C parapsilosis appears to be more invasive than other species of Candida.

Over 200 cases of fungal endocarditis were reported during the past 20 years; 75 percent were due to species of Candida.\(^1\)\(^-\)\(^3\) Untreated endocarditis due to Candida is uniformly fatal. Cure with antifungal chemotherapy alone was claimed in isolated instances,\(^4\) the survivors representing 7 to 14.5 percent.\(^1\)\(^,\)\(^5\)\(^-\)\(^8\) Combined medical and surgical treatment resulted in cure in 29 (55 percent) of the reported cases.\(^1\)\(^,\)\(^3\)\(^,\)\(^5\)\(^,\)\(^7\)\(^,\)\(^8\)

We report the findings in a heroin addict with fortuitously detected endocarditis due to Candida parapsilosis and nonobstructive asymmetric septal hypertrophy. A cure was effected with medical therapy alone. Data from this hospital suggest that C parapsilosis invades the bloodstream more frequently than other species of Candida.

**CASE REPORT**

A 43-year-old man was hospitalized on July 2, 1975, with a right foot that had been painful and swollen for one day. He had had heroin since 1967 and had entered the program for treatment with methadone hydrochloride in November 1974, and had normal findings on physical examination.

Nine weeks prior to admission, the patient noticed generalized weakness, polyarthralgias, and a transient swelling of the dorsum of his right foot following blunt trauma. One day prior to admission, the patient again noted pain, swelling, and warmth over the dorsum of the right foot. On admission to the hospital, the patient’s temperature was 101.1°F (38.4°C) orally. Old “track marks” were present on both arms, and the dorsum of the right foot was warm, tender, and erythematous. No edema, lacerations, or venous cords were present. Joints and peripheral pulses were normal. Cardiac, neurologic, funduscopic, dermatologic, abdominal, and pulmonary examinations revealed no abnormality. Laboratory studies revealed the following values: white blood cell count, 8,000/cu mm, with a normal differential cell count; hematocrit reading, 35.7 percent; erythrocytic sedimentation rate (Wintrobe’s method), 42 mm/hr; blood urea nitrogen level, 13 mg/100 ml; creatinine level, 0.9 mg/100 ml; albumin level, 3.9 gm/100 ml; and globulin level, 3.2 gm/100 ml. X-ray films of the ankle, foot, and chest and also an electrocardiogram were normal. The urine contained traces of protein. Two consecutive cultures of blood were obtained.

For presumed bacterial cellulitis the patient received penicillin for eight days. His fever abated within 24 hours, and the cellulitis improved by the end of the week. On the eighth day of hospitalization, isolation of C parapsilosis from both initial cultures of blood was reported. Eight subsequent cultures of blood obtained on the ninth, tenth, and 15th days of hospitalization also yielded C parapsilosis. Rare C parapsilosis and also C albicans were isolated from the stool but not from the pharynx, foot, anus, rectum, sigmoid colon, or urine.

On the 20th day of hospitalization, an otherwise normal phonocardiogram revealed a midystolic click (Fig 1). Cardiac catheterization showed normal values for right-sided, pulmonary capillary wedge, and left ventricular pressures, and no valvular gradients at rest or during exercise. Four of the 14 selective 2 ml samples of blood taken at the time of cardiac catheterization were positive for C Parapsilosis. The patient was started on a regimen of 3 gm of flucytosine (5-fluorocytosine; 5-FC) orally per day and 40 mg of amphotericin B intravenously on alternate days. The latter dosage was subsequently decreased to 30 mg, with resolution of transient renal insufficiency (creatinine level, 2.6 mg/100 ml).

One week after the start of antifungal therapy, a grade 2 midystolic apical murmur was first noted. An echocardiogram revealed asymmetric septal hypertrophy (septal thickness, 18 mm) but no aortic or mitral valvular vegetations or detectable mitral valvular prolapse. A phonocardiogram on the 44th day of hospitalization documented a late systolic crescendo murmur which was intensified by handgrip and was believed to be due to mild mitral regurgitation. No diastolic murmurs were auscultated or recorded.

The minimal inhibitory concentration (MIC) and the minimal fungicidal concentration of amphotericin B against the isolate of C parapsilosis were 0.70µg/ml and 1.56µg/ml, respectively. Although the MIC of flucytosine was greater than 100µg/ml, therapy with the drug was continued for seven weeks (total dose, 131 gm) because of possible in vitro
synergy. Therapy with amphotericin B was continued for a total of 14 weeks (total dose, 1.72 gm). Serum fungicidal levels were 1:5 before and 1:20 after the drug was administered. Weekly cultures of blood remained sterile after the second month of hospitalization. No evidence of arterial embolization was noted throughout the course of hospitalization, and the patient was discharged on the 121st day of hospitalization.

