

# Marantic Endocarditis: A Rare Early Presentation Of Invasive Ductal Carcinoma Of The Breast

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## Abstract

Non-bacterial thrombotic endocarditis also known as Libman-sack endocarditis is a rare disease involving mostly mitral and aortic valves. It's more commonly associated with malignancy than autoimmune disease. It can be diagnosed definitively postmortem and antepartum. It presents with signs and symptoms of arterial thromboembolism. Embolization is the most common symptom of marantic endocarditis. This can present as stroke, myocardial infarction, acute intestinal ischemia, pulmonary thromboembolism, splenic infarction, or transient ischemic attack. The pathophysiology involves the presence of sterile growths and fibrin deposits on heart valves. We present a case of a 35-year-old female who initially presented with the embolic complication of marantic endocarditis. She had an early diastolic murmur and a left arm weakness on her first presentation to the hospital. Further workup revealed vegetation on the aortic valve on echocardiography. Her blood culture as well as related tumor markers were negative. She developed a lump in her right breast after 1 month which on investigation turned out to be an invasive ductal carcinoma breast. Through this report, we highlight the importance of considering the workup for malignancy every time a patient comes with such symptoms.

**Keywords:** Endocarditis, Ductal Carcinoma, Thromboembolism.

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## 1. Introduction

Non-bacterial thrombotic endocarditis also known as Libman-sack endocarditis is a rare disease involving mostly mitral and aortic valves.<sup>1</sup> It is more commonly associated with malignancy than autoimmune disease.<sup>1</sup> It can be diagnosed definitively post-mortem and antepartum it presents with signs and symptoms of arterial thromboembolism.<sup>2</sup> Embolization is the most common symptom of marantic endocarditis. This can show up as a stroke, myocardial infarction, acute intestinal ischemia, pulmonary thromboembolism, splenic infarction or transient ischemic attack. The pathophysiology involves the presence of sterile growths and fibrin deposits on heart valves.<sup>2</sup>

When a patient presents with signs of embolism and has valvular lesions on echocardiography, we emphasize the importance of clinical suspicion for marantic endocarditis as a differential diagnosis, often against the background of malignancy.<sup>3</sup>

## 2. Case Presentation

A 35-year-old Pakistani female presented with a history of cough for 4-5 days, high-grade fever for one day and

sudden left arm weakness for a few hours. She had associated nausea, headache and one episode of vomiting.

Her past medical and surgical history revealed that she had open cholecystectomy, Roux-en-Y hepatojejunostomy and right hemi hepatectomy.

On physical examination, significant findings were HR 130/min, RR 31/min SpO2 92% at room air, BP 94/57mmHg and temperature 101F. Her GCS was 14/15. Her q-SOFA Score was 3/3. She was dehydrated and was drenched in sweat, had a dry tongue, reduced skin turgor, sunken eyes, and was pale and lethargic. Peripheral pulses were feeble. No pedal oedema was seen. On abdominal examination, the abdomen was soft with right hypochondriac tenderness on deep palpation, surgical scar marks with no other significant finding.

Cardiovascular examination revealed apex beat in the 5<sup>th</sup> intercostal space midclavicular line. On auscultation 1<sup>st</sup> and second heart sounds were audible which were of normal intensity with an early diastolic murmur at the aortic area (third left intercostal space) heard loudest on expiration and leaning forward, non-radiating with a grade 2/4. The chest was bilaterally clear with no crackles. On neurological examination, she had power 3/5 in the left upper limb and 5/5 in all other limbs. Deep tendon reflexes and tone were normal. A positive Babinski sign was present on the right side. Her breast examination on presentation was non-significant.

Initial baseline investigations were sent and the patient was resuscitated. Pan cultures were sent. Initially, a fluid bolus was given to which the patient responded as tachycardia improved and GCS also got better so she was started on maintenance fluids. The patient was given a STAT dose of ceftriaxone 2g IV within 1 hour of arrival. She was then admitted to the Intensive care unit. Initially, the patient was managed on the lines of sepsis as the sofa score was 3/3, with broad-spectrum antibiotics targeting gram-positive, gram-negative and atypical bacteria until cultures were awaited. Her serum electrolyte abnormalities were treated with KCL infusion and Oral rehydration salt.

