Concomitant Stroke and Candida Parapsilosis Native Valve Endocarditis: Report of One Case and Literature Review

Chuei-Shiun Li¹, Chi-Ren Huang¹, Cheng-Hsien Lu¹, Chun-Chung Lui², Chun-Chih Chien³, and Wen-Neng Chang¹

Abstract- Cerebrovascular stroke due to Candida (C.) parapsilosis native valve endocarditis (NVE) is rarely reported. Herein, we report a 53-year man with C. parapsilosis NVE and acute ischemic stroke. Diabetes mellitus and recent dental manipulation were the preceding events. Cranial magnetic resonance imaging study revealed occlusion of left common carotid artery, and infarcts of the pons and territory of the branch of left middle cerebral artery. With a total of 4,051 mg amphotericin B therapy and aortic valve replacement, the patient survived with right hemiplegia and dysarthria. In the English literature, there have been 12 patients with C. parapsilosis NVE including our patient over the past 25 years. Intravenous drug abuse was the most common predisposing factor for this infective disorder, followed by hematological malignancy and central venous catheterization. Fever and ischemic phenomenon of lower legs were the common clinical manifestations. Cerebrovascular stroke was present only in our case. Of these 12 patients, one administered fluconazole and miconazole therapy died, while 11 with amphotericin B therapy and one patient with fluconazole monotherapy survived.

Key Words: Candida parapsilosis, Cerebrovascular stroke, Native valve endocarditis

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INTRODUCTION

Fungal infections, especially those due to Candida (C.) species, are important opportunistic infections, particularly in critically ill patients and those in an immunocompromised state. Further, fungal involvement has been determined in 1.3-6% of infective endocarditis cases, and C. parapsilosis has been detected in 11-12% of the endocarditis cases caused by fungal infection¹². Cerebrovascular symptoms have been noted for 17% of patients with fungal endocarditis⁵. Rubinstein et al.⁹ reported 5 cases of C. parapsilosis native value endocarditis (NVE), one case involving cerebral hemorrhage and another case involving cerebral infarct proven by necropsy. Based on a review of the literature, 12 cases of C. parapsilosis fungal endocarditis in heroine addicts died²⁰. Herein we report a case of C. parapsilosis NVE with concomitant stroke, and review relevant cases in the literature.
CASE REPORT

In November 2000, a 53-year-old man was sent to the emergency room (ER) because of acute right-limb weakness and dysarthria. His past medical history was unremarkable except for poorly controlled diabetes mellitus (DM) for 10 years, betel nut chewing for several years, and teeth extraction due to bleeding gums and periodontitis three months previously. Physical examination revealed that the patient was drowsy, with a blood pressure was 126/80 mmHg, heart rate 96 /min, and body temperature 36.8 °C. Cardiac auscultation revealed a grade II/VI systolic murmur over the apex. Right hemiparesis, dysarthria and right central facial palsy were also noted on examination. Except for mild elevation in erythrocyte sedimentation rate, other laboratory studies including complete blood cell count, liver and renal function tests, electrolytes and urine analysis, were all within normal limits. Chest X-rays and brain computed tomography (CT) studies were also unremarkable.

On the second day of admission, the patient’s neurological condition deteriorated. Limitation in horizontal gazing of both eyes, with more severe involvement in the right eyes, and right hemiplegia developed. A cranial magnetic resonance image (MRI) study revealed occlusion of the left common carotid artery (Fig. 1) and infarcts over the territory of the left middle cerebral artery branch and the pons (Fig. 2). Transthoracic cardiac echocardiography revealed vegetation in the aortic valve and severe aortic regurgitation. Initial blood cul-

Figure 1. MR angiography. (A) and (B) show the occlusion of left common carotid artery

Figure 2. Diffusion-weighted imagings. (A) shows infarct of the pons (arrowheads) and (B) shows infarct of the territory of left middle cerebral artery branch (arrowheads)
tures grew yeast-like microorganism. Further blood cultures for fungus and subsequent identification showed growth of *C. parapsilosis*. With strain-specific antifungal-susceptibility tests performed according to the standard method\(^4\), the minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) values for amphotericin B/fluconazole were 0.13/1.5 µg/mL and 0.5/>200 µg/mL, respectively. Therapy of 4,051 mg intravenous amphotericin B was administered, and aortic valve replacement was also performed during the course of amphotericin B treatment. Pathologic examination of the aortic valve showed necrotizing inflammation. Over a two-year follow up period, the patient had clear consciousness, although right hemiplegia and severe dysarthria remained unresolved.

### REVIEW OF THE LITERATURE

The English literature pertaining to cases of NVE due to *C. parapsilosis* infection reported over the past 25 years (1978-2002) was reviewed for this study. A totally of 11 cases with this infectious disorder were included in this study, and their clinical data were analyzed\(^{4-14}\). The clinical data for our patient (Case 1) and the other 11 reported patients (Cases 2-12) are listed in Table. Of the other 11 reported cases, intravenous drug abuse was the most common preceding event, followed by hematologic malignancy and central venous catheterization. Of the involved cardiac valves of the other 11 reported cases, aortic valve involvement was noted in 4, mitral valve in 4, and tricuspid valve in 1. Two cases, reported

