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Case Report

CASE REPORT

A classical case of non-bacterial thrombotic endocarditis from pancreatic adenocarcinoma presenting as multiple strokes, myocardial infarction and acute limb ischaemia

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Abstract

Non-bacterial thrombotic endocarditis (NBTE) classically presents in the context of pancreatic adenocarcinomas. Echocardiography is useful to investigate for valvular vegetations, and institution of early treatment is crucial as this can be complicated by multiple systemic emboli, leading to significant morbidity or mortality in serious cases. Treatment options involve anticoagulation with unfractionated heparin, and the role of surgical intervention is unclear. In this report, we describe a classical case of a middle-aged lady with unresectable pancreatic adenocarcinoma who developed NBTE complicated by multiple systemic emboli. She eventually succumbed from poor neurological status from multiple cerebral emboli. Awareness of this condition is required by clinicians for early diagnosis and prompt treatment.

INTRODUCTION

Non-bacterial thrombotic endocarditis (NBTE) is common between patients 40 and 80 years of life with no sex predilection. The incidence of malignancy-related NBTE is largely unknown, but estimates in autopsy populations range from 0.6 to 1.26% (1, 2). NBTE may also present in patients with rheumatic and autoimmune conditions, hypercoagulable states, sepsis, indwelling catheters and acquired immune deficiency syndrome, but for the purposes of this case report we will focus on patients with malignancy (3, 4). The highest rates are reported in patients with pancreatic adenocarcinomas (10.34%), although they may also occur in other adenocarcinomas such as the lung and prostate (1.55% collectively) (2), with a propensity for vegetations to affect the aortic and mitral valves (1). We describe a case of a patient with a known history of pancreatic adenocarcinoma who presented with multiple systemic embolization phenomena.

CASE REPORT

A 54-year-old woman with a known history of chemotherapy-naive unresectable pancreatic adenocarcinoma presented with an acute onset of left-sided weakness and unsteady gait with tendency to veer towards the right. This was associated with a

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change in behaviour 3 weeks prior to admission, but otherwise, there was no nausea, vomiting, giddiness, loss of consciousness, double vision or dysphagia. The patient had a past medical history of hyperlipidaemia treated with simvastatin 40 mg every night. There was no history of antibiotic use prior to admission.

Upon examination, the Glasgow Coma Scale (GCS) was 15. The patient was observed to be anaemic with scleral icterus and associated hepatomegaly with an irregular edge. There was dysmetria on the right, and left upper limb power was graded 3 on the Medical Research Council scale. Heart sounds were dual, with no murmurs were heard on cardiac auscultation.

In the emergency department, she experienced a partial seizure that aborted spontaneously. Post-ictally, there was interval development of right gaze preference, with a GCS drop to 13 (E3V4M6).

Computed tomography (CT) scan of the brain (Fig. 1) performed showed the presence of multiple hypodensities in the cerebellum. Significant laboratory abnormalities included leukocytosis with neutrophilia, a hypochromic microcytic anaemia and hyponatraemia (serum osmolality 265 mmol/kg, urine osmlolality 492 mmol/kg and urine sodium 103 mmol/l).

Upon arrival in the ward, power on the left upper and lower limbs was zero, accompanied by areflexia and upgoing plantar reflexes. GCS continued to drop to three (E1V1M1). The patient was started empirically on intravenous ceftriaxone in view of leukocytosis after blood cultures were taken.

Magnetic resonance imaging (MRI) of the brain showed the presence of massive infarction in the right middle cerebral artery territory, a watershed infarct in the left cerebral hemisphere (Fig. 2) and multiple acute lacunar infarcts in the cerebellum (Fig. 3), the left thalamus and left posterior temporal/occipital lobe. Magnetic resonance angiography (MRA) of the brain showed complete occlusion of the right proximal M1 artery (Fig. 4).

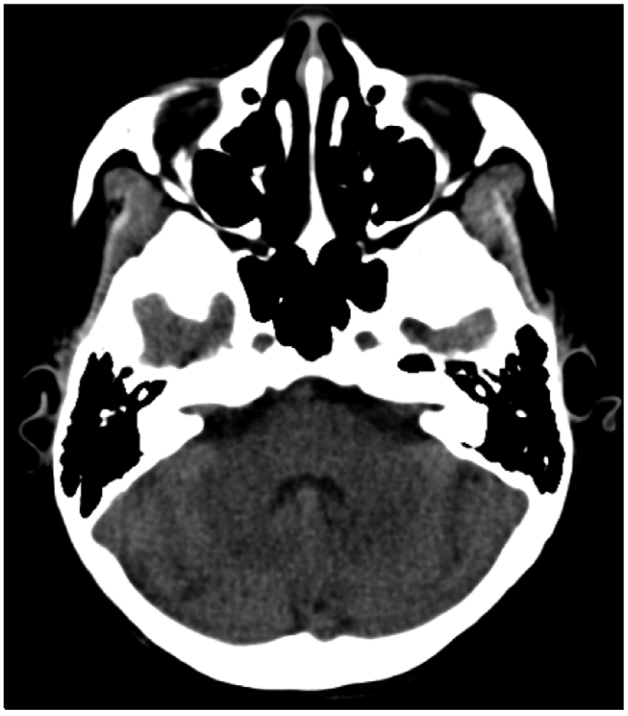

Figure 1: Non-contrasted computed tomographic scan of the brain with multiple hypodensities in the cerebellum.

