CASE REPORT

Syphilitic pancreatitis: A rare mimicker of our time

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We present an unusual case of syphilitic pancreatitis and ascending aortitis in a 41-year-old HIV-negative male patient presenting to a tertiary institution with obstructive jaundice. After a battery of investigations that included computed tomography (CT) and 18F-labelled fluorodeoxyglucose positron emission tomography/CT (18F-FDG PET/CT) imaging, syphilis serology and histology, a diagnosis of tertiary syphilis was made. The patient responded favourably to antibiotics, with resolution of all lesions on FDG PET/CT 13 weeks after initiation of therapy. Even though tertiary syphilis is a rare entity, it should be earmarked as a mimicker of other pathological conditions, including, in this case, primary pancreatic malignancy.


Syphilis, caused by the bacterium *Treponema pallidum*, is a serious public health concern owing to its worldwide reach and associated complications. According to a global health estimate in 2015, syphilis was responsible for 92 272 deaths.

Syphilis may follow a course traditionally divided into primary, secondary, latent and tertiary stages over a period of many years. Primary syphilis is characterised by the appearance of a single painless lesion (the chancre) at the site of inoculation. Primary lesions resolve spontaneously, even in untreated cases. The secondary stage occurs 6 - 8 weeks later, when mucocutaneous lesions are most common, although dissemination to any organ is possible. This stage also demonstrates spontaneous resolution. In the latent stage, clinical manifestations are absent. Few infected individuals progress to tertiary syphilis.

Tertiary syphilis typically manifests as gummatous (‘benign syphilis’), cardiovascular syphilis or neurosyphilis. It does, however, occasionally present in unusual forms and should be recalled by its moniker as ‘the great mimicker’. Acquired syphilis of the pancreas is very rarely observed. Patients with syphilis of the pancreas have a variable clinical picture, ranging from asymptomatic to features of chronic pancreatitis, pancreatic tumours or diabetes mellitus. Patients frequently present with nonspecific symptoms. Syphilis of the pancreas may occur in a sclerous and gummatous form; a combination of the two forms is also found. The symptoms of syphilitic pancreatitis differ slightly from those of other pancreatic diseases, and the pancreas only is so seldom affected that the symptoms are frequently masked by those of involvement of the other viscera.

We present the case of a 41-year-old man, who was initially being worked up for a pancreatic tumour; however, several investigations including histopathology and 18F-labelled fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) were compatible with tertiary syphilis with pancreatic involvement. This is a rare case, and a good teaching case of tertiary syphilis mimicking a pancreatic tumour.

**Ethical approval**
The study was approved by the Health Research Ethics Committee of Stellenbosch University (ref. no. C19/01/003), and the patient signed an informed consent form.

**Clinical presentation and management**
The patient, an HIV-negative man, initially presented to a peripheral hospital with a 3-week history of obstructive jaundice. An ultrasound scan demonstrated a dilated common bile duct and pancreatic duct, as well as hypoechoic liver lesions, upon which a preliminary diagnosis of metastatic cholangiocarcinoma was made. The patient was referred to Tygerberg Hospital, Cape Town, South Africa (SA), where an in-depth history revealed other symptoms, including nausea, early satiety, weight loss, anorexia, shortness of breath and recent onset of night sweats. Side-room investigations revealed a (normal) random finger-prick blood glucose of 6.5 mmol/L and anaemia, with a haemoglobin level of 8.5 mg/dL. At that stage, total bilirubin and conjugated bilirubin were 155 (reference range 5 - 21) µmol/L and 136 (reference range 0 - 3) µmol/L, respectively. The patient was admitted to a surgical ward for blood transfusion and further work-up. On admission, the lipase level was 108 (normal range 7 - 60) U/L.

The following day, a CT scan of the abdomen demonstrated an ill-defined hypoattenuating mass in the head of pancreas, with upstream parenchymal atrophy of the pancreatic body and tail (Fig. 1). Because of the pancreatic head mass, abrupt cut-off of the main pancreatic duct and markedly dilated common bile duct (double-duct sign) were observed. No plane of separation was identified between the mass and...
The mass appeared to infiltrate the medial aspect of the first part of the duodenum. Peritoneal deposits adjacent to the visceral surface of hepatic segment 5 and anterior to segment 3 (within the falciform ligament) were documented (Fig. 2). Interpretation of peripancreatic nodes was compromised owing to minimal intra-abdominal fat. Based on these imaging features, a diagnosis of unresectable pancreatic head cancer with peritoneal metastases was made. No intrahepatic metastases were evident.

The patient was initially scheduled for a Whipple procedure based on the findings of the CT scan and the clinical presentation. However, 5 days after his initial presentation, he underwent a staging laparotomy and omental biopsy of the presumed pancreatic cancer. Histology of the biopsy specimens exhibited fibroconnective tissue with non-necrotising granulomatous inflammation, which consisted of multinucleated giant cells, epithelioid macrophages and lymphocytes in a background of fibrosis (Figs 3 and 4). Features of malignancy were absent and a Ziehl-Neelsen stain was negative for mycobacteria. As the patient was feeling much better, he was discharged and requested to return, within 1 month, for a review of his test results at the infectious disease department. Thereafter, culture and a nucleic acid amplification test (Xpert MTB/RIF, USA) were performed, which were negative for tuberculosis. The patient was subsequently referred to the medical outpatient department because of a possible diagnosis of sarcoidosis.

