

A Case Report on Non-Bacterial Endocarditis in a Young Lady with Metastatic Colon Cancer

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1. Abstract

Non-bacterial thrombotic endocarditis (NBTE) presented a diagnostic dilemma in a 54-year-old woman with metastatic colon cancer. A large mass on the tricuspid valve initially suggested tumoral invasion. However, prompt anticoagulation led to complete resolution, indicating NBTE. This case highlights the challenges of differentiating NBTE from metastatic disease in high-risk patients. While transthoracic and transesophageal echocardiography (TTE and TEE) raised suspicion of tumor spread, anticoagulant therapy achieved successful resolution, potentially offering an alternative management approach. The case report proposes considering novel oral anticoagulants (NOACs) like apixaban for such scenarios.

2. Introduction

Endocarditis is defined as the inflammation of the endocardium, the lining of the cardiac chambers and valves, and is characterized by vegetations, most commonly caused by infection with bacteria or fungi. Non-infective endocarditis, also known as non-bacterial thrombotic endocarditis (NBTE) or aseptic endocarditis, refers to a rare condition characterized by the formation of sterile vegetations. Without treatment, these can lead to valvular dysfunction, heart failure, systemic embolism and death.[1] Marantic or non-bacterial thrombotic endocarditis involves the deposition of large, friable, sterile vegetations predominantly on the cardiac valves. These vegetations have been associated with disseminated intravascular coagulation and systemic embolization.[2] NBTE differs from culture-negative endocarditis, which refers to infectious ori-

gins based on clinical history and symptomatology that have not been readily identified or difficult to culture. It is most commonly a postmortem finding (autopsy series 0.9 – 1.6%) and seen in advanced malignancy.[3] NBTE vegetations are most frequently left sided, with two-thirds involving the mitral valve and the remainder occurring on the aortic valve. Rarely, both valves can be affected. Due to the small size of the many vegetations seen in NBTE, pathology may frequently escape detection by TTE. In patients in whom there is a high suspicion of NBTE in the setting of an unclear TTE scan, a TEE is indicated.[4] Based on autopsy reports, patients with an underlying malignancy are six times more likely to develop NBTE compared to the general population (1.25% vs. 0.2%). Solid tumor cancers are associated more commonly with NBTE, with mucin-secreting adenocarcinomas having the highest observed rates.[3]

3. Case Presentation

a 54-year-old female presented with a 15-day history of dyspnea, hemoptysis, pleuritic chest pain and fatigue. She had a history of diabetes mellitus type 2, hyperlipidemia, and metastatic colon cancer (to liver and lung). She was on chemotherapy regimen for malignancy from 2 years ago and the last session of chemotherapy was 20-day ago. Her sister had colon cancer, too. She had porta-cath in right subclavian vein. The physical exam was normal, with the exception of sinus tachycardia and pallor. Empirical treatment was start (include levofloxacin and enoxaparin).

According to clinical signs and symptoms we performed TTE for

cardiac cause of dyspnea. We found a large mobile mass on Tricuspid valve (Figure 1). Our first differential diagnosis were tumor metastatic invasion and infective endocarditis and thrombus. Despite the high level of inflammatory markers, she did not have other signs and symptoms suggestive for infective endocarditis and blood culture was negative for three times. other laboratory findings were as follows:

Trop-I= neg, LDH=842, ESR=125, Alb=3.3, D-dimer= 2241

Regarding the TEE finding (Figure 2) and life expectancy more than 6 month, our multidisciplinary team (cardiologist, cardioseer-geon, oncologist, Infectious disease specialist) decided that operation is the best choice for our patient. Enoxaparin was held and

heparin started. Few days later, before the scheduled operation, TTE was repeated (Figure 3) for more detailed information, but the mass was disappeared. For pulmonary embolism assessment, pulmonary CT angiography was done and it was negative (Figure 4). Therefore, metastatic invasion of tricuspid valve was excluded and our plan changed to continuing anticoagulation therapy with heparin.