A transthoracic echocardiogram (TTE) showed the presence of a 7 mm by 4 mm mobile echodensity on the aortic valve (Fig. 5) with moderately severe left ventricular systolic dysfunction (ejection fraction of 32%) and regional wall motion abnormalities. Serum troponin increased from 2.79 to 9.32 μg/l.

Two days later, the patient started developing a cold left foot. The left foot had absent dorsalis pedis and posterior pedal pulses and started becoming pale in comparison with the right

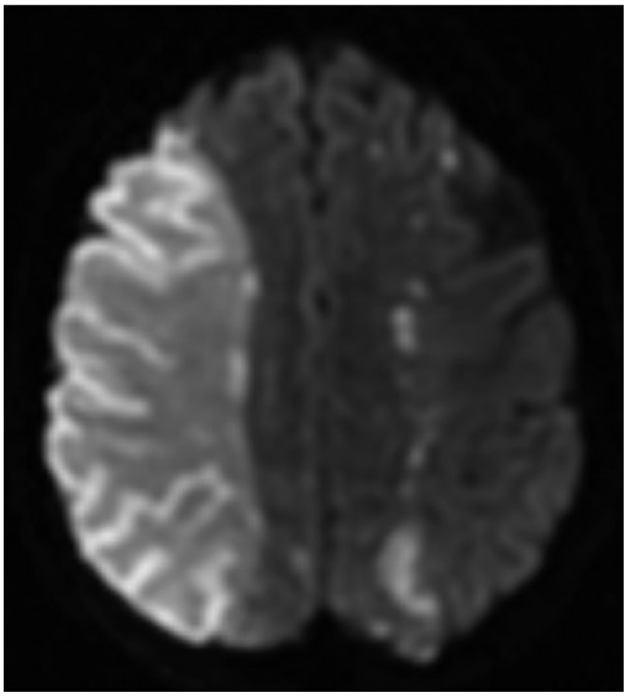

Figure 2: MRI of the brain. Diffusion-weighted imaging showing a right middle cerebral artery and left watershed infarct.

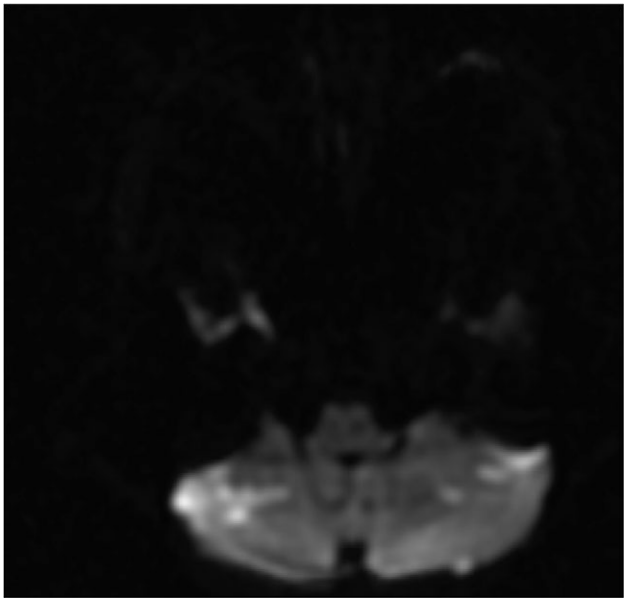

Figure 3: MRI diffusion-weighted imaging showing multiple hypodensities in the cerebellum.

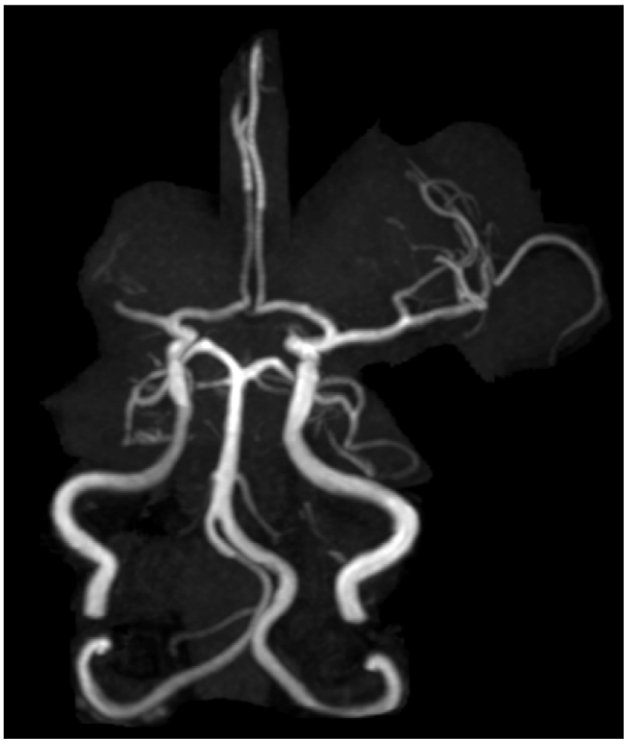

Figure 4: MRA showing a complete occlusion of the proximal M1 segment of the right middle cerebral artery.

