance (TOE)	Conserved	No	Fragile, voluminous masses on two cusps and the narrowing tissue
9	M/37	Aortic	Voluminous vegetation, hyperechogenic and obstructive (TTE); little regurgitation, perivalvar hyperechogenic appearance (TOE)	Conserved	No	Dense voluminous vegetation on the ventricular face of the aortic valve
10	F/21	Mitral prosthetic valve	Voluminous vegetation on the ventricular surface of the prosthetic valve (TTE); abscess and aortic regurgitation (TOE)	Conserved	No	Major tissue destruction (abscesses); several crumbly vegetations (> 20 mm)
11	M/30	Aortic	Dense vegetation (20×13 mm) with major valvar regurgitation (TTE and TOE)	Conserved	No	Mass fixed on the cusp; no abscess
12	M/34	Aortic	Dense hyperechogenic appearance of the aortic valve and the narrowing tissues; the vegetation was obstructive (TTE, confirmed by TOE for the narrowing tissue aspect)	Left ventricular hypertrophy; normal left ventricular function	No	Destruction of the tissue causing narrowing of the aortic valve with interventricular communication

TOE, transoesophageal echography; TTE, transthoracic echography.

Figure 1 Echocardiographic example of *Candida* species aortic valvar endocarditis, with destruction of the narrowing tissue. There was initially a bulky, echogenic mass on the aortic cusps (A). Rapidly, the echocardiographic aspect of the interventricular septum became unusual with a large number of hyperechogenic points. Anatomical observation revealed a large number of micro-abscesses of the narrowing of the aortic valve (B). S, interventricular septum; V, left ventricular cavity; A, left atrium.

right atrium without tricuspid valve destruction), and the third had an infected indwelling central venous catheter.

In seven of the 12 patients, the vegetations were described as being abnormally large (fig 1). The size of each vegetation was not precisely described on all the echocardiography reports. The mean size (in four patients) was 20 mm (range 11–32 mm). Vegetations were obstructive in two cases. One patient with aortic endocarditis had a heterogeneous, hyperechogenic appearance of the interventricular septum (fig 1). Echocardiographic appearances suggestive of the presence of an abscess were seen in three cases. In one patient, there appeared to be an aneurysm within an aortic cusp. A frequently used phrase (seven cases) in the echocardiography reports describing the echocardiographic appearances of the vegetations was “a voluminous mass adhering to the valvar or paravalvar structures”. In 11 of the 12 patients, the adjectives “dense” and “hyperechogenic” were used (fig 1). In all cases, there was a notable discrepancy between the large size of the vegetation and the rather mild grade of the associated valve regurgitation (fig 2).

SURGICAL FINDINGS

Surgical findings were available in 10 patients. Two patients died rapidly before surgical intervention. All patients were admitted to an intensive care unit because of severe septic shock. Complete destruction of the valve and the surrounding tissue was observed in six

Figure 2 Transoesophageal view of an aortic valve fungal endocarditis, with voluminous, hyperechogenic vegetation and moderate valvular regurgitation.

cases. In seven cases, the anatomical description of the vegetation indicated the presence of an infiltrated and retracted appearance of the infected cardiac valve. In two cases, the perioperative description of the vegetation was similar to that of bacterial endocarditis. The size of the vegetation was never precisely described by the surgeon because of the extent of fungal lesions.

There was a good correlation between the echocardiographic and surgical findings in all but two cases. In one of these, echocardiography overestimated the extent of tissue destruction. In the other, a heterogeneous, hyperechogenic appearance of the interventricular septum was noted on echocardiography.

At surgery, multiple interventricular communications were found. Surgery was successful in all patients. A new model of biological valve was used in the last three patients in the series. This was a stentless valve capable of replacing the damaged valves and also the surrounding tissues. It had a stentless soft root which could be used as a patch, permitting the surgeon, for example, to close the interventricular communication in one of the 12 patients.

Seven patients were discharged alive. All seven were still alive after two years of follow up. Three patients died in the 15 days following the surgical treatment: two of these died suddenly, while the third patient died in septic shock.

