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CONCISE ARTICLE

Candida parapsilosis endocarditis: a comparative review of the literature

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Abstract Fungal endocarditis (FE) is an uncommon disease, and while accounting for only 1.3–6% of all cases of infectious endocarditis, it carries a high mortality risk. Although *Candida albicans* represents the main etiology of FE, *C. parapsilosis* is the most common non-albicans species. We report the case of a 32-year-old man with a history of prior intravenous drug (IVD) use hospitalized with endocarditis due to *C. parapsilosis* and review all 71 additional cases documented in the literature. A retrospective analysis of the 72 *C. parapsilosis* cases compared to 52 recently reviewed cases of *C. albicans* endocarditis was conducted to identify organism-specific clinical peculiarities. The most common predisposing factor for *C. parapsilosis* endocarditis (41/72; 57.4%) involved prosthetic valves followed by IVD use (12/72; 20%). Peripheral embolic and/or hemorrhagic events occurred in 28/64 (43.8%) patients, mostly in cerebral and lower limb territories. Overall mortality was 41.7%. Combined surgical and clinical treatment was associated with a lower mortality. Few patients received the newer antifungal agents, and it would appear that more experience is required for their use in the treatment of *C. parapsilosis* endocarditis.

Introduction

Although fungal endocarditis (FE) accounts for only 1.3–6% of all infective endocarditis cases, it carries a high mortality risk and has increased in incidence over the last two decades [1, 2]. The latter may be explained by improved diagnostic methods, a greater exposure to medical therapies that predispose to fungal infection, an increase in the incidence of intravenous drug (IVD) use and a more frequent use of invasive procedures for diagnosis and therapy [1, 3]. Fungal endocarditis is associated with a higher incidence of embolic events than bacterial endocarditis. An additional diagnostic challenge is that some common clinical signs and symptoms of endocarditis, including the presence of cardiac murmurs, may be absent [4].

The incidence of invasive candidiasis has increased during the past years [5], with *Candida* species being the most common agents involved in fungal endocarditis, followed by *Aspergillus* species. In a review of 152 cases of FE, *Candida* spp. was responsible for 94.1% of yeast endocarditis and *Aspergillus* spp. for 71.8% of mold endocarditis [1]. Among yeast-related endocarditis, *C. albicans* was the most frequent strain isolated (46%), followed by *C. parapsilosis* (17%). The latter was the most common pathogen isolated in IVD users [4]. *Candida parapsilosis* is also associated with nosocomial infections related to vascular devices, which may be explained in part by its ability to produce a biofilm on foreign bodies and catheters [6].

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We report here a case of relapsing *C. parapsilosis* endocarditis in an IVD user-patient and review the additional 71 cases published in the literature. A comparison of outcome differences with 52 *C. albicans* endocarditis cases was also conducted with the aim of identifying organism-specific clinical peculiarities.

Materials and methods

We conducted an OVID-MEDLINE search without language restriction from January 1968 through October 2006 to identify cases published in any language. The keywords "*Candida parapsilosis*", "endocarditis" and "fungal endocarditis" were used. Additional references were retrieved from reviews on the topic. Only reports with sufficient information on epidemiological and clinical data for patients over 16 years old were included. The review was also restricted to cases of "definite infective endocarditis" according to the modified Duke's criteria [7].

To evaluate potential clinical and epidemiological disagreement, the 72 cases of *C. parapsilosis* endocarditis were compared with 52 cases of *C. albicans* endocarditis recently reviewed [1].

Collected data were recorded in a database especially designed for the study. Analyses were performed by chi-square test, Fisher's exact test, and Student's *t* test, as appropriate. Two-sided tests were used and $p<0.05$ was considered to be statistically significant. In the multivariate analysis, the dependent variable was mortality, and only variables with a $p<0.2$ in terms of outcome were included in a stepwise logistic regression model. Calculations were made using the EPIINFO statistical program, ver. 3.3.2 (Centers for Disease Control and Prevention, Atlanta, GA).