The patient has remained well, and no relapse has been seen on follow-up visits (including cultures of blood) for longer than 18 months after the completion of therapy. A repeat phonocardiogram obtained nine months after discharge (Fig 2) still showed the murmur of mitral regurgitation, and an echocardiogram (Fig 3) revealed for the first time a prolapse of the posterior mitral leaflet.

**RESULTS OF THE MYCOLOGIC SURVEY**

Yeasts are observed in slightly over 5 percent of the cultures submitted to the hospital's microbiology laboratory; slightly less than half are classified as to species. Of these, *C albicans* was most common isolate, while *C parapsilosis* represented only 8 percent (7/87) of isolates (Table 1). During a five-year period, 34 patients had contamination of an intravenous catheter without fungemia or dissemination; *C parapsilosis* was isolated in six, a higher proportion, but this was not significant at the 5 percent level. Fungemia (usually associated with an intravenous catheter) occurred in 42 patients, and in two-thirds of these, the fungemia was transient. The remaining 14 patients manifested persistent fungemia or disseminated fungal disease (or both). The present patient is the only one with diagnosed endocarditis. In patients with fungemia, *C parapsilosis* was isolated at a significantly higher frequency than in all patients, *i.e.*, 26.7 percent (12/45) vs 8.0 percent (7/87) (P < 0.01 by the t-test).

**DISCUSSION**

In this patient with persistent fungemia with *C parap-
endocarditis, initially developed insidiously, with a mild anemia and an elevated erythrocyte sedimentation rate. More typically, fungal endocarditis is characterized by fever and the effects of bulky vegetations, ie, heart failure and major arterial embolization. The two most common conditions predisposing to endocarditis due to Candida (ie, open-heart surgery and prolonged intravenous therapy with fluids and antibiotics) were not present, but heroin addiction, the third most common risk factor, was present. In our patient with resting nonobstructive asymmetric septal hypertrophy and a midystolic ejection click, the development of the murmur of mitral regurgitation during therapy and the subsequent prolapse of the posterior mitral leaflet supports the diagnosis of endocarditis involving the mitral valve or its chordae tendineae. To our knowledge, this is the first report of fungal endocarditis seen in a patient with asymmetric septal hypertrophy.

The present experience suggests that medical therapy alone may be successful when the diagnosis of fungal endocarditis is made early. There are no valid comparisons of outcome after medical therapy vs combined medical and surgical therapy. The higher incidence of survival in patients with fungal endocarditis after combined therapy (55 percent), which was calculated from several reports in the literature, is based on the recovery of Candida in resected tissues. In contrast, in the few medical cures of “endocarditis” due to Candida, the diagnosis rested on candidemia alone; and, therefore, the nevertheless poor response to medical therapy may have been overestimated.

Our patient was infected with the species most commonly associated with endocarditis due to Candida in the heroin addict. Fifty cases of endocarditis due to Candida in heroin addicts have been reported, and the various species were isolated in the following frequencies: C parapsilosis (parakrusei), 25 cases; C albicans, five cases; C krusei, five cases; C tropicalis, four cases; C stellatoidea, four cases; C quilliermondii, four cases; and unspecified species, three cases. Nine patients received no therapy and died, ten received antifungal chemotherapy alone (one survivor; 10 percent), and 31 patients received combined chemotherapy and surgery (13 survivors; 42 percent). The association of C parapsilosis with endocarditis in heroin addicts was believed to be related to contamination of the drug with this yeast. In our survey, C parapsilosis was significantly more often associated with fungemia, compared to other species. This suggests that C parapsilosis is more capable of invasion of the bloodstream than other species of Candida. The impression is supported by the intermediate frequency of isolation of C parapsilosis from contaminated intravenous catheters.

ACKNOWLEDGMENT: Ms. Susan Vozel and Ms. Kim Bartley provided excellent secretarial assistance.

REFERENCES


Table 1—Frequency of Isolation of Yeasts

<table>
<thead>
<tr>
<th>Isolated Organism</th>
<th>1st Quarter of 1975 (All Sites)</th>
<th>Contamination of Intravenous Catheter</th>
<th>Fungemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>C albicans</td>
<td>53 (61)</td>
<td>21 (90)</td>
<td>21 (47)</td>
</tr>
<tr>
<td>C tropicalis</td>
<td>13 (15)</td>
<td>5 (14)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>C parapsilosis</td>
<td>7 (8)**</td>
<td>6 (17)</td>
<td>12 (27)**</td>
</tr>
<tr>
<td>Torulopsis glabrata</td>
<td>5 (6)</td>
<td>3 (9)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>C neoformans</td>
<td>0</td>
<td>0</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Other yeast†</td>
<td>9 (10)</td>
<td>0</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Yeasts/patients</td>
<td>87/72</td>
<td>35/34</td>
<td>45/42</td>
</tr>
</tbody>
</table>

*Numbers within parentheses are percents.

**Difference of all sites vs fungemia significant at 1 percent level.

†Includes C krusei, C stellatoidea, C quilliermondii, and Rhodotorula sp.

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