Pancreatic cancer with multiple liver metastasis complicating multi organ infarcts from Marantic endocarditis and Trousseau's syndrome

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European Journal of Medical Case Reports
Volume 8(6):113–117
DOI: 10.24911/ejmcr.173-1641049029

ABSTRACT

Background: Marantic endocarditis and Trousseau's syndrome are historically linked with pancreatic cancer. The patient had catastrophic embolic events which caused multi organ infarct due to underlying advanced pancreatic cancer. Doctors should be aware of early signs and symptoms of pancreatic cancer and conduct necessary clinical assessments and investigations that can prevent any severe complications.

Case Presentation: A middle-aged healthy gentleman who presented with left-sided weakness, slurred speech, left-sided sensory neglect, mild headache, and fever. CT head showed acute right-sided temporal ischemic changes with subsequent magnetic resonance imaging (MRI) head showed multiple infarcts in the brain. A transesophageal echocardiogram reported possible MV vegetation. MRI of the liver was done due to deranged LFTs which showed multiple liver metastasis with a primary mass in the tail of the pancreas. Left leg ultrasound Doppler showed a large left leg deep vein thrombosis involving the femoral vein as he complained of left leg pain for 2 months and went to GP with right leg pain 3 months ago which was treated as a right ankle sprain. The clinical events explained that most likely he developed Trousseau's syndrome 3 months ago and the embolic phenomena were due to rare Marantic endocarditis (Non-bacterial thrombotic endocarditis) secondary to pancreatic cancer. Ultrasound-guided biopsy of liver metastasis was planned, but sadly the patient passed away the next day.

Conclusion: The diagnosis of early pancreatic cancer with imaging poses a challenge sometimes, therefore the pancreatic protocol of CT or MRI is the first line of investigation. Moreover, the cause of unprovoked thrombo-embolism should be investigated to rule out any underlying malignancy.

Keywords: Pancreatic cancer, marantic endocarditis, trousseau's syndrome.

Received: 01 January 2022 **Accepted:** 17 April 2024 **Type of Article:** CASE REPORT **Specialty:** Gastroenterology

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Background

Pancreatic cancer, which is the sixth most common cause of cancer death in the UK, is a notorious disease due to its late presentation, early metastasis, and poor survival rates. Early pancreatic cancer symptoms are often vague and nonspecific (frequently epigastric discomfort or dull backache), and their significance is frequently overlooked. More than two thirds occur in the head of the pancreas and classically present with painless, progressive, obstructive jaundice. Tumors in the body and tail of the pancreas generally occur in patients presenting with nonspecific pain and weight loss and are much less likely to cause obstructive signs and symptoms. Patients sometimes present with epigastric pain which radiates to the back, obstructive jaundice with pale stool and dark-colored urine, acute pancreatitis, unexplained weight loss, malabsorption symptoms, but often the thromboembolic events are the early and only symptoms as we can see in this case.

Case Presentation

We are now writing the clinical events sequentially during the patient's hospital stay. A 41-year-old, healthy, and fit gentleman with no past medical history was admitted with left-sided weakness, slurred speech, and facial drop. He also had a fever and mild headache at admission. He denied having any cough, shortness of breath, chest pain, palpitations, abdominal pain or bowel-bladder symptoms. He had two doses of COVID-19 vaccine and never had COVID-19. Repeated COVID-19 PCR swabs were negative throughout the hospital stay. He was not on any regular medications or over-the-counter medications. There was no family history of any stroke, heart attack, or cancer and no history of recent travel to abroad. He has smoked 5-10 cigarettes per day since adolescence and drinks 1-2 cans of beer occasionally. He has a stable relationship with his female partner. He denied any use of illicit drugs. At admission, on systemic examination, he only had left-side

