

CASE REPORT

Marantic endocarditis: incidental infarcts leading to diagnosis of pancreatic cancer

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SUMMARY

Non-bacterial thrombotic endocarditis (NBTE) is a well-described phenomenon associated with malignancies due to hypercoagulable state. In the setting of pancreatic cancer, NBTE is more commonly diagnosed postmortem. We describe a case of a man who was diagnosed with pancreatic carcinoma after incidental finding of NBTE. Imaging incidentally revealed multiple strokes, bilateral renal and splenic infarcts, while subsequent workup for cardioembolic source demonstrated a 1.1×0.7 cm mitral valve vegetation. As multiple blood cultures were sterile and patient lacked clinical signs of infection, an underlying malignancy was suspected. CT abdomen demonstrated a dilated pancreatic duct, MRI showed a 2.8×2.2 cm pancreatic head mass. Endoscopic biopsy of the mass revealed pancreatic adenocarcinoma. Other than NBTE, there were no other clinical or laboratory findings to clearly suggest pancreatic cancer. Thus, incidental discovery of this mitral valve vegetation led to the diagnosis of pancreatic malignancy.

BACKGROUND

Non-bacterial thrombotic endocarditis (NBTE), also known as marantic endocarditis, is well documented in the literature phenomenon. This condition arises secondary to hypercoagulable state and has been associated with various malignancies, most commonly, gynaecologic.¹ Pancreatic cancer is the third leading cause of cancer-related deaths in the USA with a 5-year survival rate less than 10%.² Whereas globally, pancreatic cancer is responsible for 331 000 deaths annually and is the seventh most common cause of cancer-related deaths.³ The morbidity and mortality from pancreatic cancer is due to hypercoagulable state resulting in increased incidence of embolic events.¹ Here, we report a case of NBTE as the presentation of underlying pancreatic malignancy. What makes our case unique is that diagnosis of marantic endocarditis in the setting of pancreatic cancer is made post-mortem in 1.2% of patients during autopsy.⁴ The diagnostic challenge of marantic endocarditis in living patients is due to the small size of these vegetations, which are often not large enough to be diagnosed on echocardiography; thus, it is not surprising that the first ever antemortem case was reported in 2008.^{4,5} Healthcare professionals need to be aware of the association between marantic endocarditis and pancreatic malignancy,

as it may lead to diagnosis and treatment of underlying neoplastic process.

CASE PRESENTATION

A 66-year-old cachectic male with history of heavy alcohol use, but no known medical history presented to the emergency department after a mechanical fall while attempting to climb into his truck. He denied presyncopal symptoms preceding the fall. Imaging showed a left inferior pubic ramus fracture which orthopaedic surgery concluded was non-operative. Although the patient was alert and oriented, he was noted to have slow responses to questions and scanning speech. MRI of the brain revealed multiple subacute to acute strokes of differing ages: posterior right periventricular white matter infarcts and right posterior cerebellar infarction (figure 1). Patient was evaluated by neurology, started on atorvastatin, aspirin and clopidogrel. Transthoracic echocardiography (TTE) was negative for cardioembolic source. His clinical course was complicated by increased oxygen requirement due to aspiration pneumonia, which resolved after a course of antibiotics. Patient was discharged home in stable condition.

Three days later, the patient returned to the emergency department with nausea, vomiting and abdominal pain. On presentation, he was noted to have melena.

Patient was afebrile, with normal vital signs. He was cachectic, but awake, alert and oriented. Cardiac examination revealed regular rhythm with no murmur auscultated, lungs were clear to auscultation bilaterally, abdomen was non-tender with no palpable masses, and skin examination showed no jaundice or rashes. Other than anaemia, all laboratory studies including hepatic function panel were normal.

CT of abdomen and pelvis showed a duodenal ulcer with contained perforation. He had a non-surgical abdomen and was taken to interventional radiology for mesenteric angiogram which showed no source of bleeding, but the gastroduodenal artery was prophylactically embolised. Incidentally, CT imaging also revealed bilateral renal and splenic infarcts (figure 1). Due to the previously noted strokes and new multi-organ infarctions, concern for a cardiac source of emboli was again raised.