Case report

A 32-year-old man with a history of prior IVD use was hospitalized with acute thromboembolic stroke and *C. parapsilosis* candidemia. Transoesophageal echocardiography (TEE) revealed a 6-mm-sized floating vegetation in the aortic valve. In view of the intermediary susceptibility to fluconazole presented by the blood isolate of *C. parapsilosis* (MIC4 mg/l), combined therapy with caspofungin [70 mg intravenous (i.v.) as first day loading dose, followed by 50 mg/day i.v.] and voriconazole [800 mg daily (p.o.) first day loading dose, followed by 400 mg/d p.o.] was administered for 12 weeks. The patient refused a surgical aortic valve replacement and was discharged with a proposed suppressive therapy of voriconazole (400 mg/day p.o), but was subsequently lost to follow-up. Three months after hospital discharge, he was re-hospitalized due to an episode of thromboembolic ischemic stroke linked to relapsed *C. parapsilosis* endocarditis. The patient acknowledged non-compliance to the voriconazole treatment previously prescribed. Voriconazole (400 mg/day p.o.) was restarted. A new TEE showed a vegetation in the aortic valve associated with a perforation and a mycotic aneurysm in the right coronary cuspid. A moderate to severe valve insufficiency was also found. In view of these findings and the severe hemodynamic compromise, the decision was taken to replace the aortic valve by a porcine xenograft valve (Schilling N° 25). The post-operative period was uneventful, and the patient was discharged from the hospital under voriconazole therapy (400 mg/day p.o.) – and again was lost to follow-up. One year following surgery, the patient was re-admitted with severe cardiac failure due to severe aortic insufficiency associated with paravalvar leak. He admitted to having followed the antifungal treatment for only 4 months following his last discharge. Blood cultures yielded *C. parapsilosis* once again, and a TEE revealed vegetations in the aortic prosthetic valve. The patient died suddenly two days after admission. The authorization to perform the autopsy was not given.

Results

Including our own case, we retrieved a total of 80 cases of endocarditis due to *C. parapsilosis*. Of these, 72 met the inclusion criteria (Appendix). Most cases were published prior to the availability of the newer antifungal compounds, such as echinocandins and second-generation triazoles.

Clinical presentation, risk factors and complications

Of the 72 patients meeting the inclusion criteria of this review, 71% (51/72) were male, and the mean age was 48.73 years (±15.8 years). Forty-one (57%) patients had isolated prosthetic valve involvement, and 31 (48.6%) had isolated native valve involvement; in four subjects, both native and prosthetic (relapsing infection) valve involvement occurred. Globally, the most frequent predisposing factor was prior cardiac surgery for valve replacement (57%) (Table 1). Late-onset infection, defined here as 6 months following surgery, occurred in 21/33 (63.3%) patients with prosthetic valve involvement for whom data were available. The second most frequent predisposing factor was IVD use (12/72 patients; 16.6%). Eleven of the 72 patients (15.2%) presented simultaneously with more than one predisposing factor. An absence of predisposing factors was observed in only 4/72 (5.6%) patients.

Data on embolic or hemorrhagic complications were available for 64 (88.8%) of the 72 patients. Of these, 28 (43.8%) presented complications, with the most common

Table 1 Main predisposing factors, age, associated mortality rate and affected valves observed in 124 reported cases of *Candida parapsilosis* and *C. albicans* endocarditis[a]

	C. albicans		*C. parapsilosis*		OR (95% CI)	*p* value
	n	Percentage	*n*	Percentage		
Number of patients	52		72			
Predisposing factors						
Prosthetic valve	29	55.8	41	57	0.95 (0.4–2.0)	0.94
IVD use	4	7.7	12	16.6	0.42 (0.1–1.5)	0.23
Intravenous parenteral nutrition	0	0.0	5	6.9	0 (0–1.58)	0.06
Broad spectrum antibiotics	1	1.9	4	5.6	0.33 (0–3.3)	0.29
Abdominal surgery	4	7.7	5	6.9	1.12 (0.2–5.1)	0.56
Previous valvular disease	7	13.5	3	4.8	3.58 (0.8–18.5)	0.06
Immunosuppression[b]	5	9.6	4	6.4	1.81 (0.4–8.6)	0.30
Other	3	5.6	3	4.1	1.41 (0.2–9.2)	0.49
None	2	3.8	4	5.6	0.68 (0.1–4.6)	0.50
Mean age (years±SD)	42.5	14.2	43.8	14.7	-	-
Mortality rate	17	33	30	41.7	-	-
Valve						
Aortic	27	51.9	41	56.9	-	-
Mitral	14	26.9	21	29.1	-	-
Tricuspid	5	9.6	3	4.1	-	-
Combination	6	11.5	-	-	-	-
Ventricular wall	-	-	2	2.8	-	-
Pulmonary	-	-	1	1.4	-	-