<table>
<thead>
<tr>
<th>No</th>
<th>Ref.</th>
<th>Age</th>
<th>Sex</th>
<th>Valve</th>
<th>Risk factors</th>
<th>Symptoms and signs</th>
<th>Treatment</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1</td>
<td>PR</td>
<td>53</td>
<td>M</td>
<td>A</td>
<td>DM, dental procedure</td>
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<td>AmB (4051mg) + AVR</td>
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<td>2</td>
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<td>72</td>
<td>M</td>
<td>T</td>
<td>Post-operation hyperalimentation, CVC</td>
<td>Low grade fever, murmur, dyspnea, ischemic leg</td>
<td>AmB (3022mg)--&gt; fluconazole</td>
<td>Survived</td>
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<tr>
<td>3</td>
<td>(6)</td>
<td>29</td>
<td>F</td>
<td>A</td>
<td>HIV, intravenous drug abuser</td>
<td>High fever, intermittent claudication</td>
<td>AmB (&lt;1000mg) + embolectomy + AVR--&gt; fluconazole (800mg/d) 6 weeks</td>
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<tr>
<td>4</td>
<td>(7)</td>
<td>ND</td>
<td>ND</td>
<td>L</td>
<td>Hematologic malignancy</td>
<td>ND</td>
<td>AmB--&gt; fluconazole</td>
<td>Survived</td>
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<tr>
<td>5</td>
<td>(7)</td>
<td>ND</td>
<td>ND</td>
<td>R</td>
<td>Hematologic malignancy</td>
<td>ND</td>
<td>Fluconazole + G-CSF</td>
<td>Survived</td>
</tr>
<tr>
<td>6</td>
<td>(8)</td>
<td>35</td>
<td>F</td>
<td>M</td>
<td>Hematologic malignancy, Bone marrow transplantation, bacteremia history, Hickman catheter</td>
<td>Poor intake, mild fever, anorexia, weight loss</td>
<td>AmB (2000mg) + MVR--&gt; fluconazole (200mg/d) 4 months</td>
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<tr>
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<td>26</td>
<td>M</td>
<td>A</td>
<td>Intravenous drug abuser</td>
<td>Ischemic leg</td>
<td>AmB (1400mg) + 5-FC + AVR + embolectomy</td>
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<td>56</td>
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<td>M</td>
<td>ND</td>
<td>ND</td>
<td>Fluconazole (400mg/d) + miconazole + MVR</td>
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<tr>
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<td>Fever, ischemic leg</td>
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<tr>
<td>10</td>
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<td>F</td>
<td>M</td>
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<td>ND</td>
<td>AmB (1120mg) + MVR</td>
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<tr>
<td>11</td>
<td>(13)</td>
<td>30</td>
<td>M</td>
<td>A</td>
<td>Intravenous drug abuser</td>
<td>Fever, fatigue, dyspnea, weight loss, palmer petechiae</td>
<td>AmB (1340mg) + 5-FC + AVR</td>
<td>Survived</td>
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<tr>
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<td>(14)</td>
<td>43</td>
<td>M</td>
<td>M</td>
<td>Intravenous drug abuser</td>
<td>Weakness, cellulitis of leg, joint pain</td>
<td>AmB (&gt;1720mg) + 5-FC</td>
<td>Survived</td>
</tr>
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</table>

No: Patient number; Ref.: reference; PR: presented patient; ND: not described; M: male; F: female; DM: diabetes mellitus; CVC: central venous catheter; HIV: human immunodeficiency virus infection; AmB: amphotericin B; AVR: aortic valve replacement; GM-CSF: granulocyte-macrophage colony-stimulating factor; 5-FC: 5-fluorocytosine; MVR: mitral valve replacement.
by Girmenia C(7), did not mention which valve was involved. Of the clinical manifestations of the other 11 reported cases, fever and ischemic phenomenon of lower legs were common. Concerning the therapeutic regimen of the other 11 reported cases, amphotericin B was the most commonly used antifungal agent, followed by fluconazole, 5-fluorocytosine and miconazole. Cardiac valve replacement and/or embolectomy were the common surgical interventions. The prognosis included survival in 10 and death in 1.

**DISCUSSION**

In total, there were 12 cases of NVE caused by *C. parapsilosis* infection in this study. Our patient (Case 1) did not have history of drug abuse, malignant hematological diseases and central venous catheterization but he had DM and recent dental manipulation. These preceding events may have played an important role in the development of *C. parapsilosis* NVE since Candida species are frequently found in the oral cavity of diabetic patients (51%) and 0.5% of implicated Candida species are *C. parapsilosis*(15).

In this study, aortic valve, mitral valve and tricuspid valve were the commonly involved cardiac valves. This relative frequency of cardiac-valve involvement for these cases of *C. parapsilosis* NVE is consistent with that demonstrated for overall fungal endocarditis(2). Our patient (Case 1) presented with cerebrovascular stroke which was not mentioned in any of the other 11 reported *C. parapsilosis* NVE cases(5-14). Because of the concurrence of DM, fungemia and infective endocarditis, the pathogenesis of multiple cerebral infarcts of our patient may be complicated. An embolic process may be a possible component of the pathogenesis. However, infection-related atherosclerosis may be another component, and this association has been noted in both cardiovascular and cerebrovascular insult caused by infectious disorders(16-19).

The therapeutic strategies for fungal endocarditis are administration of an antifungal agent and valve replacement(20). For our patient, susceptibility to both antifungal (amphotericin B, fluconazole) agents was demonstrated for the isolated strain of *C. parapsilosis*, however, the MFC value for fluconazole was much higher. All 10 of the reviewed patients who received amphotericin B therapy survived. The mortality rate for *C. parapsilosis* NVE was lower than the mortality rate of overall fungal endocarditis (41-43%)(13). However, the number of cases in this study was too small to achieve a statistical significance. Further large-scale studies are needed to produce conclusive statistical verification.

**REFERENCES**


