

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

Acta Neurol Taiwan 2004;13:131-135

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 infection^(1,2). Cerebrovascular symptoms have been noted for 17% of

patients with fungal endocarditis⁽²⁾. Rubinstein et al.⁽³⁾ reported 5 cases of *C. parapsilosis* native valve 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 died⁽²⁾. Herein we report a case of *C. parapsilosis* NVE with concomitant stroke, and review relevant cases in the literature.

From the Departments of ¹Neurology, ²Radiology, and ³Clinical Pathology, Chang Gung Memorial Hospital-Kaohsiung, Kaohsiung, Taiwan.

Received June 7, 2004. Revised July 14, 2004.

Accepted August 16, 2004.

Reprint requests and correspondence to: Wen-Neng Chang, MD. Department of Neurology, Chang Gung Memorial Hospital, Kaohsiung, Kaohsiung, Taiwan.

E-mail: cwenneng@ms19.hinet.net

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-

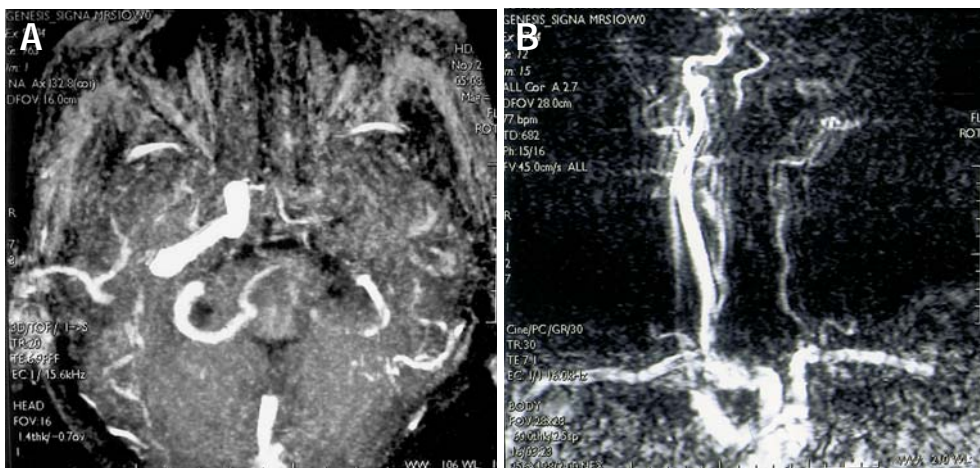


Figure 1. MR angiography. (A) and (B) show the occlusion of left common carotid artery

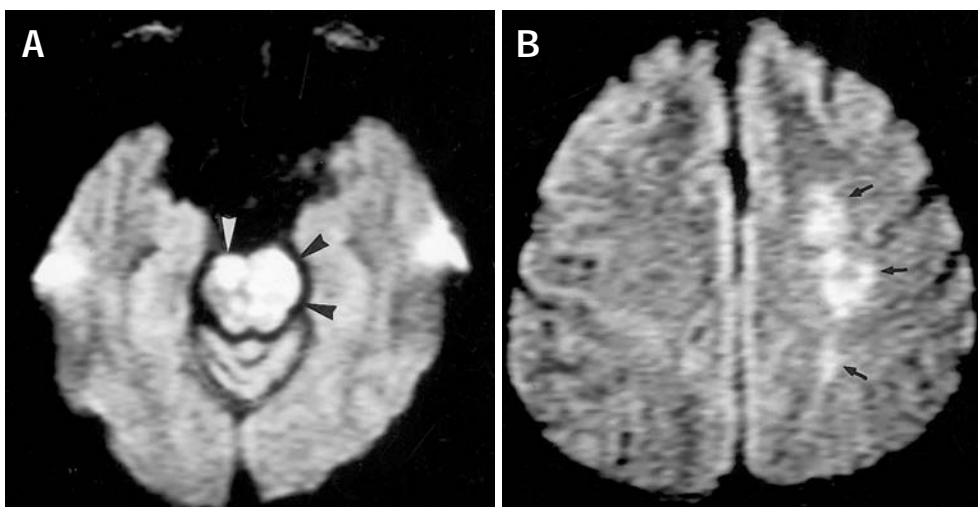


Figure 2. Diffusion-weighted imaging. (A) shows infarct of the pons (arrowheads) and (B) shows infarct of the territory of left middle cerebral artery branch (arrowheads)

Table. Clinical data of the 12 patients with native valvular endocarditis due to *Candida parapsilosis* infection