OR, Odds ratio; 95% CI, 95% confidence interval; IVD, intravenous drug

[a] More than one predisposing factor may be present for each patient

[b] Includes one case of esophageal cancer, one case of allogenic bone marrow transplantation, one case of advanced HIV infection and to cases of diabetes

sites being the lower limbs (ten; 35.7%) and the brain (six; 21.4%), followed by the lung (three; 10.7%) and the upper limbs (two; 7.1%). Seven (25%) of 28 patients presented intracranial hemorrhage, probably secondary to mycotic aneurysms.

Table 1 summarizes the characteristics of the 52 reported cases of *C. albicans* [1] and the 72 cases of *C. parapsilosis* endocarditis. The latter showed a trend towards a more frequent history of prior parenteral nutrition and valvular disease.

Therapy and outcome

Single, combined or sequential medical antifungal therapy was received by 28 (38.0%), 25 (34.7%) and 16 (22.2%) patients, respectively. Amphotericin B deoxycholate was the most frequently prescribed antifungal drug in 41 patients (56.9%), followed by 5-fluocytosine (23 patients; 31.9%) and fluconazole (20 patients; 27.7%). Other antifungal treatments were lipid formulations of amphotericin B (six patients; 8.3%) and miconazole and ketoconazole (five patients; 6.9%). Five patients were treated with the newer antifungal drugs caspofungin (three patients; 4.1%) and voriconazole (two patients; 2.7%). Medical treatment was not specified in two cases (2.7%). Combined surgical and medical treatment was performed in 42/72 (58.3%) patients. Interestingly, surgical therapy was more commonly performed in native valve patients (72.4%) than in patients with prostheses [45.7%; Odds Ratio (OR) 3.1; 95% confidence interval (CI) 1.0–8.9; $p=0.05$].

Neither mean age nor gender was associated with outcome. A trend was observed toward a higher mortality among patients with *C. parapsilosis* endocarditis less than 65 years (OR 3.18; 95%CI 0.85–11.83; $p=0.07$). Of note, this was restricted to patients that underwent cardiac surgery (OR 5.2; 95%CI 0.81–32.98; $p=0.08$).

The mortality rate was lower among patients undergoing adjunctive surgical therapy (33.3%) than among those treated only with antifungals (53.3%), but the difference was not statistically significant (OR 0.4; 95%CI 0.2–1.1; $p=0.14$). Surgery was not related to a lower incidence of embolic and/or hemorrhagic complications, which were observed in 43.9% of surgical-associated therapy and 40.9% of the non-surgical cases (OR 1.1; 95% CI 0.4–3.2; $p=0.96$). This result could be due to the higher incidence of embolic events in the early course of FE.

Even in a multivariate analysis adjusted for gender, age (two blocks; ≥ or < than 65 years), combined surgical

therapy or not and type of valve (native or prosthetic), an adjuvant surgical treatment was significantly associated with a better outcome (OR 0.3; 95% CI 0.1–1.0; p=0.05) (Table 2).

Discussion

The first case of endocarditis due to *C. parapsilosis* was reported in 1940 [8]. In the years that followed, this agent was predominantly reported as an etiology of endocarditis, notably in IVD users [9]. However, *C. parapsilosis* is now considered to be an important emerging pathogen of invasive candidiasis, only surpassed by *C. albicans* [10], and this will probably have consequences on FE microbiology in the near future [11, 12]. *C. parapsilosis* strains associated with invasive disease are more likely to produce biofilm structures [13] that are morphologically different from those produced by *C. albicans* [14].