INVESTIGATIONS

Repeat TTE was again negative for valvular vegetation or intracardiac shunt.



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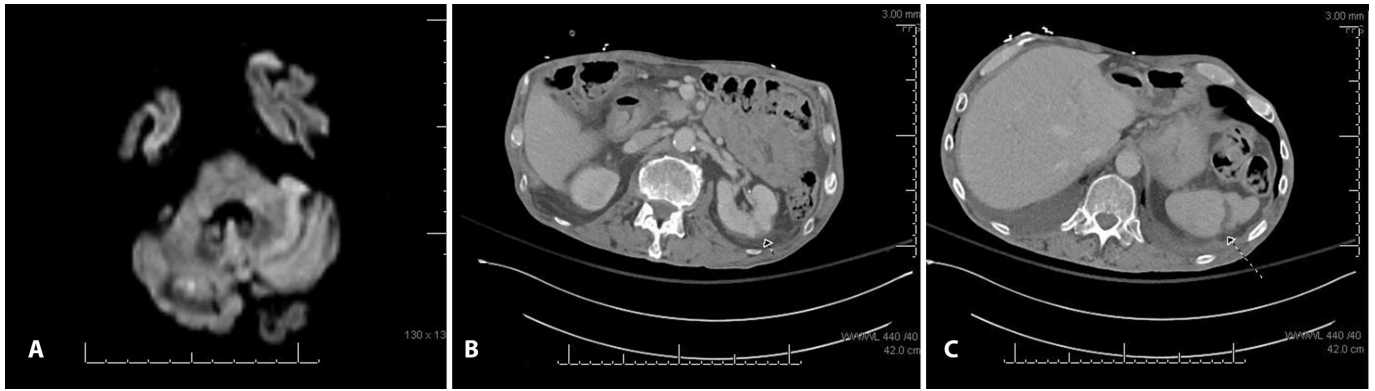


Figure 1 (A) Brain MRI showing a focus of restricted diffusion in right cerebellum. (B) CT of abdomen demonstrating wedge-shaped area of renal cortical hypoattenuation. (C) CT of abdomen demonstrating age-indeterminate splenic infarct.

As four sets of serial blood cultures taken over the course of a month remained negative and lack of evidence to explain multiorgan embolic events, a transoesophageal echocardiography (TEE) was ordered. Follow-up (TEE) revealed a 1.1×0.7 cm vegetation on the posterior leaflet of the mitral valve (figure 2). CT abdomen on initial presentation showed a 5 mm dilation of the main pancreatic duct with no definite evidence of obstructing lesion (figure 3). Outpatient non-emergent MRI was recommended; however, abdominal MRI was ordered inpatient due to suspected malignancy in the setting of NBTE. MRI revealed a 2.8×2.2 cm soft tissue mass in the pancreatic head that resulted in pancreatic duct stricture (figure 3). Endoscopic ultrasound demonstrated an irregular 14 mm hypoechoic mass with poorly defined endosonographic borders, invading into the portal vein. The parenchyma of the pancreas appeared to have honeycombing and lobularity. The pancreatic duct was dilated to 6 mm with a mural nodule seen within pancreatic duct at the genu. Needle aspiration was performed and cytology revealed pancreatic adenocarcinoma.

DIFFERENTIAL DIAGNOSIS

- ▶ Culture-negative infective endocarditis: patient had no evidence of infective endocarditis on clinical examination and no signs or symptoms of underlying infection.