Discussion

Cardiac infections by *Candida* species are rare but have usually had a dismal prognosis. Vo and colleagues reported an 80% mortality rate in a series of 44 patients described in various published reports.³ Several investigators have suggested that the definitive eradication of fungal endocarditis may not be possible, based on the observed frequency of late recurrence. Branco and associates have emphasised the importance of early surgical intervention in view of the high rate of embolic events, often in multiple locations, and the frequent occurrence of perivalvular destruction leading to heart failure.⁴

Endocarditis is probably not the most common cardiac location of fungal infection: in a necropsy series of 51 patients, Walsh and colleagues found 31 cases of myocarditis, 13 of

endocarditis, and four of pericarditis; in three cases all three locations were involved.⁵ Myocarditis was generally asymptomatic and was statistically linked to the presence of HIV infection. The two HIV patients in our series had voluminous and extensive masses adherent to the endocardium but neither had diffuse myocarditis. Numerous yellowish grainy spots, with a surrounding haemorrhagic halo, were observed throughout the myocardium. Similar appearances were described by Andriole and colleagues in a series of 21 necropsied cases of fungal endocarditis.⁶ In 38% of cases of candida endocarditis from published necropsy series, symptoms began soon after thoracic surgery.

Other clinical settings are associated with fungal endocarditis. In a report by Lozano and associates, 50% of patient with fungal endocarditis were drug addicts and 60% had pre-existing valvular disease.⁷ Branco and colleagues reported a series of 10 patients with fungal endocarditis, in eight of whom the infection developed on a prosthetic valve; none of these patients was an intravenous drug user.⁴

In the present series, four of the 12 patients were intravenous drug users and a further four patients had either a prosthetic valve, a pacemaker, or an indwelling central venous catheter. Pre-existing valvular disease was only seen in patients with left sided infection.

Fungal valvular infection is aggressive and difficult to treat surgically. There is a high risk of embolisation, and serious perioperative bleeding may occur when infected tissue is resected.⁸ Usually surgery is complicated by the need for radical debridement and reconstruction of the valvar root. Some investigators have suggested that immediate surgical intervention is associated with a better long term outcome.⁹ Fungal prosthetic valve endocarditis is particularly serious, and the first episode is usually a result of nosocomial candidaemia.¹⁰ Recurrent episodes are frequent.¹¹ In prosthetic valve fungal endocarditis, urgent surgical intervention is recommended and antifungal drug treatment should be continued for life.

Echocardiography has become a mainstay in the diagnosis of endocarditis. Transthoracic echocardiography alone is often sufficient to establish the diagnosis, as demonstrated by Lengyel, who found that transthoracic and transoesophageal echocardiographic findings were concordant in 83% of cases.¹² However, transoesophageal echocardiography is superior for defining the anatomical extent of the valvar lesions and guiding the surgical strategy.¹² In the subgroup of patients with suspected endocarditis on prosthetic valves, transoesophageal echocardiography is preferable.¹³ In addition, Erbel and colleagues have shown that transoesophageal echocardiography can identify a high risk subgroup among patients with infective endocarditis.¹⁴ Nguyen and associates drew attention to the diagnostic value of transoesophageal echocardiography in candidal prosthetic valve endocarditis, but did not report on specific echocardiographic features of the vegetations or the myocardium.¹⁵ Other case reports have occasionally described large

vegetations on transthoracic echocardiography.^{16, 17} Tischler and Vaitkus published a meta-analysis of the findings at echocardiography.¹ They found that vegetation size was < 10 mm in approximately 50% of cases of bacterial endocarditis. In our study, the diagnosis was made on transthoracic examination in all patients. Large vegetations—around 20 mm in diameter—were common. These were usually hyperechogenic and dense. Transoesophageal examination was helpful in ascertaining the extent of particularly large vegetations, in detecting abscesses, and in looking for other evidence of tissue destruction. In three cases in our series (a man of 32, a man of 34, and a woman of 60), echocardiography underestimated the extent of disease as determined at surgery. This may have been related to the delay between echocardiography and surgical intervention. In our opinion it is important to highlight the hyperechogenic appearances of valvar or perivalvar lesions. These are particularly characteristic of candidal infection.

CONCLUSIONS

Candidal cardiac infection is a rare condition with a poor prognosis. Our study emphasises the unusual echocardiographic features of endocarditis caused by *Candida* species. Transthoracic echocardiography of the vegetations is striking because of their heterogeneous and dense appearance. These characteristic appearances should suggest the diagnosis of candida rather than other forms of endocarditis and hence influence the treatment strategy. When this dense heterogeneous appearance is found not only in the vegetations but also in the adjacent myocardium, early surgical intervention may be warranted.

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