Recent changes in fungal epidemiology may also be related to the wide use of azoles in combination with the new prophylactic and therapeutic strategies for fungal infections. More specifically, there is a consensus that the percentage of *Candida* non-albicans species accounting for nosocomial *Candida* infections is increasing, in part due to the widespread use of fluconazole [15]. The most probable source of infection in the outbreaks of *C. parapsilosis* infective endocarditis reported to date was determined to be intraoperative contamination (e.g. cardiac bypass equipment, tears in surgical gloves worn by carrier surgeons) [16, 17].

The core findings of this review reveal that the aortic valve was the most commonly involved valve, with 42.5% of cases occurring in native valves. The most common predisposing factor in patients with native valve involvement was IVD use. Overall mortality among these patients was as high as 41.7%, with a lower mortality among those treated with adjuvant surgery. Only five cases treated with new antifungal drugs have been reported to date, which precludes the drawing of any firm conclusion on their role in the treatment of *C. parapsilosis* endocarditis.

Table 2 Variables associated with mortality in 64[a] patients presenting with endocarditis due to *C. parapsilosis*: multivariate analysis

	OR	95% CI	p value
Age (≥ or <65 years)	0.34	0.08–1.45	0.14
Gender	1.0	0.29–3.39	0.99
Adjuvant surgery	0.33	0.01–1.02	0.05
Type of valve (native or prosthetic)	0.56	0.17–1.82	0.34

[a] Eight patients were excluded from the analysis: four patients without data on the type of involved valve and four patients with sequential native and prosthetic valve involvement

Only four (5.7%) patients did not present any predisposing factor for *C. parapsilosis* endocarditis. However, Rubinstein and Lang reported that as high as 12% of patients presenting with FE have no identifiable predisposing factors [18]. In general, the predisposing factors observed were similar to those of patients with endocarditis due to *C. albicans* [19]. A comparison of *C. albicans* and C. *parapsilosis* endocarditis cases shows that FE due to these pathogens rarely originates without a predisposing factor and occurs more frequently in prosthetic valves. In addition, a history of IVD use was present in 20% of patients with *C. parapsilosis* infection. In contrast, *C. albicans* seems to be less frequently associated with IVD use and is observed predominantly in patients with underlying abnormal valves, mostly with rheumatic disease (Table 1). Our data suggest also that *C. parapsilosis* is more prevalent than *C. albicans* in patients receiving parenteral nutrition (Table 1).

Embolic and/or hemorrhagic complications were present in 43.8% of patients, most commonly as cerebral thromboembolic events, which is in accordance with the incidence rate reported by Ellis et al. [4]. In general, the occurrence of embolic events in patients with fever should always be seen as a potential diagnostic of infective endocarditis. In particular, a fungal etiology must be considered, given the high likelihood of thromboembolic events reported in these cases [20].

Survival in patients with FE is poor and barely exceeds 50% [18]. Although *C. parapsilosis* endocarditis has been associated with a higher mortality when compared to endocarditis caused by other *Candida* species [19], this could not be confirmed in our comparison with *C. albicans* cases (Table 1).

The ideal treatment for *Candida* endocarditis has not been formally tested in prospective randomized controlled studies. In the present review, combined surgical and medical therapy was associated with a lower mortality rate. In clinical practice, surgery is generally regarded as the standard treatment for FE. The American College of Cardiology (ACC) and The American Heart Association (AHA) guidelines stipulate surgical indications for FE (Class I recommendation). In addition, the recent Infectious Diseases Society of America (IDSA) guidelines on *Candida* endocarditis recommend that it should be treated by valve replacement, either for native or prosthetic valves [21]. Unfortunately, the heterogeneity of the population affected, allied to the relative rarity of FE, makes the performance of prospective studies impractical [4].