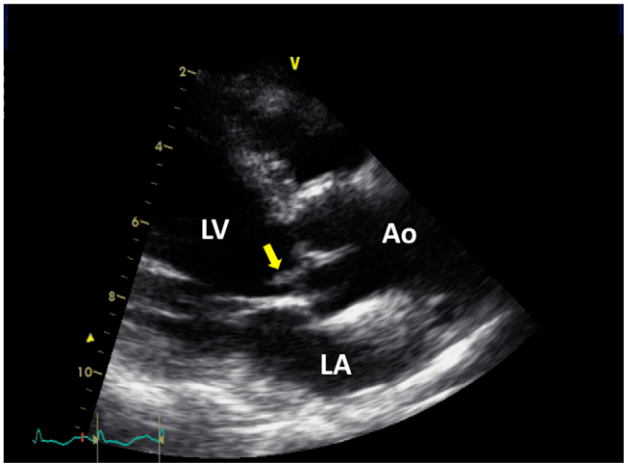

Figure 5: TTE at the parasternal long axis window showing a mobile echodensity attached to the ventricular surface of the aortic valve, consistent with that of a vegetation.

which was normal. Despite antibiotics, the patient continued to have a persistent fever of 38 degrees. Repeated blood cultures have returned negative.

The coagulation profile was done for the patient and the platelet count of 177×10^9/l, prothrombin time of 16.3 s, international normalized ratio of 1.39 and activated thromboplastin time of 33.1 s were not suggestive of disseminated intravascular coagulation. Polymerase chain reaction for fastidious organisms was not performed as the patient had multisystem involvement in the presentation and it was deemed that it would not change management.

At this point, in view of the already poor prognosis from the treatment refractory advanced pancreatic cancer, a family conference was held with family members, and a consensus was made not to subject the patient to further investigations that may be futile in terms of reversing the eventual outcome. Best supportive care was opted for, and she passed away peacefully 3 days later.

DISCUSSION

Patients with malignancy have a hypercoagulable state, and NBTE is a condition whereby there is valvular deposition of fibrin and platelets (5). Patients often present, as in this case, with signs and symptoms of systemic embolization from the vegetations. The vegetations are particularly prone to embolization, as they have little inflammatory reaction at the site of attachment with little cellular organization (6). Embolization to the cerebral (presenting as focal neurological deficits) and cardiac vessels (presenting as myocardial infarction) result in the most morbidity (6). Cardiac murmurs are infrequent (7). In a patient with underlying malignancy and an echocardiogram detected vegetation, persistent fever in the presence of serial negative blood cultures coupled with lack of response to antimicrobial therapy should increase suspicion of NBTE.

Patients with suspicion of cerebrovascular involvement should undergo an MRI scan in preference to a CT scan of the brain as they have higher sensitivity and specificity in diagnosing embolic strokes (8). NBTE patients have multiple widely distributed strokes of various sizes vis-à-vis patients with infective endocarditis who present with either a single lesion, multiple closely spaced lesions in a single arterial territory or multiple punctate disseminated lesions. Transoesophageal echocardiogram (TOE) is more specific than TTE in detecting vegetations, and TOEs have been shown to be helpful in diagnosing NBTE in stroke patients (9, 10). Optimal treatment is both heparin and treatment of the underlying cancer (11). Anticoagulation with lifelong unfractionated heparin either intravenously or via the subcutaneous route has been shown to reduce the incidence of recurrent episodes of thromboembolism (12). For valvular lesions with recurrent embolism or heart failure, surgical intervention may be considered (13, 14).

In this case, histology was not obtained as this was not to change the patient's management. While it is theoretically possible that the cardiac vegetation is due to secondary metastases, by the principle of Ockham's razor, NBTE seems like the most consistent diagnosis. Concurrent pancreatic adenocarcinoma and cardiac metastases would be rare, as would end-stage malignancy presenting acutely with concurrent ischaemic stroke and acute limb ischaemia in the absence of NBTE.

In summary, we present a case of NBTE in a lady with advanced pancreatic adenocarcinoma. Consider NBTE in patients presenting with multiple embolic phenomena in the context of a past medical history of cancer due to severe potential morbidity from the disease. Diagnosis may be clinched by echocardiography. Treatment modalities involve treating the underlying cause, anticoagulation and in certain cases, surgery.

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None.

CONFLICT OF INTEREST STATEMENT

None declared.

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ETHICAL APPROVAL

No ethical approval is required.

CONSENT

We were unable to obtain consent from the patient as the patient passed away. Attempts to obtain consent from the next-of-kin was unsuccessful as well.

GUARANTOR

Dr Ching-Hui Sia.

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