- ▶ NBTE secondary to malignancy: patient’s age, cachectic appearance and negative infectious workup made malignancy high on our differential.
- ▶ Antiphospholipid syndrome: antinuclear antibody was negative, and given the patient’s age and lack of clinical symptoms, systemic lupus erythematosus and secondary antiphospholipid syndrome were less likely diagnoses. However, primary antiphospholipid syndrome can truly be ruled out by negative laboratory workup with lupus anticoagulant, anticardiolipin antibody or anti- β2 glycoprotein-I antibody at least 12 weeks apart.⁶

TREATMENT

In the setting of mitral valve NBTE complicated by cerebral, renal and splenic infarcts, the patient was started on systemic anticoagulation for prevention of recurrent thromboemboli. Treatment of his underlying malignancy is also crucial. On hospital discharge, patient followed up with surgical, medical and radiation oncology.

OUTCOME AND FOLLOW-UP

Given his poor performance status and borderline resectable tumour with the involvement of portal vein, he was deemed not a surgical candidate at this time. He elected to pursue

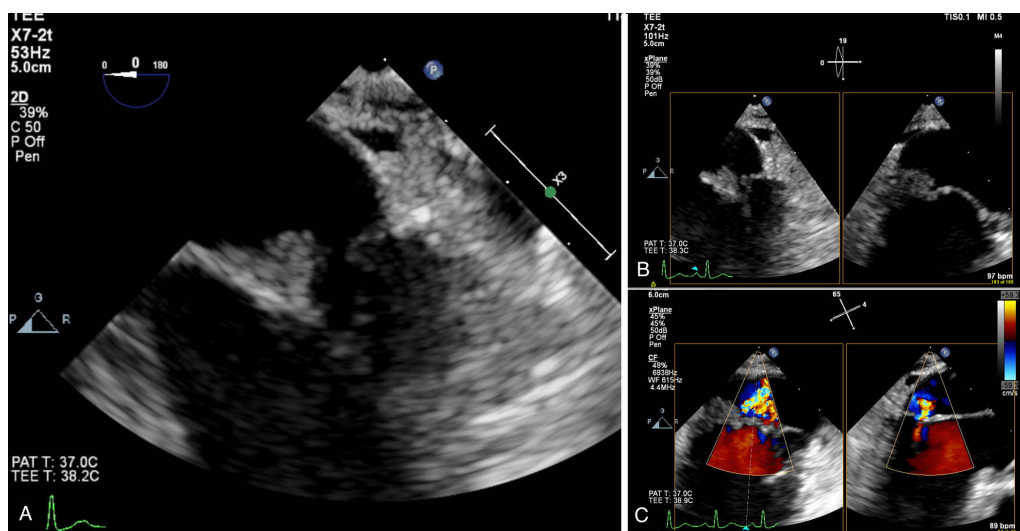


Figure 2 (A and B) Transoesophageal echocardiography showing a 1.1×0.7 cm vegetation on the posterior leaflet of the mitral valve. (C) The presence of mitral valve regurgitation.