Retrospective studies based on well-documented cases may be a feasible alternative. In their recent meta-analysis, Steinbach et al. suggest that patients who underwent combined surgical and medical therapy may have presented a lower mortality rate (OR 0.56; 95% CI 0.16–1.99). A higher

mortality has been reported in patients infected by *C. parapsilosis* (OR 1.51; 95%CI 0.39–5.52) and with left-sided endocarditis (OR 2.36, 95%CI 0.55–10.07) [19]. However, methodological limitations should be considered when analyzing these results. For example, in very critically ill patients, a surgical procedure may be precluded, thus leading to a falsely higher mortality in the group with medical treatment alone. Moreover, a high number of patients with FE probably underwent surgery because endocarditis due to these agents are more frequently related per se to the classical indications for surgical treatment, such as thromboembolic events and the presence of large vegetations [22]. In the present review, thromboembolic events may have commonly indicated a surgical procedure, which explains why operated patients did not present a lower incidence of this complication in a cross-sectional analysis. Finally, isolated reports show that a single medical treatment for *Candida* endocarditis may be sufficient – in particular if the most potent and less toxic antifungal drugs are used [23].

We observed a lower mortality rate among patients that underwent adjuvant surgery. Multivariate analysis revealed that this tendency persisted even with adjustment for type of valve (native or prosthetic), gender and age (≥ or < than 65 years). However, there was a lack of data for determining if patients treated with surgery had more severe disease and also on the delay between the diagnosis of endocarditis and the surgical procedure.

Since the mid-1990s, new antifungal drugs, such as second-generation triazoles (voriconazole and posaconazole), have become available which are well tolerated and active against fluconazole-less susceptible or fluconazole-resistant *Candida* species and which reach high body tissue concentrations, including in the central nervous system. Echinocandins (caspofungin, anidulafungin and micafungin), which have an innovative mechanism of action, are rapidly fungicidal for *Candida* species and are rarely associated with adverse events [24]. They present a good activity in the biofilm, which could be considered of interest in terms of FE in patients with prosthetic valves. *Candida parapsilosis* is less susceptible to echinocandins, but the clinical impact of the in vitro results have still to be evaluated [25]. However, apart from the lack of well-controlled clinical studies using these new compounds, high costs and the risk of resistance among fungal species are potential concerns for their widespread use. An early diagnosis allied to rapid and efficient treatment may potentially improve the outcome of FE.

This study presents some of the limitations that are common to retrospective studies. First, there is an important heterogeneity among included patients, and the clinical management of cases was not uniform. Second, data on patients treated with the new antifungal compounds are scarce, thus precluding any definitive conclusion. Finally, given that some of the relevant information is lacking in the reports, the retrospective analysis of treatments with the aim of comparing single medical or combined medical plus surgical treatment remains limited.

Conclusions

More experience is required with the use of newer antifungal agents in the treatment of *C. parapsilosis* endocarditis. These drugs may permit more efficient therapy since they are related to a higher efficacy and fewer side effects. As a result, the indication for surgical therapy may be reduced. Prospective randomized studies are required to answer these questions, although their feasibility is uncertain.

Appendix

Table 3 Details of 71 previously reported cases of *Candida* parapsilosis (1968–2006)

Authors	Reference	Age	Gender[a]	Type of valve[b]	Valve[c]	Predisposition[d]	Concomitant surgery	Medical therapy[e]	Outcome	Complications
Abgueguen et al. 2002	[1]	81	M	P	Ao	Prosthetic valve and long-term antibiotic therapy and abdominal surgery	Yes	Amp B + fluconazole	Dead	No
Aoyagi et al. 1989	[2]	56	M	N	Mi and Ao	Absent	Yes	Unspecified drug	Survival	No
Auger et al. 1983	[3]	49	M	P	Mi	Prosthetic valve	Yes	Amp B, then 5-FC	Survival	Ischemic stroke

Table 3 (continued)