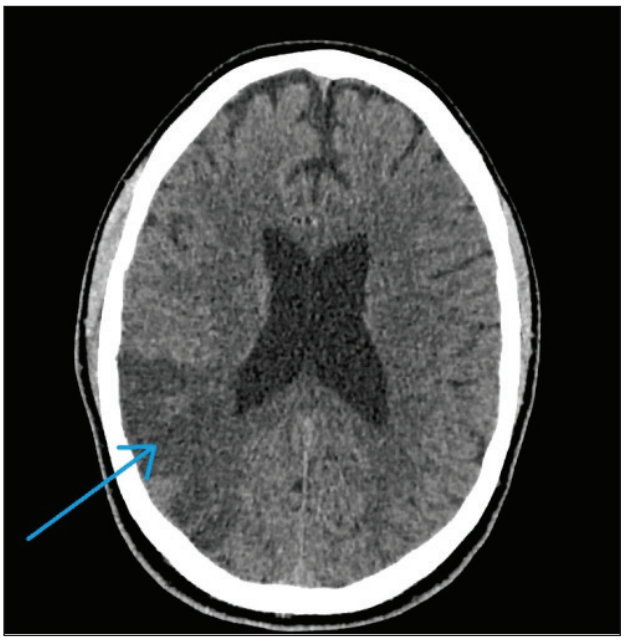

Figure 1. *CT of the head: Right temporal gyrus acute ischaemic stroke with mild mass effect, no intracranial haemorrhage. 194 × 196 mm (96 × 96 DPI).*

hemiparesis with mild left-side sensory neglect and upper motor neuron type of facial nerve palsy with no signs of meningism. GCS was 15. Cardiovascular, respiratory, and abdominal examinations were unremarkable. Vital signs were stable except for a mild rise in temperature of 37.8°C. He was admitted to the stroke team. NIHSS was 2 at admission. He underwent computed tomography (CT) of the head which showed right temporal gyrus acute ischemic stroke with mild mass effect, and no intracranial hemorrhage (Figure 1). He was not thrombolysed as the onset of symptoms was more than 4.5 hours and due to the sub-acute CT head changes as per the stroke consultant. Blood tests showed high CRP 202, WBC 20.8 with normal hemoglobin, renal function, HbA1C, and lipid profile. The electrocardiogram showed sinus tachycardia and the chest X-ray was normal with no foci of infection. Vasculitis and auto-immune screen were negative. HIV, hepatitis, and syphilis screening were negative. He also mentioned about left leg pain for a few weeks. Ultrasound Doppler of the left leg showed a large occlusive thrombus from the left common femoral vein to the superficial femoral vein. He was started on a treatment dose of low molecular weight heparin. He later had magnetic resonance imaging (MRI) of the head and magnetic resonance of the carotids which showed multifocal cerebral and cerebellar infarcts with cytotoxic oedema, and normal carotid arteries (Figure 2a-c). The echocardiogram showed low normal left ventricle function with an ejection fraction of 57%, apex and septum dyskinetic, and chambers were not dilated. The anterior and posterior mitral valve was mildly thickened but mobile with mild mitral regurgitation, trace tricuspid regurgitation, and pulmonary regurgitation. He continued to spike his temperature and even has been on broad-spectrum antibiotics since admission. The microbiology team advised to start on IV meropenem, IV vancomycin, and IV metronidazole. He started being treated for infective endocarditis. He didn't have any peripheral signs of infective endocarditis. On 9th day, the liver function test was done and came back deranged with bilirubin 13.7, alanine aminotransferase 212, alkaline phosphatase 188, gamma-glutamyl transferase 415, albumin 29 with normal INR and platelets. Previous liver function tests were normal. He underwent CT of the chest, abdomen, and pelvis with contrast to find out the cause of continued fever and deranged liver function test. The result showed multiple liver metastasis without obvious primary tumor, bilateral kidney infarcts and splenic infarcts, and bilateral small pulmonary embolism in both lower lobes (Figure 3). The cardiology team was contacted for a transesophageal echocardiogram (TOE) to rule out infective endocarditis. TOE was done in theatre which showed myxomatous mitral valve and mitral valve vegetation. A cardiology multidisciplinary team meeting was held for the management. They advised not to surgical intervention and to continue with medical management with intravenous antibiotics. Blood culture came back negative three times.