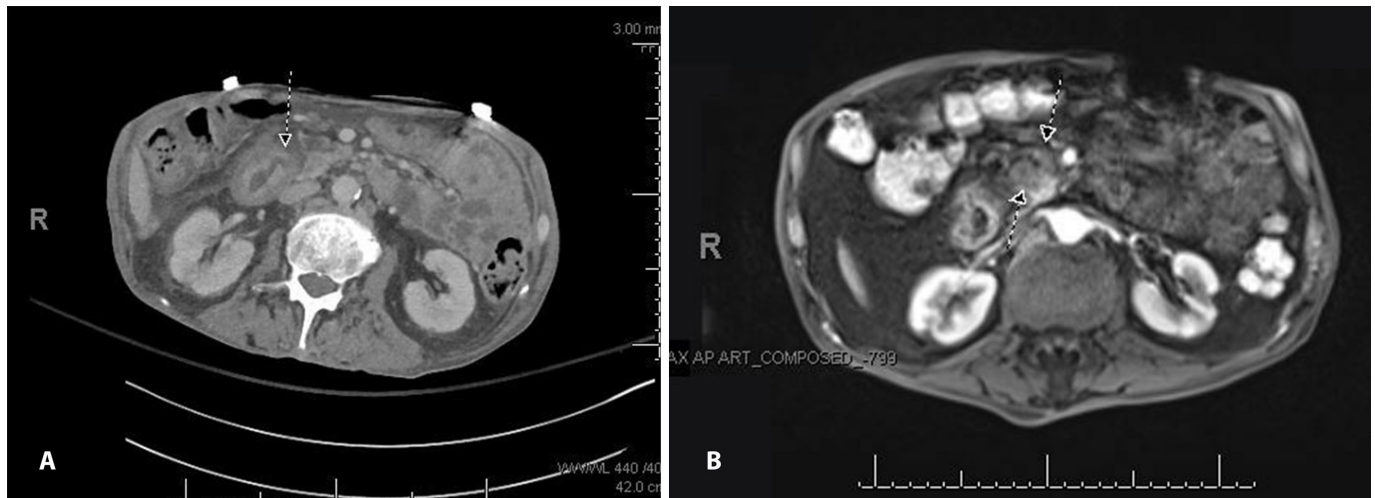


Figure 3 (A) Dilation of main pancreatic duct up to 5 mm shown on abdominal CT. (B) Abdominal MRI demonstrating an ill-defined soft tissue in the pancreatic neck/head measuring 2.8×2.2 cm, obstructing the pancreatic duct.

neoadjuvant therapy with chemo and radiation and may still consider surgery in the future if his performance status improves and tumour responds.

DISCUSSION

In 1888, Zeigler used the term thromboendocarditis to describe thrombi depositing on heart valves. Later, the term evolved into cachectic, or marantic, endocarditis; while finally in 1936, Gross and Friedberg coined 'non-bacterial thrombotic endocarditis'.^{4 7 8} NBTE most commonly affects patients between the fourth and eighth decade of life, without a specific gender predilection.⁴ NBTE results from deposition of thrombi composed of platelets and sterile fibrin on heart valves, with associated morbidity and mortality stemming from embolisation of these into the central nervous system.⁹ Mitral and aortic valves are the most common sites of vegetation.¹⁰ Although the pathogenesis of this process still remains unclear, underlying malignancy or high-inflammatory states result in elevated levels of cytokines (tumour necrosis factor and interleukin-1), which in turn cause local tissue damage with activation of coagulation cascade resulting in vegetation formation.⁹ The first ever antemortem case of marantic endocarditis as the presentation of underlying pancreatic malignancy was published in 2008 by Smeglin *et al.*^{1 5} In pancreatic cancer, these vegetations are often too small and friable, leaving remnants that are not large enough to be identified by echocardiography, making it difficult to diagnose NBTE in a living patient.⁴ Yet, these lesions have significant morbidity with the overall reported incidence of embolic events being 42%, most commonly affecting spleen, kidney, brain and heart, respectively.^{4 11}

In addition to the treatment of underlying malignancy, the most important guidelines when it comes to treatment of NBTE focus on the use of anticoagulation to prevent recurrent thromboembolic events.

Unfortunately, these stem from general anticoagulation guidelines in malignancy, as there is scarcity of studies specifically in NBTE. Therefore, some suggest the use of low-molecular-weight heparin as the preferred antithrombotic agent, whereas others argue that unfractionated heparin is the therapy of choice.^{9 12 13} Meanwhile, the role of direct oral anticoagulants in cancer-related thrombotic events, and in NBTE in particular, needs to be addressed in further studies.¹³

Learning points

- ▶ Pancreatic cancer is the third leading cause of the cancer-related deaths in the USA with a 5-year survival rate less than 10%.² Whereas globally, pancreatic cancer is responsible for 331 000 deaths annually and is the seventh most common cause of cancer-related deaths.³
- ▶ Non-bacterial thrombotic endocarditis (NBTE) is a rare but known presenting feature of pancreatic cancer.
- ▶ Healthcare professionals must suspect NBTE in the setting of multiorgan infarcts and lack of infectious signs or symptoms. It is prudent to obtain a transoesophageal echocardiography in the setting of negative transthoracic echocardiography.
- ▶ Treatment of NBTE consists of systemic anticoagulation and treating the underlying malignancy.

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