Unfortunately, the platelet count was low (Plt=24000). Thus, we could not exclude the HIT (heparin induce thrombocytopenia), heparin was stopped and apixaban replaced. Platelet count increased gradually and After 3 days, the patient underwent TTE again and fortunately the tricuspid valve vegetation completely resolved. We continued apixaban with a lifelong intention and followed the patient for 1 year without any thrombotic or bleeding event.

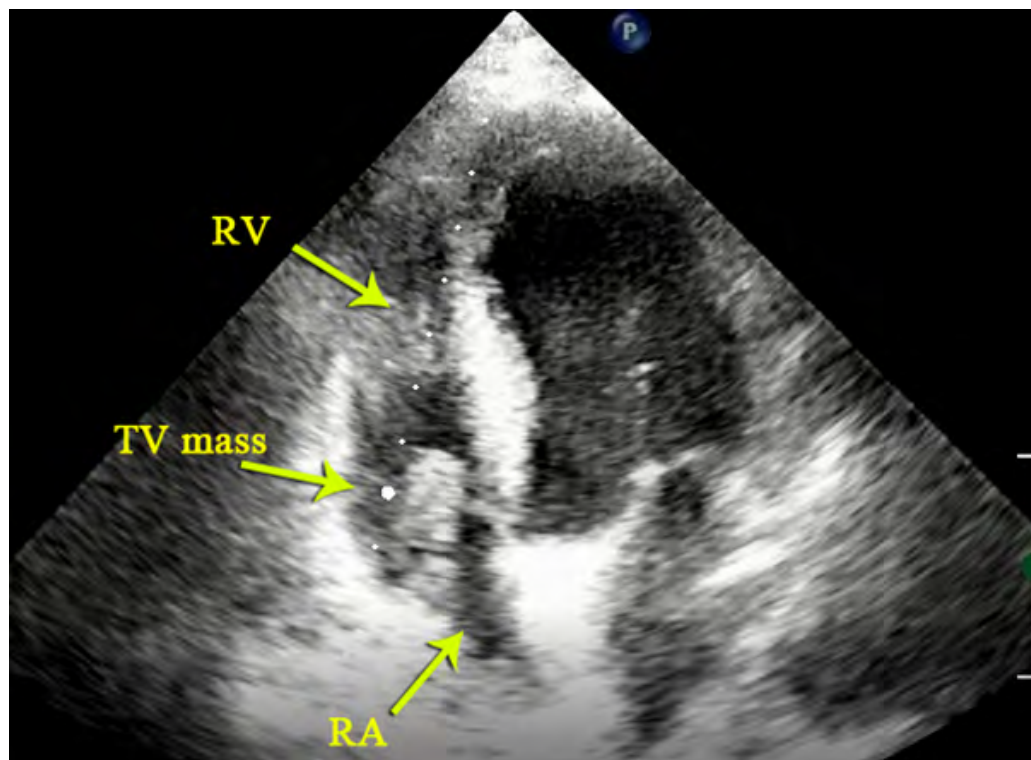


Figure 1: initial transthoracic echocardiography image showing tricuspid vegetation in apical 4-chamber view. RA: right atrium, TV: tricuspid valve, RV: right ventricle.