The patient became more confused and a repeat CT of the head was done which showed the evolution of multifocal cortical and cerebellar infarcts with new prominent involvement of the left dorsolateral frontal lobe and left anterior parietal regions, not visible on previous scans. No intracranial hemorrhage or local mass effect or ventricular dilatation was found. He had another CT of the chest, abdomen, and pelvis with contrast which showed multifocal low attenuation liver lesions which are stable. The lesion could be a liver abscess or metastasis with no source of primary tumor. The bilateral kidney and splenic infarcts are stable with no lymphadenopathy and bony lesions.

The Gastroenterology team was contacted, and we agreed with the plan of an MRI of the liver for further study. Non-invasive liver tests: autoimmune liver antibodies, alpha-1 antitrypsin, serum ceruloplasmin, and iron studies were normal. MRI of the liver reported that the primary malignancy is in the tail of the pancreas with hypo vascular liver metastasis. The scan was limited due to motion artefacts though (Figure 4). Ultrasound-guided biopsy of the liver lesion was planned. Cancer screening showed high CA-19-9, >10,000.0, normal alpha feto protein, and prostate-specific antigen level. Antiphospholipid antibodies were negative. Brucella, Bartonella, Chlamydia, Amoeba, and Cat-scratch disease screen were negative. We took a further history from his mom who mentioned that the patient had right leg pain 3 months ago and it was treated as an ankle sprain by the GP. Then he had an ambulatory emergency care presentation in the hospital a month later with left leg pain and was treated as left leg cellulitis. He was discharged on the same day with an oral antibiotic. D-Dimer was 6801 and CPR 24 at that time.