Authors	Reference	Age	Gender[a]	Type of valve[b]	Valve[c]	Predisposition[d]	Concomitant surgery	Medical therapy[e]	Outcome	Complications
Baddour 1995	[4]	45	M	P	Ao	Prosthetic valve and abdominal surgery	No	Amp B, then Amp B lipidic complex, then fluconazole (long-term suppressive therapy)	Survival	No
Blinkhorn et al. 1992	[5]	37	M	N	Ao	IVD	Yes	Valve replacement and embolectomy and Amp B + 5-FC	Survival	Lower limbs embolism
Brandstetter and Brause 1980	[6]	24	M	N	Ao	IVD	Yes	Valve replacement + mp B and 5-FC	Survival	No
Cancelas et al. 1994	[7]	35	F	N	Mi	Allogeneic bone marrow transplant	Yes	Amp B, then fluconazole (twice)	Survival	No
Caparrós and Cabrera 2002	[8]	48	M	N	Ao	Long-term antibiotic therapy	Yes	Embolectomy + liposomal Amp B	Dead	Lower limbs embolism
Cheng and Yu. 1970	[9]	29	M	N and P	Mi and Tri	Cardiac surgery Prosthetic valve	Yes	Valve replacement	Dead	Ischemic stroke and pulmonary embolism (autopsy)
Chuei-Shiun Li	[10]	53	M	P	Mi	Diabetes mellitus	Yes	Amp B	Survival	Ischemic stroke
Czwerwiec et al. 1993	[11]	58	M	P	Ao	Prosthetic valve	No	Amp B, then fluconazole (long-term suppressive therapy)	Survival	Intracerebral hemorrhage
Darwazah et al. 1999	[12]	67	M	P	Ao	Prosthetic valve	Yes	Valve replacement + liposomal Amp B and 5-FC	Survival	Ischemic stroke
De Belder et al. 1989	[13]	44	M	N	Ao	Ruptured oesophagus and consequent surgery	Yes	Amp B and 5-FC	Survival	Ischemic stroke
Diekema et al. 1997	[14]	79	M	P	Ao	Prosthetic valve	Yes	Amp B	Dead	No
Diekema et al. 1997	[14]	70	M	P	Ao	Prosthetic valve	No	Amp B	Survival	No
Diekema et al. 1997	[14]	58	M	P	Ao	Prosthetic valve	No	Amp B	Dead	No
Diekema et al. 1997	[14]	78	M	P	Ao	Prosthetic valve	No	Amp B	Dead	No
Dismukes et al. 1973	[15]	47	NR	P	Ao	Prosthetic valve	No	Amp B	Dead	NR

Table 3 (continued)

Authors	Reference	Age	Gender[a]	Type of valve[b]	Valve[c]	Predisposition[d]	Concomitant surgery	Medical therapy[e]	Outcome	Complications
Galgiani et al. 1977	[16]	36	M	N and P	Ao	Prosthetic valve	Yes (three times)	Amp B, then 5FC, then Amp B + 5FC	Dead	No
Galgiani et al. 1977	[16]	50	M	P	Aortic	IVD and prosthetic valve	Yes (twice)	Amp B, then 5FC, then Amp B and 5FC, then miconazol	Dead	No
Garzoni et al. 2006	NP	32	M	N and P	Aortic	IDU and ancient abdominal surgery	Yes	Voriconazol and caspofungin, then voriconazol	Dead	Ischemic stroke
Girmenia et al. 1996	[17]	NR	NR	NR	NR	Hematological malignancy	No	Amp B, then fluconazole	Survival	NR
Girmenia et al. 1996	[17]	NR	NR	NR	NR	Hematological malignancy	No	Fluconazole	Survival	NR
Gladstone et al. 1976	[18]	31	M	N	Mitral	IVD	No	Amp B and 5-FC	Survival	Lower limbs embolism
Gomes et al. 1976	[19]	55	M	N	Aortic	IVD	Yes	Amp B and 5-FC	Survival	No
Gottlieb et al. 1974	[20]	23	M	N	Aortic	IVD and bicuspid aortic valve	Yes	Amp B	Dead	Intracerebral hemorrhage
Grehl et al. 1972	[21]	51	M	P	Aortic	Prosthetic valve	Yes (twice)	Amp B , then 5-FC indefinitely	Survival	No
Herling et al. 1984	[22]	67	F	N	Aortic	Prosthetic valve	Yes	Valve replacement + Amp B	Survival	No
Hoeprich et al. 1974	[23]	20	F	N	Aortic	IVD and cardiac surgery other	No	5-FC, then Amp B and clotrimoxazol	Dead	No
Inoue et al. 1998	[24]	57	M	N	Aortic	Parenteral nutrition chemotherapy and abdominal surgery	Yes	Fluconazole	Survival	No
Isalska et al. 1988	[25]	37	F	P	Mitral	Prosthetic valve	No	Amp B, then Amp B and 5FU, then fluconazole	Survival	Intracerebral hemorrhage
Johnston et al. 1994	[26]	68	M	P	Aortic	Prosthetic valve	No	Amp B + 5-FC, then ketoconazole	Dead	NR
Johnston et al. 1994	[26]	41	F	P	Aortic	Prosthetic valve	No	Amp B	Dead	NR
Johnston et al. 1994	[26]	53	M	P	Aortic	Prosthetic valve	No	Amp B + 5-FC	Dead	NR
Johnston et al. 1994	[26]	65	M	P	Aortic	Prosthetic valve	No	Amp B + 5-FC	Dead	NR
Johnston et al. 1994	[26]	78	F	P	Aortic	Prosthetic valve	No	Amp B	Dead	NR
Jones et al. 2002	[27]	82	M	P	Ao	Prosthetic valve	Yes	Amp B	Dead	Lower and upper limb embolism

