

# Medical therapy of a left-sided native valve endocarditis with neurologic sequela

Choon S. Ng, MBBS, Shawal Mohamad, MBChB BAO, MMED, Oteh Maskon, MRCPI, MSc Cardiology.

## ABSTRACT

يمكن أن يصاحب التهاب الشغاف عدد كبير من العلامات والأعراض. ويعد الاضطراب العقلي الحاد المصاحب لهذه الحالة من الأمور النادرة، والتي يمكن أن يصاحبها اختلال عصبي وهذا كله يحاكي أعراض السكتة الدماغية وذلك لدى المرضى الشباب. نستعرض في هذا المقال حالة مريض يبلغ من العمر 33 عاما وقد أتى إلى المستشفى وهو يعاني من شلل حاد في الشق الأيمن واضطراب عقلي وذلك بعد أسبوعين من استئصال أحد أسنانه. ولقد تطابقت نتائج الأشعة الطبقيّة مع نتائج التصوير بالرنين المغناطيسي والتي أشارت إلى ظهور احتشاء جديد في الشرايين الدماغية الأمامية وكذلك الشرايين اليسرى الوسطى. فيما كشف تخطيط القلب عن وجود نمو جرثومي في تفرعات الصمام المترالي الخلفي. وأظهر اختبار عينة الدم مدى حساسية المكورات العنقودية-بيتا الانحلالية لمادة البنسلين. ولذلك فقد قمنا بإعطاء المريض مضاد جنتاميسين لمدة أسبوعين عبر الوريد، بالإضافة مضاد بنزيل البنسلين لمدة 6 أسابيع عبر الوريد أيضا. ونلقى الضوء في هذا المقال على أهمية أخذ التهاب الشغاف بعين الاعتبار لدى المرضى الشباب الذين يشكون من اضطرابات عصبية بعد استئصال الأسنان.

Infective endocarditis could present with a plethora of signs and symptoms. Among the rarity of its presentation is acute confusion associated with neurological deficits, mimicking stroke especially in the young population. We report a case of a 33-year-old young man with acute right-sided hemiparesis and confusion 2 weeks after tooth extraction. The brain CT and MRI was consistent with new infarction on the left middle and anterior cerebral arteries' territory. Echocardiography unveiled the existence of posterior mitral valve leaflet vegetation. Blood culture grew Group B beta-haemolytic *Streptococcus*, sensitive to penicillin. Two weeks of intravenous gentamicin with 6 weeks of intravenous benzylpenicillin were administered. In this case report, we highlight the importance of recognition of infective endocarditis in a young patient presenting with cerebrovascular accident following tooth extraction.

*Saudi Med J* 2015; Vol. 36 (6): 743-746  
doi: 10.15537/smj.2015.6.11420

From the Department of Medicine, National University of Malaysia Medical Center, Kuala Lumpur, Malaysia.

Received 5th February 2015. Accepted 30th March 2015.

Address correspondence and reprint request to: Dr. Choon S. Ng, Department of Medicine, National University of Malaysia Medical Center, Kuala Lumpur, Malaysia. E-mail: csng2009@gmail.com

A wide variety of organisms have been attributed to infections of native heart valves. Among them are *staphylococci*, *streptococci*, and the group of *Haemophilus*, *Aggregatibacter* (previously *Actinobacillus*), *Cardiobacterium*, *Eikenella corrodens*, *Kingella* (HACEK) organisms. Aortic or mitral valves (left-sided) accounts for the vast majority of endocarditis cases in non-intravenous drug users. Right sided infective endocarditis contributes 5-10% of all cases of endocarditis, usually among intravenous drug users.<sup>1</sup> Emboli from left-sided valvular vegetation can become dislodged or fragmented into the brain via systemic circulation, resulting in neurological complications. In contrast with the right sided embolus, the right sided infective endocarditis may cause embolic phenomenon due to preexisting congenital heart diseases such as patent foramen ovale, atrial septal defect, or ventricular septal defect. In this case report, we highlight the importance of recognition of infective endocarditis with an embolic stroke in a young confused patient with normal cardiac valve following a simple dental extraction procedure.

**Case Report.** A 33-year-old man presented to the University Kebangsaan Malaysia Medical Center, Kuala Lumpur, Malaysia, with acute confusion. He was last seen at 9 pm the day prior and became less responsive at 11 am on the day of admission. He was living alone and was noted by paramedics semiconscious (Glasgow Coma Scale of 10/15: eye opening 3, verbal response 2 and motor response 5 [E3V2M5]) with urinary incontinence. No fits noted. Further, history obtained from family members revealed that he had intermittent onset of fever for a week, associated with upper

respiratory tract symptoms. He was treated empirically with lung infection, and was given intravenous Ceftriaxone (2-days duration) before discharge with an oral antibiotic (ceftibuten) of 5-day duration. Two weeks prior to the admission, he underwent a tooth extraction. Further history obtained from family members revealed that he had history of consuming ecstasy pills as well as visiting prostitutes (high risk behaviors). He was the youngest among 3 siblings, single, living alone, and working as a lorry driver and water dispenser. There was no significant childhood or family histories.