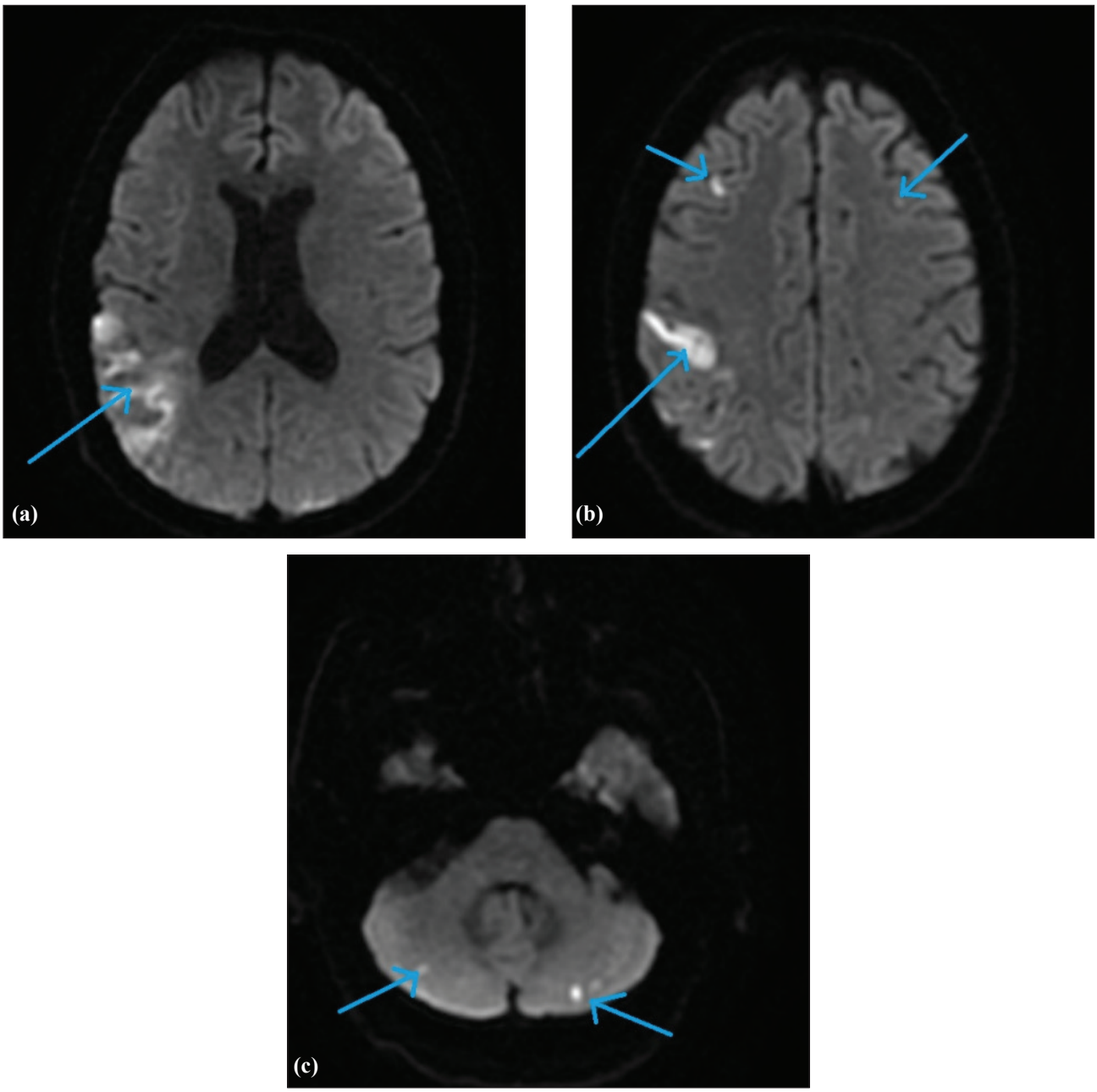

Figure 2. *(a) MRI of the head DWI sequence: Multifocal cerebral and cerebellar infarcts with cytotoxic oedema. 167 × 184 mm (96 × 96 DPI). (b) MRI of the head DWI sequence: Multifocal cerebral and cerebellar infarcts with cytotoxic oedema. 160 * 175 mm (96 × 96 DPI). (c) MRI of the head DWI sequence: Multifocal cerebral and cerebellar infarcts with cytotoxic oedema. 165 * 165mm (96 × 96 DPI.*

Unfortunately, he became more unwell, confused, and disoriented. The palliative team was involved, and it was decided after the discussion with the family to keep him comfortable and not for further investigation or intervention. He passed away peacefully the next day. It is clear that most likely he had Trousseau's syndrome 3 months ago and the embolic phenomena were due to Marantic Endocarditis secondary to advanced pancreatic cancer.

Discussion

Marantic endocarditis

Marantic endocarditis, currently named as non-bacterial thrombotic endocarditis (NBTE) is a consequence of a hypercoagulable state due to chronic inflammatory conditions, autoimmune diseases, and malignancy with complex pathogenesis. It is characterized by the deposition of fibrin thrombi in previously undamaged heart valves with the absence of bloodstream bacterial infection. It has rarely been reported as antemortem [1].

As the vegetations are more friable, the NBTE can cause systemic thrombo-embolism more rapidly and extensively than infective endocarditis. Sometimes the patients' neurological manifestations precede the diagnosis of advanced pancreatic cancer. The preferred diagnostic test for NBTE is TOE which is more sensitive in the detection of vegetation than the transthoracic approach. Recommended treatment is therapeutic anticoagulation