Table 3 (continued)

Authors	Reference	Age	Gender[a]	Type of valve[b]	Valve[c]	Predisposition[d]	Concomitant surgery	Medical therapy[e]	Outcome	Complications
Jones et al. 2002	[27]	59	M	P	Ao	Prosthetic valve	Yes	Amp B, then liposomal Amp B and 5-FC, then fluconazole	Survival	No
Kaloterakis et al. 2003	[28]	59	M	N	Tri	Parenteral nutrition antibiotic therapy	Yes	Liposomal Amp B, then fluconazole	Survival	No
Kontou-Kastellanou et al. 1990	[29]	27	M	P	Ao	Prosthetic valve	Yes	Valve replacement and Amp B	Survival	No
Lejko-Zupanc and Kozelj 1977	[30]	62	M	P	Mi	Prosthetic valve	No	Amp B, then fluconazole	Survival	No
Li et al. 2004	[10]	53	M	N	Ao	Diabetes mellitus and dental manipulation	Yes	Amp B	Survival	Ischemic stroke
Lipton et al. 1984	[31]	NR	F	N	Mi	IVD	No	Amp B	Survival	Intracerebral hemorrhage
López-Ciudad et al. 2006	[32]	59	F	N	Ventricular wall	Abdominal surgery Parenteral nutrition and antibiotic therapy	No	Caspofungin and voriconazole	Survival	No
Lozano et al. 1994	[33]	26	M	N	Ao	IVD	Yes	Fibrinolysis + Amp B and 5-FC	Survival	Lower limb embolism
Martin et al. 1979	[34]	30	M	N	Ao	IVD	Yes	Amp B and 5-FC	Survival	No
Martin et al. 1987	[35]	67	F	P	Mi	Prosthetic valve	Yes	Valve replacement + Amp B, then ketoconazole, then miconazole.	Dead	NO
Mayrer et al. 1978	[36]	43	M	N	Mi	IVD	No	Amp B + 5-FC	Survival	No
Melgar et al. 1997	[37]	47	M	N	Ao	Absent	Yes	Amp B, then ketoconazol, then amp B, then fluconazole	Survival	No
Melgar et al. 1997	[37]	47	F	P	Mi	Prosthetic valve	Yes	Amp B, then fluconazole	Survival	No
Moudgal 2005	[38]	51	M	P	Ao	Prosthetic valve	No	Amp + 5 FU, then caspofungin + fluconazole, then Amp B lipid complex	Survival	No