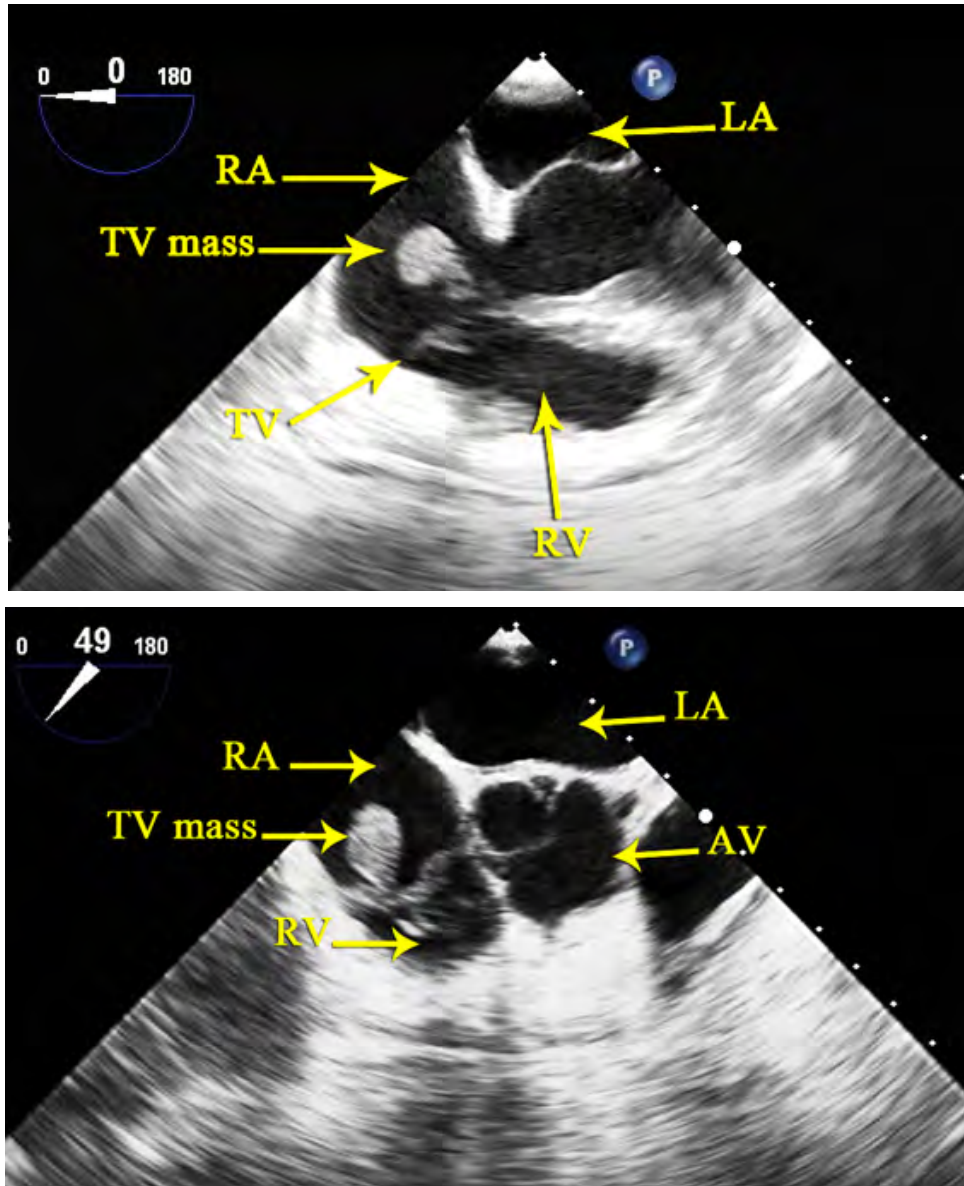


Figure 2: transesophageal echocardiography in RV inflow-outflow view. These images show a well-defined mass on the tricuspid valve. RA: right atrium, LA: left atrium, AV: aortic valve, TV: tricuspid valve, RV: right ventricle.

