Tri-valvular Nonbacterial Thrombotic Endocarditis Presenting as a Stroke in the Young

Miriam Angeline G. Antonio, MDa and Vincent B. Macalintal, MD, FPNAb

ABSTRACT

This is a case of a 44 year old single, Filipino, female who presented with dysarthria, left central facial paresis, left hemianopsia and left hemiparesis. Magnetic Resonance Imaging showed an acute infarction of the right posterior cerebral artery territory. 2d echo and transesophageal echocardiography were done and vegetations were observed on the mitral, aortic and tricuspid valves giving a diagnosis of endocarditis. With the absence of fever and negative blood cultures, infective endocarditis was less likely. On further workup, computed tomography scan of the abdomen showed a probable malignant ovarian mass. This finding led to a diagnosis of nonbacterial thrombotic endocarditis as the cause of the stroke. Endocarditis as a cause of an embolic event in the brain is uncommon and nonbacterial thrombotic endocarditis is rare. It commonly affects the left sided heart valves. Multivalvular involvement which includes the right sided heart valves are rarely reported. Nonbacterial thrombotic endocarditis has a high mortality so therefore early detection and management is crucial and can be life-saving.

INTRODUCTION

Stroke in the young is relatively uncommon and accounts for 3% of all stroke cases. Though rare in this age group, malignancy shows an increased stroke risk in young patients. In one study, 7% of young stroke patients were found to have an underlying cancer.¹ The mechanism by which a cancer patient is at an increased risk of stroke is an inherent hypercoagulable state. This setting can then lead to a rare condition that can also cause ischemic strokes in susceptible patients, and this is a nonbacterial thrombotic endocarditis. Nonbacterial thrombotic endocarditis is a non infectious endocarditis characterized by deposition of sterile vegetation consisting of fibrin and platelet aggregates. Left sided heart valves, namely the mitral and aortic, are commonly involved but in very rare cases, the right side may be involved as well.2

A thorough workup and a prompt diagnosis and treatment of this condition can

help improve the outcome in these patients. This report presents a case of nonbacterial thrombotic endocarditis in a newly diagnosed ovarian cancer patient who presented with an acute ischemic infarction. In this case, the mitral, aortic and tricuspid valves were affected.

CASE PRESENTATION

Our patient is a 44-year-old female, single, Filipino, works as a manager, with an unremarkable medical history. She is not on any maintenance medication or supplements, and has no history of fever, palpitations or chest pains. She is a non smoker, non alcoholic beverage drinker, and denies any illicit drug use. She has no history of pregnancies nor oral contraceptive use. She had left hemianopsia, left central facial paresis and left hemiparesis. Blood pressure was 120/80 mmHg, heart rate was 80 beats per minute. There was no documented fever. ECG was normal sinus rhythm. An MRI was done which showed an acute ischemic infarction in the right posterior cerebral

PhilJNeurol 21 ISSN 0117-3391

^aFourth Year Resident, Asian Hospital and Medical Center ^bConsultant, Asian Hospital and Medical Center

artery territory. She was initially started on antiplatelets. Hypercoagulable workup was requested, which included antiphospholipid syndrome panel, protein C and S, and homocysteine. Results were unremarkable. 2 D e c h o a n d T r a n s e s o p h a g e a l echocardiography were done which showed mitral, aortic and tricuspid valve vegetations.

Infective endocarditis was considered so she was started on Intravenous Penicillin. However, blood cultures turned out negative. Antibiotics and antiplatelets were still continued and she was discharged two weeks later with improvement of neurologic deficits. Transesophageal echocardiography was repeated two weeks later and it was noted that there was a decrease in the size of the vegetations, and the previously seen tricuspid valve vegetation was no longer appreciated.

A few weeks later, the patient was readmitted due to chest heaviness and shortness of breath. Chest Xray showed pleural effusion. Computed tomography of the abdomen revealed a large lobulated complex solid ovarian mass. She underwent exploratory laparotomy with tumor debulking. Biopsy of the mass was compatible with a high grade serous carcinoma.

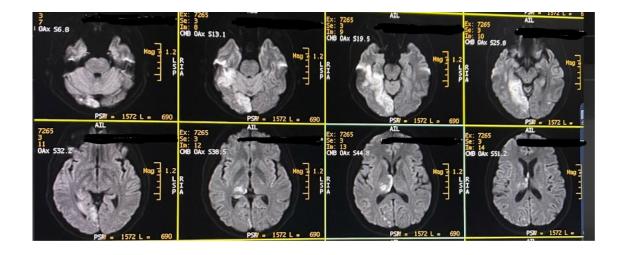
Now with a setting of an ovarian adenocarcinoma, a hypercoagulable state secondary to malignancy seems to be the probable cause of the valvular vegetations, leading to a diagnosis of nonbacterial thrombotic endocarditis.

The patient has undergone chemotherapy and is currently on Apixaban 5 mg/tablet, one tablet twice a day. A repeat 2D echocardiography was done four months after initiation of anticoagulation. Findings did not show the previously noted valvular vegetations.