Initial physical examination revealed blood pressure of 123/72 mm Hg, heart rate of 82 beats per minute, temperature of 39.3°C, with oxygen saturation under room air of 100%. No Kussmaul's breathing was noted. Pupils were 3 mm equal reactive bilaterally. Neck stiffness was present. However, other signs of meningism (Kernig's sign and Brudzinski's sign) were absent. There was an expressive dysphasia. Right sided pyramidal signs were present as evidenced by right facial sagging, hyper-reflexia, and upgoing plantar response, with power of 0/5 over right upper and lower limbs. Cardiovascular examination revealed presence of both normal first and second heart sounds with an apical pansystolic murmur (grade 3/6). Other systemic reviews were normal. No malar rashes were noted, and he had neither peripheral signs of infective endocarditis nor heart failure.

The result of the dextrostix was 11.6 mmol/l (normal range [NR] 4.4 - 6.1 mmol/l). Blood investigations revealed the leucocytosis (white blood count = 20.7 x10<sup>9</sup>/L [NR: 4.1 - 11.4 x10<sup>9</sup>/L]) with neutrophil predominant (88.8%). There was normocytic normochromic anemia (hemoglobin 10.7x10<sup>9</sup>/L [NR: 11.6 - 15.1 x10<sup>9</sup>/L], mean cell volume 87.7 fl [NR: 80.6 - 95.5 fl], and mean corpuscular hemoglobin concentration 32 g/dL [NR: 31.9 - 35.3 g/dL]), but no evidence of bleeding. The platelet count was normal (297x10<sup>9</sup>/L [NR: 171 - 399x10<sup>9</sup>/L]). Renal function test was otherwise, normal. The acute phase reactant was elevated (C-reactive protein of 39.53 mg/dL [NR: <0.5 mg/dL]). Retroviral and hepatitis screenings were negative. Magnetic resonance imaging of the brain demonstrated high signal intensity involving the left middle cerebral artery territory (Figure 1). No hydrocephalus or midline shift.

**Disclosure.** Authors have no conflict of interests, and the work was not supported or funded by any drug company.

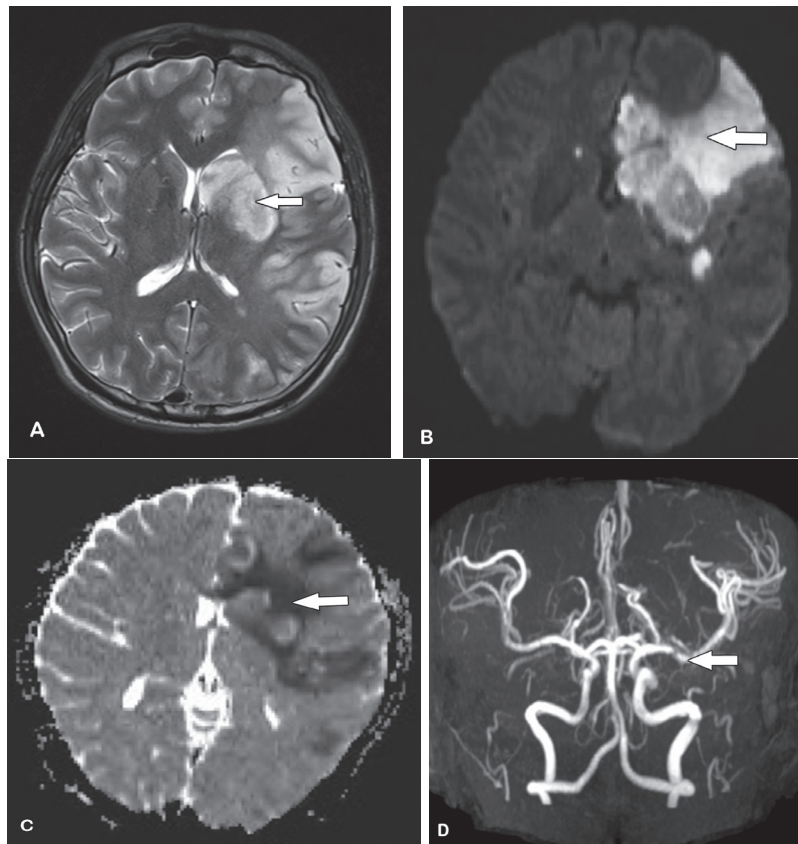
No thrombus was seen within the venous sinuses. Transthoracic echocardiography revealed the presence of an oscillating mass of 3.4 x 1.4 cm at the posterior mitral valve leaflet (Figures 2A & 2B), with mild to moderate mitral regurgitation and mild tricuspid regurgitation (maximum tricuspid regurgitation gradient 22 mm Hg), but no mitral stenosis and normal aortic valve. No regional wall motion abnormality was noted. The ejection fraction was 70%. Cerebrospinal fluid analysis was carried out to exclude meningeal pyogenic infection from septic emboli. It unveiled the absence of polymorphs or lymphocytes, normal glucose level, but slightly raised protein content (586 mg/L). Opening pressure was 350 mm H<sub>2</sub>O, with negative Indian ink staining and acid fast bacilli smear. Blood culture was positive for group B *beta-haemolytic Streptococcus*, which was sensitive to both penicillin (minimal inhibitory concentration: 0.047 µg/ml) and ampicillin. However, no growth was found in culture of the cerebrospinal fluid. Tuberculin skin test was negative.