As there was a murmur on cardiovascular examination a transthoracic echocardiography was done which showed an ejection fraction of 60% mild mitral regurgitation, severe aortic regurgitation, mild tricuspid regurgitation with RSVP 30mmHg and vegetation attached to left coronary cusp measuring 0.5 x 1.0 cm.

For precise details Trans-Esophageal Echocardiography was also performed which showed an Ejection Fraction of 60%, large mobile 0.5 x 1.4 vegetation (Figure 1) on the left coronary cusp with severe Aortic Regurgitation (Figure 2) and mild mitral regurgitation.

Vegetation with isolated left arm weakness raised the suspicion of septic emboli to the brain so a CT brain plain was done which showed no acute bleed of ischemia, then magnetic resonance imaging and magnetic resonance venography of the brain was arranged which showed evidence of T2 and FLAIR cortical oedema seen in the right superior parietal lobe. It appeared isotense on T1 and shows signal loss on SW1. There were few filling defects seen in the right superior parietal region superficial cortical veins concerning cortical venous thrombosis (Figure 3).

All this led to a diagnosis of infective endocarditis leading to septic embolization as one of the major (echocardiography evidence of vegetation) and two minor (fever, embolic phenomenon) modified duke criteria were fulfilled. Intravenous antibiotics were modified (gentamycin, ceftriaxone and vancomycin) and awaiting blood C/S turned out to be negative.

After adequate resuscitation and stabilization patient was referred to a cardiac surgeon for aortic valve replacement surgery. She underwent AVR and the vegetation was sent for histopathology. She was started on warfarin and was regularly being followed for INR to keep in the therapeutic range i.e. 2.0-3.0.

Histopathology report of the aortic valve revealed sterile vegetations and mild myxoid degeneration. To evaluate the other causes of endocarditis a panel of laboratory investigations including carcinoembryonic antigen

(CEA), anti-nuclear antibodies (ANA), Antiphospholipid antibodies, RA factor, HIV screening, CA 19-9 were sent which were negative except CA 125 levels which were mildly raised.

The further plan was to do a full body contrast-enhanced computed tomography to see for any unseen malignancy but due to a few complications of the patient which included deranged renal function tests, pleural effusion leading to chest tube insertion.

The patient was discharged home with no neurological focal deficit, afebrile, vitally stable, resolution of pleural effusion, INR in therapeutic range and well oriented in time, place and person and was asked to follow up with fresh renal function tests to proceed with CECT abdomen, pelvis, chest and neck.

After 1 month of discharge, she noticed a lump on the right upper outer quadrant of her right breast which was tender on palpation. O/E there was a lump 2.5 x 2.5cm at 11 o'clock in the right breast. No lymphadenopathy was present on examination. Her breast USG was done which showed a focal hypoechoic lesion right breast BIRAD III. Her mammography showed an area of architectural distortion with linear pleomorphic calcification in the right breast BIRAD IV.

Tru-cut biopsy right breast lump was taken and the histopathological report revealed invasive ductal carcinoma. Estrogen receptors were positive, progesterone receptors were weakly positive and HER2/Neu receptors were negative.



**Figure 1: Large mobile 1.4 x 0.5 vegetation on the left coronary cusp of the aortic valve**

The bone scan was negative for any bone metastasis. Contrast-enhanced computed tomography abdomen, chest and pelvis showed fairly well-defined homogeneously enhancing soft tissue density mass lesions in the upper quadrant of the right breast with mild peri lesional soft tissue stranding, mild overlying skin thickening and few subcentimeter sized oval shaped ipsilateral axillary lymph nodes. Diagnosis of Stage II breast carcinoma was made and was planned for chemotherapy with doxorubicin 75mg/m<sup>2</sup> and

cyclophosphamide 600mg/m<sup>2</sup> to be repeated every 4 weeks for 6 cycles.

The patient is undergoing chemotherapy at the moment with regular follow-ups.



Figure 2: Severe aortic regurgitation showing eccentric jet.