Table 3 (continued)

Authors	Reference	Age	Gender[a]	Type of valve[b]	Valve[c]	Predisposition[d]	Concomitant surgery	Medical therapy[e]	Outcome	Complications
Otaki and Kitamura 1993	[39]	55	F	P	Mi	Prosthetic valve	Yes	Fluconazole	Dead	Intracerebral hemorrhage
Record et al. 1971	[40]	57	M	P	Ao	Prosthetic valve	No	Amp B, then 5FC	Dead	Intracerebral hemorrhage
Rubenstein et al. 1975	[41]	42	M	N	Ao	No	Yes	Amp B	Dead	No
Rubenstein et al. 1975	[41]	17	M	N	Mi	Rheumatic heart disease	Yes	Amp B	Dead	Ischemic stroke
Rubenstein et al. 1975	[41]	42	M	P	Mi	IVD	No	Amp B and 5FU	Dead	Intracranial haemorrhage
Rubenstein et al. 1975	[41]	62	F	N	Mi	Cardiac surgery other	No	Amp B	Dead	Upper limb embolism
Rubenstein et al. 1975	[41]	35	F	N	Tri	Rheumatic heart disease	No	Amp B	Dead	Pulmonary embolism
Rudd et al. 1980	[42]	53	F	P	Ao	Prosthetic valve	Yes	Amp B	Survival	Lower limb embolism
Saito et al. 2001	[43]	72	M	N	Tri	Parenteral nutrition	No	Amp B and fluconazole	Survival	No
Samelson et al. 1980	[44]	36	F	N and P	Mi	Intervertebral disc prosthetic valve	Yes	Different drug therapies: Amp B, 5-FC, miconazole and ketoconazole	Survival	Ischemic stroke, cerebral abscess, septic thrombophlebitis
Senba et al. 1992	[45]	56	M	N	Mi	No	Yes	Valve replacement + fluconazol and miconazole	Survival	No
Severo et al. 1987	[46]	33	M	P	Mi	Cardiac surgery Prosthetic valve	No	Ketoconazole	Dead	Ischemic stroke
Stulz et al. 1980	[47]	34	F	P	Mi	Prosthetic valve	Yes	Amp B	Survival	No
Sunazawa et al. 1995	[48]	42	F	N	Pul	Cardiac surgery other	Yes	Unspecified drug	Survival	No
Tonomo et al. 2004	[49]	22	M	NR	VW	Abdominal surgery antibiotic therapy and parenteral nutrition	Yes	Miconazol, then fluconazole intercalated with miconazol.	Survival	Pulmonary embolism
Veraldi et al. 2000	[50]	29	F	N	Ao	HIV infection	Yes	Valve replacement + surgical embolectomy + Amp B alternated with fluconazole	Survival	Lower limb embolism
Vivas et al. 1985	[51]	54	M	N	Mi	Rheumatic heart disease	No	Amp B	Dead	No
Wallbridge et al. 1993	[52]	58	M	P	Mi	Prosthetic valve	No	Amp B and 5FC, then fluconazole	Dead	No

Table 3 (continued)

Authors	Reference	Age	Gender[a]	Type of valve[b]	Valve[c]	Predisposition[d]	Concomitant surgery	Medical therapy[e]	Outcome	Complications
Wang et al. 1998	[53]	42	F	N	Ao	Cardiac surgery other	Yes	Fluconazole, then Amp B, then fluconazole	Survival	Lower limb embolism
Watanakunakorn et al. 1968	[54]	40	M	P	Ao	Prosthetic valve	Yes	Amp B	Dead	No
Zahid et al. 1994	[55]	48	M	P	Mi	Prosthetic valve	No	Amp B, then 5-FC, then fluconazole	Survival	No

NR, No report; NP, not published
[a] M, Male; F, female
[b] N, Native; P, prosthetic
[c] AO, aortic; Mi, mitral; Tri, tricuspide; Pul, pulmonary; VW, ventricular wall
[d] IVD, Intravenous drug use
[e] 5FC, 5-fluocytosine; Amp B, amphotericine B

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