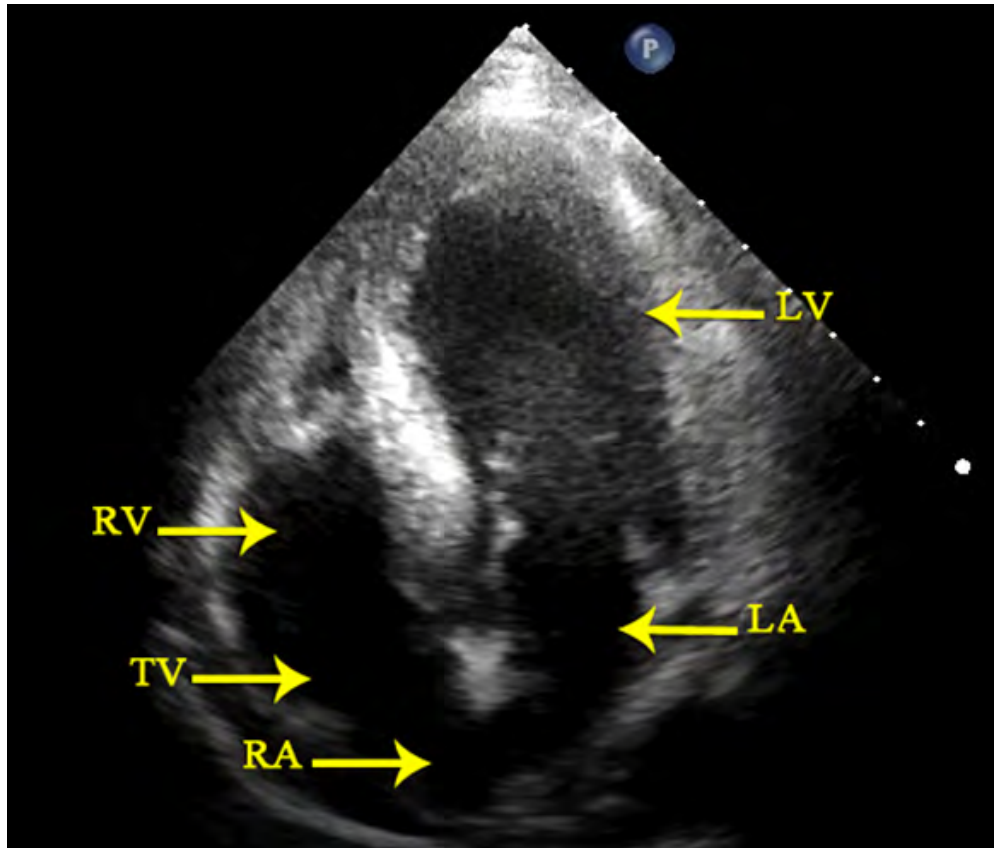


Figure 3: apical 4-chamber view in transthoracic echocardiography (TTE). mass is disappeared after anticoagulation therapy.

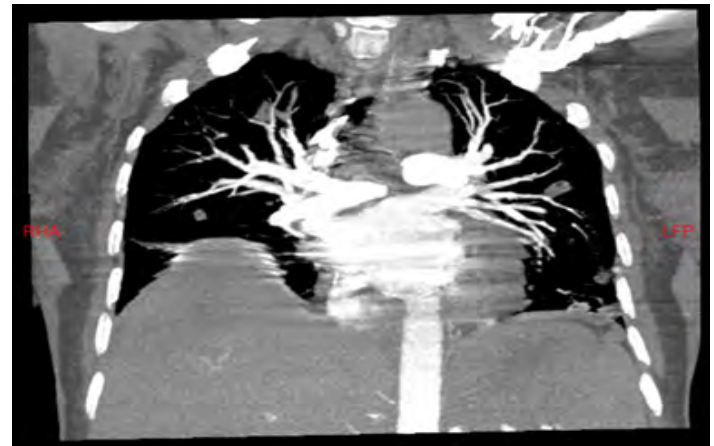
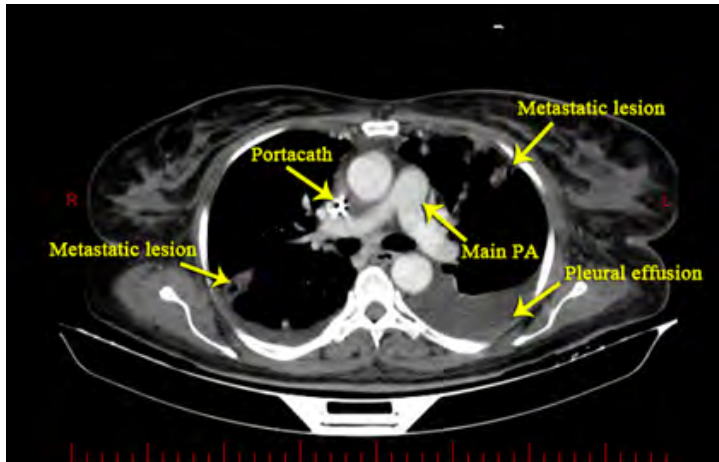


Figure 4; pulmonary CT angiography that show no evidence for embolism.