A diagnosis of acute embolic stroke secondary to left-sided (mitral valve) endocarditis was reached. Cardiothoracic consultation was sought, but surgical intervention was not warranted, and he was treated conservatively. He was given intravenous gentamicin 160 mg twice daily for 2 weeks and was planned for intravenous benzylpenicillin 3 mega international units 6 times per day for a total duration of 6 weeks. No nephrotoxicity was noted throughout the treatment. Repeated transthoracic echocardiography one month post-treatment revealed complete resolution of vegetation, with only mild mitral regurgitation but no other valvular lesions. He was able to sit up by himself and feed himself, although his speech has not yet fully recovered.

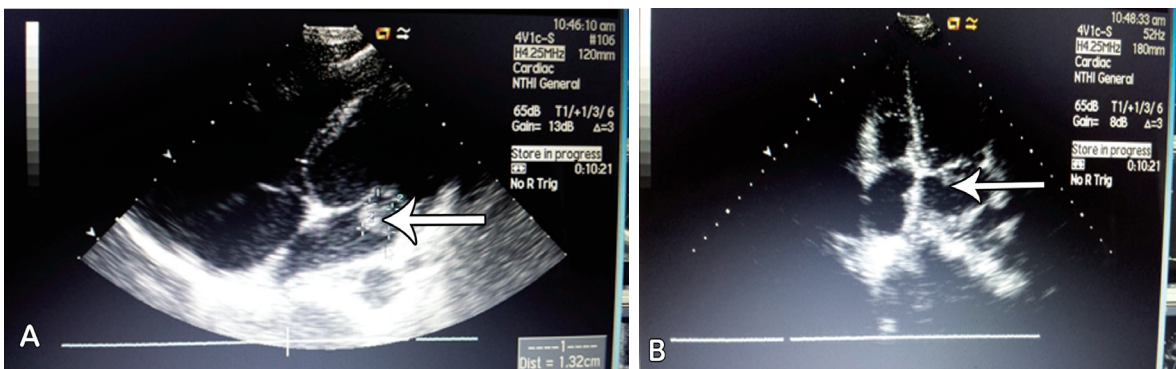
**Discussion.** This patient had one major and 3 minor criteria, which fulfilled the Duke criteria for infective endocarditis. These include positive echocardiogram (major criteria), fever of 39.3°C (minor criteria), single positive blood culture (minor criteria), and infarction (minor criteria). Up to 30% of the incidence of systemic emboli has been reported in cases of infective endocarditis,<sup>1</sup> commonly involving the central nervous system (CNS). Previous studies<sup>2,3</sup> reported a 10% stroke rate. Such neurologic sequela mainly affects the middle cerebral artery (>40%).<sup>4</sup> It results in considerable morbidity and mortality with health cost implications. Other less common CNS involvements of infective endocarditis include hemorrhages, aneurysms, meningitis, abscess, or even silent brain emboli. Therefore, MRI is advocated as a crucial imaging modality in detecting more cases of

such CNS emboli;<sup>5</sup> particularly, left-sided infective endocarditis. A prospective study in Sweden<sup>6</sup> has shown that the cerebrovascular complications arise by 65% of the patients with left-sided infective endocarditis. One of the major highlight in this case illustration is the history of tooth extraction 2 weeks prior to the

current presentation. This raises the concern of whether endocarditis prophylaxis would be beneficial in this patient without any underlying cardiac conditions. The American Heart Association and American College of Cardiology recommendation in 2007,<sup>7</sup> advocates the use of antibiotic prophylaxis for high risk patients



**Figure 1** - Magnetic resonance imaging of brain. A) T2-weighted axial view depicting hyper-intensities in the left middle cerebral artery territory. B) The diffusion weighted image and C) the apparent diffusion coefficient map showing restricted diffusion indicating recent infarct. D) Magnetic resonance angiography showing focal filling narrowing at M1 segment of left middle cerebral artery suggesting stenosis.