### 3. Discussion

Marantic endocarditis is an old name for non-bacterial thrombotic endocarditis (NBTE). As the name suggests it is very often associated with an embolic event which includes ischemic stroke, transient ischemic attack, mesenteric ischemia, splenic infarction or any other thromboembolic phenomenon. It mostly affects the left heart valves i.e. mitral and aortic valves.<sup>3</sup> On valvular leaflets, marantic endocarditis is characterized by sterile vegetation made up of fibrin-platelet thrombi<sup>3</sup>. NBTE mostly occurs in patients suffering from SLE or advanced cancer. We report a rare case of marantic endocarditis associated with invasive ductal carcinoma breast initially presenting with the symptoms of ischemic stroke. In 2022 a case was reported of an 83 years old female with a known case of breast CA for 12 years who presented with a day history of left-sided weakness on workup she turned out to have large aortic and mitral valves vegetations with a diagnosis of marantic endocarditis.<sup>4</sup>

Another case was reported of a young male presented with similar complaints, previously healthy and fit, diagnosed with mitral vegetation and a detailed workup revealed he had pancreatic CA with liver metastasis, by Mir Rahman.<sup>5</sup>

In our case, the only finding linked with endocarditis was an early diastolic murmur heard in the aortic area. Although less than 50% of the marantic endocarditis cases have associated murmurs.<sup>6</sup>

Cerebral venous thrombosis being a rare complication of infective endocarditis was seen in our case and proved with MRI findings has also been reported earlier by Dorée Augustia<sup>7</sup> in a young male who initially presented with sudden severe headaches with signs of meningeal irritation with right hemiparesis and right hypoesthesia. Our patient had an initial infarction-free CT scan which was followed by multiple filling defects seen in the right superior parietal region superficial cortical vein concerning cortical venous thrombosis.

Because sterile thrombotic lesions are friable, embolization is common in them as lack of inflammation causes poor adhesion to the valves on which they reside<sup>3</sup>. The release of pro-inflammatory cytokines is the central event in the pathogenesis. These cytokines damage endothelial cells, resulting in the formation and deposition of immune complexes as well as platelet and fibrin complexes on the cardiac valves. In the background of this process is a hypercoagulable state brought on by cancer or systemic inflammation.

It can be challenging to tell the difference between sterile lesions and those caused by infective endocarditis. Small, sessile lesions with irregular borders, broad bases, friability, and varying densities are among the echocardiographic features presenting primarily on the mitral and aortic valves, as demonstrated by our case report. Although Transesophageal echocardiography (TEE) is more sensitive to rule out any vegetation but still transthoracic echocardiography (TTE) plays a vital role and is the first choice with TEE being reserved for unrevealing cases. Although we had evidence of vegetation on TTE we confirmed it with TEE to be sure. As the patient had severe aortic regurgitation we had to shift her for valve replacement and her valve histopathology revealed sterile vegetation so culture-negative endocarditis organisms were not investigated. Blood culture-negative endocarditis is a significant diagnosis that needs to be excluded in patients.

Even with therapeutic dose anticoagulation, new valvular vegetation can form, removing the source of the immune-mediated deposition of thrombus is the mainstay of treatment for marantic endocarditis [3,1]. Anticoagulation with Low molecular weight heparin should be used and the patient should be placed on lifelong anticoagulation as recurrent thromboembolism has been reported in some patients after its stoppage. Histopathology report of the trust disposes of showing invasive ductal carcinoma with previously negative blood culture finding and evidence of aortic valve

vegetation on TOE/TTE made a definite diagnosis of marantic endocarditis secondary to invasive ductal breast carcinoma.

#### 4. Conclusion

We present the first reported case of non-bacterial thrombotic endocarditis secondary to invasive ductal carcinoma breast. This was treated with neo-adjuvant chemotherapy which was to be followed by mastectomy and therapeutic anticoagulation. We consider the significance of the requirement for high clinical suspicion of NTBE in patients with embolic signs and valvular vegetations on echocardiography. It is essential to make an early diagnosis of marantic endocarditis to treat the underlying cause, search for malignancy could be started earlier, identified and treated with chemotherapy as well as surgery where needed. Also, the early initiation of therapeutic anticoagulation is important. This is due to the close correlation between the two conditions.

#### Institutional Review Board Approval

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M.B, Z.R, F.I, F, K.R, M.A - Conception of study

M.B, Z.R, F.I, F, K.R, M.A - Experimentation/Study

Conduction

M.B, Z.R, F.I, F, K.R, M.A -

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