4. Discussion

Non-bacterial thrombotic endocarditis (NBTE) is a rare condition with a 1.1% to 1.6% incidence in patient-series from autopsy studies. [5, 6] Non-bacterial thrombotic endocarditis occurs in patients with a predisposing factor and/or a hypercoagulable state, such as systemic lupus erythematosus (SLE), APLs (Libman–Sacks endocarditis), cancer (marantic endocarditis), disseminated intravascular coagulation (DIC), or various other chronic diseases (tuberculosis or autoimmune disease).[7, 8] Among the patients

with malignancies, the three most frequent cancers are lung adenocarcinoma, breast, and pancreatic cancer. Stroke was the most frequent clinical presentation at admission (60%), while HF was observed in 21% and acute coronary syndrome in 7% of patients. Transthoracic echocardiography was able to confirm the diagnosis in 45% of patients. The mitral valve was more often affected (62%) than the aortic valve (24%).[9] Nevertheless, involvement of the right-side cardiac valves, such as pulmonary and tricuspid valves,

is relatively rare.[10] NBTEs are usually found incidentally, during imaging for other causes, or in patients with embolic syndromes. Usually, if not already done, a TTE is performed, which might give a good view of the tricuspid valve. However, especially due to the propensity of NBTE to be found on mitral and aortic valves, a TEE is done for confirmatory measures. Multiple sets of blood cultures are also needed to rule out subacute bacterial endocarditis. Hypercoagulable studies are warranted in patients where clinical suspicion is high. PET could also be considered to rule out culture-negative endocarditis by organisms such as *Tropheryma whippelii*. Cardiac CT and/or MRI are less often used due to the efficiency, ease and low-radiation benefits of echocardiography. [11] According to American College of Chest Physicians current guidelines, treatment of NBTE with heparin or LMWH is preferred over no anticoagulation, in addition to treating the underlying condition.[12] Recent studies have suggested that heparin or LMWH would be preferred in cases with malignancy-associated NBTE, while Vitamin K antagonists (VKA) agonists like warfarin may be preferred in antiphospholipid syndrome-associated NBTE.[11] The treatment of the underlying cause (i.e. SLE or cancer) is crucial to prevent recurrent NBTE. Anticoagulation treatments should be considered in all patients and balanced against the individual patient's bleeding risk. [8] Patients may be anticoagulated with low-molecular-weight heparin, vitamin K antagonists, or unfractionated heparin. There are no data to support the use of direct oral anticoagulants in NBTE. In a randomized open-label multicenter study comparing rivaroxaban and warfarin in patients with thrombotic APLs, the use of rivaroxaban was associated with an increased rate of thrombo-embolic events and major bleeding. [13] The role of surgery is controversial and remains to be clarified. However, surgery should be considered in patients with severe valve dysfunction or with large vegetations. [9] Direct oral anticoagulants as rivaroxaban, apixaban or edoxaban are equally acceptable alternatives but should be used carefully in patients with gastrointestinal or genitourinary tracts tumors, due to the considerable risk of bleeding events.[14] In patients with advanced metastatic disease such as in our case, treating the underlying condition is not feasible. Like in a large subset of patients the mainstay of NBTE treatment revolves around anticoagulation.[4]

5. Conclusion

We should consider NBTE in any high-risk patient for thromboembolism that present with any type of vegetation. In this case TTE and TEE echo finding completely compatible with metastatic invasion but after a short period of anticoagulation therapy, vegetation completely disappears. Our second challenge was platelet count falling after initiating of heparin. Recent study suggests that NOAC (especially apixaban) may be considered for thromboembolic event in malignant patient.

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