**Figure 2** - Transthoracic echocardiography carried out on day 3 of admission revealed the presence of a large vegetation at the posterior mitral valve leaflets, both on A) parasternal long-axis view and B) apical view.

undergoing high risk dental procedures (including dental extraction). High risk is defined as those patients with underlying cardiac conditions associated with the highest risk of adverse outcome from infective endocarditis. Conducting trials to answer such doubts of antibiotic prophylaxis in those undergoing high risk dental procedures (like in this case), but do not correspond to the high risk group would sound reasonable but unethical. The benefit exists for this healthy group, but not enough to warrant its routine use as identified in the 2012 Cochrane Database of Systematic Reviews article.<sup>8</sup>

The successfully established medical therapy of our patient is another highlight of this case. Although in our case, the evidence of septic emboli with large vegetation may warrant surgical referral, nonetheless, medical therapy was opted. The fact that this patient recovered with such therapy could also be partly due to the favorable outcome of the younger age onset nature of such stroke from infective endocarditis.<sup>9</sup> In the our, intravenous beta-lactam (penicillin-G) was combined with aminoglycoside (gentamicin) to medically treat a virulent organism (group B *Streptococcus*), and low minimal inhibitory concentration (susceptible to penicillin). Such combination is aimed to achieve synergism, as demonstrated in a previous study<sup>10</sup> of 179 group B streptococcal isolates with effective bacterial clearance at 6-hour minimal bactericidal concentration.

We reported a case of group B streptococcal left-sided endocarditis complicated with an embolic stroke, which was successfully managed medically. It also underlined the importance of recognition of embolic stroke as part of our differentials in a young man presenting with acute confusion. This could lead to early treatment and subsequent prevention of the high morbidity and high mortality that it carries.

**Acknowledgment.** We gratefully acknowledge Associate Professor Dr Shahizon A. Mukari for reviewing the Figures for their clarity and correctness.

## References

1. Chan KL, Embil J, Salehian O. Systemic embolism in endocarditis: incidence, risk factors, clinical significance, and treatment strategies. In: Chan KL, Embil J, editors. Endocarditis: diagnosis and management. London (UK): Springer-Verlag; 2006. p. 229-240.
2. Thuny F, Avierinos JF, Tribouilloy C, Giorgi R, Casalta JP, Milandre L, et al. Impact of cerebrovascular complications on mortality and neurologic outcome during infective endocarditis: a prospective multicentre study. *Eur Heart J* 2007; 28: 1155-1161.
3. Anderson DJ, Goldstein LB, Wilkinson WE, Corey GR, Cabell CH, Sanders LL, et al. Stroke location, characterization, severity, and outcome in mitral vs. aortic valve endocarditis. *Neurology* 2003; 61: 1341-1346.
4. Sonnevile R, Mourvillier B, Bouadma L, Wolff M. Management of neurological complications of infective endocarditis in ICU patients. *Ann Intensive Care* 2011; 1: 10.
5. Cooper HA, Thompson EC, Lauren R, Fuisz A, Mark AS, Lin M, et al. Subclinical brain embolization in left-sided infective endocarditis: results from the evaluation by MRI of the brains of patients with left-sided intracardiac solid masses (EMBOLISM) pilot study. *Circulation* 2009; 120: 585-591.
6. Snygg-Martin U, Gustafsson L, Rosengren L, Alsiö A, Ackerholm P, Andersson R, et al. Cerebrovascular complications in patients with left-sided infective endocarditis are common: a prospective study using magnetic resonance imaging and neurochemical brain damage markers. *Clin Infect Dis* 2008; 47: 23-30.
7. Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2007; 116: 1736-1754.
8. Lodi G, Figini L, Sardella A, Carrassi A, Del Fabbro M, Furness S. Antibiotics to prevent complications following tooth extractions. *Cochrane Database Syst Rev* 2012; 11: CD003811.
9. Ruttman E, Willeit J, Ulmer H, Chevtchik O, Hofer D, Poewe W, et al. Neurological outcome of septic cardioembolic stroke after infective endocarditis. *Stroke* 2006; 37: 2094-2099.
10. Baker CN, Thornsberry C, Facklam RR. Synergism, killing kinetics, and antimicrobial susceptibility of group A and B streptococci. *Antimicrob Agents Chemother* 1981; 19: 716-725.