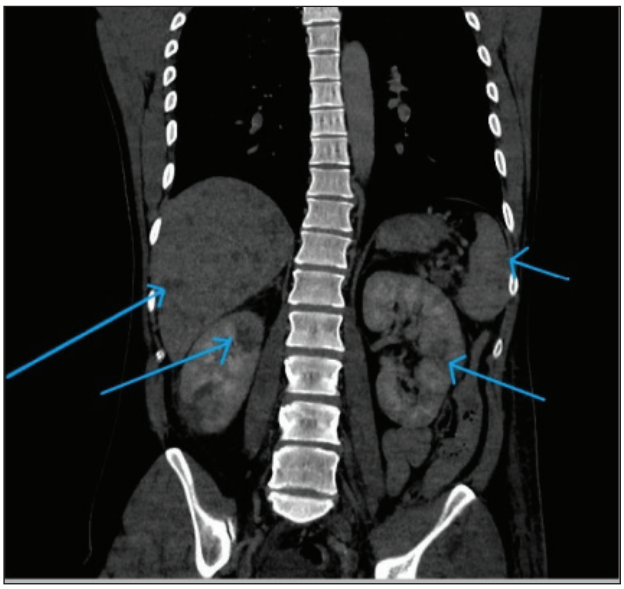

Figure 3. *CT of the chest, abdomen and pelvis with contrast: Multiple liver metastasis without obvious primary tumor, bilateral kidney infarcts and splenic infarcts, bilateral small pulmonary embolism in both lower lobes. 188 × 166 mm (96 × 96 DPI).*

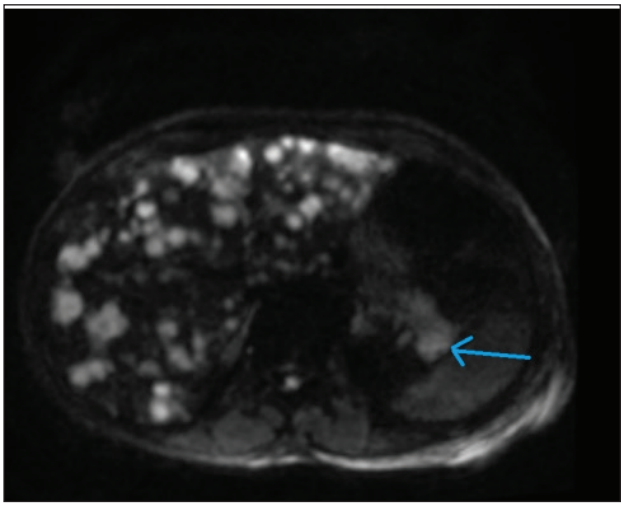

Figure 4. *MRI of the liver: Primary malignancy is in the tail of pancreas, 35 × 20 mm with hypovascular liver metastasis. The scan was limited due to motion artefacts. 220 × 172 mm (96 × 96 DPI).*

with unfractionated heparin or low molecular weight heparin and the treatment of underlying cause [2].

Trousseau syndrome

Trousseau syndrome, also commonly referred to as Trousseau's sign of malignancy to avoid confusion with Trousseau's sign of latent tetany is a type of paraneoplastic syndrome caused by adenocarcinomas, predominantly gastric, pancreatic, and pulmonary, presenting as recurrent and migrating episodes of thrombophlebitis. The pathophysiology of the phenomena is not well established, but the mucin compounds produced by adenocarcinomas have been found to interact with the selectin family of adhesion molecules, leading to thrombocyte activation and aggregation.

It can cause arterial and venous thrombosis and NBTE [3]. The treatment involves therapeutic anti-coagulation and management of underlying malignancy.

Conclusion

The diagnosis of early pancreatic cancer is challenging and needs careful and detailed clinical assessment [4]. Moreover, the cause and trigger of unprovoked thrombo-embolism should be properly investigated to rule out any underlying malignancy and the use of Wells score is important for the proper investigation and management [5].

What is new?

There are few cases of Marantic endocarditis and Trousseau's syndrome. This case highlights the severity and complexity of the diagnosis of pancreatic cancer and its complications.

List of Abbreviations

CT	Computed tomography
MRI	Magnetic resonance imaging
NBTE	Non-bacterial thrombotic endocarditis
TOE	Transesophageal echocardiogram

Conflicts of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Funding

None.

Consent for publication

Informed consent was taken from the patient to publish this case in a medical journal.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Male, 41-year-old
2	**Final diagnosis**	Advanced pancreatic cancer with liver metastasis complicated by multi organ embolic infarcts.
3	**Symptoms**	Fever, headache, left leg pain, left sided weakness, slurred speech, facial drop.
4	**Medications**	Treatment dose of LMWH, IV antibiotics.
5	**Clinical procedure**	None.
6	**Specialty**	Gastroenterology