No	Ref.	Age	Sex	Valve	Risk factors	Symptoms and signs	Treatment	Outcome
1	PR	53	M	A	DM, dental procedure	Stroke	AmB (4051mg) + AVR	Survived
2	(5)	72	M	T	Post-operation hyperalimentation, CVC	Low grade fever, murmur, dyspnea, ischemic leg	AmB (3022mg)--> fluconazole	Survived
3	(6)	29	F	A	HIV, intravenous drug abuser	High fever, intermittent claudication	AmB (<1000mg) + embolectomy + AVR--> fluconazole (800mg/d) 6 weeks	Survived
4	(7)	ND	ND	L	Hematologic malignancy	ND	AmB--> fluconazole	Survived
5	(7)	ND	ND	R	Hematologic malignancy	ND	Fluconazole + G-CSF	Survived
6	(8)	35	F	M	Hematologic malignancy, Bone marrow transplantation, bacteremia history, Hickman catheter	Poor intake, mild fever, anorexia, weight loss	AmB (2000mg) + MVR--> fluconazole (200mg/d) 4 months	Survived
7	(9)	26	M	A	Intravenous drug abuser	Ischemic leg	AmB (1400mg) + 5-FC + AVR + embolectomy	Survived
8	(10)	56	M	M	ND	ND	Fluconazole (400mg/d) + miconazole + MVR	Died
9	(11)	37	ND	A	Intravenous drug abuser	Fever, ischemic leg	AmB (2100mg) + 5-FC + embolectomy + AVR	Survived
10	(12)	36	F	M	Intravenous drug abuser	ND	AmB (1120mg) + MVR	Survived
11	(13)	30	M	A	Intravenous drug abuser	Fever, fatigue, dyspnea, weight loss, palmer petechiae	AmB (1340mg) + 5-FC + AVR	Survived
12	(14)	43	M	M	Intravenous drug abuser	Weakness, cellulitis of leg, joint pain	AmB (>1720mg) + 5-FC	Survived

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.

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⁽⁵⁻¹⁴⁾. 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 hematological 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

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%)^(1,2). 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

1. Pierrotti LC, Baddour LM. Fungal endocarditis, 1995-2000. *Chest* 2002;122:302-10.
2. Ellis ME, Al-Abdely H, Sandridge A, et al. Fungal endocarditis: evidence in the world literature, 1965-1995. *Clin Infect Dis* 2001;32:50-62.
3. Rubinstein E, Noriega ER, Simberkoff MS, et al. Fungal endocarditis: analysis of 24 cases and review of the literature. *Medicine (Baltimore)* 1975;54:331-44.
4. National Committee for Clinical Laboratory Standards. Reference method for broth dilution antifungal susceptibility testing of yeasts. Approved standard. Document M-27 A. Wayne PA: NCCLS. 1997.
5. Saito Y, Takahashi M, Sato A, et al. Isolated tricuspid valve endocarditis due to *Candida parapsilosis* associated with long-term central venous catheter implantation. *Intern Med* 2001;40:403-4.
6. Veraldi GF, Guglielmi A, Genna M, et al. Occlusion of the common iliac artery secondary of fungal endocarditis: report of a case. *Surg Today* 2000;30:291-3.
7. Girmenia C, Martino P, De Bernardis F, et al. Rising incidence of *Candida parapsilosis* fungemia in patients with hematologic malignancies: clinical aspects, predisposing factors, and differential pathogenicity of the causative strains. *Clin Infect Dis* 1996;23:506-14.
8. Cancelas JA, Lopez J, Cabezudo E, et al. Native valve endocarditis due to *Candida parapsilosis*: a late complication after bone marrow transplantation-related fungemia. *Bone Marrow Transplant* 1994;13:333-4.
9. Lozano P, Flores D, Blanes I, et al. Acute lower limb ischemia complicating endocarditis due to *Candida parapsilosis* in a drug abuser. *Ann Vasc Surg* 1994;8:591-4.
10. Senba M, Watanabe K, Yoshida K, et al. Endocarditis caused by *Candida parapsilosis*. *Southeast Asian J Trop*

- Med Public Health 1992;23:138-41.
11. Blinkhorn RJ Jr, Eckhauser ML, Snow N. Saddle embolism complicating *Candida parapsilosis* aortic valve endocarditis: cure with aortic valve replacement and prompt extraction of multiple mycotic emboli. *J Vasc Surg* 1992;16:128-9.
 12. Samelson LE, Lerner SA, Resnekov L, et al. Relapse of *Candida parapsilosis* endocarditis after long term suppression with flucytosin: retreatment with valve replacement and ketoconazole. *Ann Intern Med* 1980;93:838-9.
 13. Martin E, Pancoast SJ, Neu HC *Candida parapsilosis* endocarditis: medical and surgical cure. *Ann Intern Med* 1979; 91:870-1.
 14. Mayrer AR, Brown A, Weintraub RA, et al. Successful medical therapy for endocarditis due to *Candida parapsilosis*: a clinical and epidemiologic study. *Chest* 1978;73:546-9.
 15. Fisher BM, Lamey PJ, Samaranyake LP, et al. Carriage of *Candida* species in the oral cavity in diabetic patients: relationship to glycaemic control. *J Oral Pathol* 1987;16:282-4.
 16. Vercellotti GM. Microbes, inflammation and atherosclerosis: will old pathology lesions guide new therapies? *Trans Am Clin Climatol Assoc* 2001;112:215-22.
 17. Caligiuri G. Role of the immune response in atherosclerosis and acute coronary syndromes. *MS Md Sci (Paris)* 2004; 20:175-81.
 18. Hosoglu S, Ayaz C, Geyik MF, et al. Tuberculous meningitis in adults: an eleven-year review. *Int J Tuberc Lung Dis* 1998;2:553-7.
 19. Lan SH, Chang WN, Lu CH, et al. Cerebral infarction in chronic meningitis: a comparison of tuberculous meningitis and cryptococcal meningitis. *QJM* 2001;94:247-53.
 20. Bayer AS, Bolger AF, Taubert KA, et al. Diagnosis and management of infective endocarditis and its complications. *Circulation* 1998;98:2936-48.