DISCUSSION

This case describes a previously healthy female, newly diagnosed with ovarian cancer, who presented with an acute ischemic infarction secondary to a nonbacterial endocarditis as the initial presentation. Nonbacterial thrombotic endocarditis previously known as Marantic endocarditis is a rare non infectious endocarditis that usually involves the mitral and aortic valves. Vegetations consist of sterile fibrin and platelet aggregates.³ It is associated with advanced malignancy in 80% of cases, and

Figure 1. DWI of patient showing an acute infarct on the right thalamus, right temporoparietooccipital area. (Right posterior cerebral artery territory)



PhilJNeurol 22 ISSN 0117-3391

Figure 2. 2D echocardiography image showing (A) thickened mitral valves, (B) aortic valve, (C) Transesophageal echocardiography image showing (C) thickened tricuspid valves (D) echodense structure in the right atrium suggestive of a thrombus or a vegetation.





autoimmune diseases such as systemic lupus erythematosus and antiphospholipid antibody syndrome. Mulitivalvular involvement is rarely reported. As of this writing, only six cases of multivalvular non thromobitc endocarditis were reported, three of which were diagnosed through autopsy. The others were seen through a transesophageal echocardiography.² In our patient, through transesophageal echocardiography, she was found to have vegetations in the mitral, aortic and tricuspid valves.

This condition is usually found postmortem with a rate of 0.9 - 1.6% in an autopsy series.⁴ Patients with nonbacterial thrombotic endocarditis are usually asymptomatic until an embolic phenomenon occurs. Common sites of these embolic events are the liver, kidney and extremities but most frequently, the central nervous system. Strokes can even be the presenting symptom.⁵

In a recent study, it was found that stroke patients with cancer related nonbacterial thrombotic endocarditis have a high risk of recurrent stroke events and mortality during a 6 month follow up. 21.6% of patients included in the study had stroke recurrence.⁶

Negative blood cultures, and pathologic finding of vegetations through echocardiography and transesophageal echocardiography are essential to make the diagnosis of nonbacterial thrombotic endocarditis. Because of the high mortality, early detection and management is crucial. Management is with lifelong systemic anticoagulation and treatment of the underlying condition.

CONCLUSION

In a young patient with an unremarkable medical history presenting with an acute ischemic infarction, investigating the cause can be a challenge. An underlying malignancy should also be considered as part of the workup for stroke in the young, specifically for a hypercoagulable state. Early diagnosis and treatment may be life saving and can also improve the patient's quality of life.

REFERENCES

- Stack CA, Cole JW. The Clinical Approach to Stroke in Young Adults. In: Dehkharghani S, editor. Stroke [Internet]. Brisbane (AU): Exon Publications; 2021 Jun 18. Chapter 3. PMID: 34279884.
- Lee MH, Tsai WC, Su HM, Hsu PC. Nonbacterial thrombotic endocarditis in multiple heart valves. Kaohsiung J Med Sci. 2020 Mar;36(3):220-221. doi: 10.1002/kjm2.12151. Epub 2019 Nov 11. PMID: 31710414.
- 3. Kuipers RS, Berghuis MAT, Ogilvie AC, van Wissen SA, Riezebos RK. Non-bacterial thrombotic endocarditis manifested by ventricular fibrillation in a patient with low grade ovarian carcinoma: case report and literature review. Eur Heart J Case Rep. 2021 Apr 21;5(4):ytab120. doi: 10.1093/ehjcr/ytab120. PMID: 34109290; PMCID:PMC8183660.
- 4. Grecu N, Tiu C, Terecoasa E, Bajenaru O. Endocarditis and stroke. Maedica (Bucur). 2014 Dec;9(4):375-81. PMID: 25705308; PMCID: PMC4316883.
- 5. Zmaili MA, Alzubi JM, Kocyigit D, Bansal A, Samra GS, Grimm R, Griffin BP, Xu B. A Contemporary 20-Year Cleveland Clinic Experience of Nonbacterial Thrombotic Endocarditis: Etiology, Echocardiographic Imaging, Management, and Outcomes. Am J Med. 2021 Mar;134(3):361-369. doi: 10.1016/j.amjmed.2020.06.047. Epub 2020 Aug 19. PMID: 32827467.
- 6. Yoo J, Choi JK, Kim YD, Nam HS, Park H, Lee HS, Heo JH. Outcome of Stroke Patients with Cancer and Nonbacterial Thrombotic Endocarditis. J Stroke. 2020 May;22(2):245-253. doi: 10.5853/jos.2020.00619. Epub 2020 May 31. PMID:32635688; PMCID: PMC7341006.
- Toyoshima H, Nakanura B, Tanigawa M, Tanaka H, Nakanishi Y, Sakabe S. Nonbacterial thrombotic endocarditis

- with cryptogenic stroke. Clin Case Rep. 2021 Sep 15;9(9):e04833. doi: 10.1002/ccr3.4833. PMID: 34552744; PMCID: PMC8443433
- 8. Deppisch LM, Fayemi AO. Non-bacterial thrombotic endocarditis: clinicopathologic correlations. Am Heart J. 1976 Dec;92(6):723-9. doi: 10.1016/ s0002-8703(76)80008-7. PMID: 998478.