Subsequent review at the outpatient department revealed an asymptomatic patient with spontaneous resolution of jaundice. Cardiac examination showed a mildly displaced apex and a decrescendo diastolic murmur consistent with aortic regurgitation. Chest radiography, requested the same day, revealed that the mediastinum was widened, with an increased cardiothoracic ratio. No hilar lymph nodes or lung lesions were seen. An electrocardiogram (ECG) demonstrated no clear abnormality. Echocardiography (performed the same day) confirmed aortic valve incompetence secondary to a thoracic aortic aneurysm, with root involvement and associated pericardial effusion. A CT was performed urgently, which showed a fusiform thoracic aortic aneurysm (measuring 61 × 71 × 123 mm) involving the aortic root, ascending aorta and aortic arch, without any evidence of dissection (Fig. 5), and a pericardial effusion (measuring 14 mm in maximal diameter). In the context of an aortic root aneurysm and non-caseating granulomatous histology of the peritoneal deposit, a syphilitic aetiology was suspected for the first time.

On blood sampling, the patient tested positive for *T. pallidum* antibodies and a rapid plasma reagent (RPR) test was reactive, with a titre of 256. Subsequently, FDG PET/CT was performed to evaluate uptake in the pancreatic lesion, determine the extent of the disease, identify possible additional biopsy sites and confirm whether the aortic root

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**Fig. 1.** Contrast-enhanced computed tomography of the abdomen (portovenous phase) (pancreas protocol). The arrow marks the hypoattenuating, ill-defined mass in the head of pancreas (slice thickness 1.5 mm).

**Fig. 2.** Contrast-enhanced computed tomography of the abdomen (portovenous phase) (pancreas protocol). The arrow marks one of several soft-tissue nodules, thought to represent peritoneal metastatic deposits from a pancreatic primary lesion, but later shown to represent syphilitic gummatous inflammatory deposits (slice thickness 1.5 mm).

**Fig. 3.** Low-power view (H&E × 100) of omental biopsy, showing extensive fibrosis with non-necrotising granulomatous inflammation.
aneurysm represented an active vasculitis. PET showed moderate uptake in all lesions previously documented on CT (including the pancreatic head lesion), as well as an additional site of disease in paravertebral soft tissue, between the 4th and 5th ribs on the left (Fig. 6). Moderate, circumferential uptake was also seen in the aortic root aneurysm, which was consistent with an active inflammatory process. Interestingly, increased uptake was also observed in the pulmonary trunk. By now, all the identified pathology was considered to be attributable to tertiary syphilis.

Angiography to assess the coronary ostia showed narrowing of the left main stem and right coronary ostia. Aortic regurgitation was graded as moderate.

The patient received a once-off dose of penicillin VK (2.4 million units intramuscularly stat), followed by a 10-day course of intravenous penicillin G (4 million units 4-hourly). Serial measurements of the RPR titre demonstrated a steady decrease over the next 4 months. A repeat PET/CT scan performed 3 months later documented marked reduction in the avidity of vascular uptake and a resolution of all other lesions, including the pancreatic head mass (Fig. 7).

**Discussion**

The diagnosis of tertiary syphilis can be difficult. Our patient presented with dyspeptic phenomena, which are characteristic of the pseudotumoural form of pancreatic syphilis, but relatively nonspecific. Imaging findings were typical of a primary pancreatic malignancy. Differential diagnoses were seriously considered after an omental biopsy demonstrated granulomatous pathology. The possibility of pancreatic tuberculosis had to be entertained, especially in the SA context. While tuberculous infections are mostly associated with caseous necrotising granulomas, non-necrotising granulomas may also be present and Ziehl-Neelsen stains may be negative. A diagnosis of sarcoidosis in the absence of pulmonary disease or mediastinal lymphadenopathy would have been atypical, but only after an aortic root aneurysm was found, the diagnosis of tertiary syphilis was suspected and subsequently confirmed by the RPR test. The excellent response to penicillin, to which syphilis remains sensitive, supported the diagnosis.

To our knowledge, only a few case reports of syphilitic pancreatitis have been published since the original description of the entity by Rokitansky. These have highlighted the risk of misdiagnosis of a pancreatic malignancy. A Korean case report of syphilitic granulomatous pancreatitis described similar findings of an obstructive mass of low density in the pancreatic head. This was initially diagnosed as a primary pancreatic neoplasm, for which a Whipple procedure was performed. Macroscopically, the pancreas appeared fibrotic, with a well-preserved common bile duct. Microscopically, numerous interlobular non-caseating granulomas with multinucleated giant cells were identified. These features were consistent with the imaging findings and omental histology of our own case.

A case report by Bhowmick et al. described a patient who presented with jaundice, diabetes and hepatomegaly, which raised concern regarding pancreatic malignancy. Hepatic histology showed evidence of nonspecific granuloma and active hepatitis, but no cholestasis. The patient was treated successfully with antisyphilitic therapy. As far as we know, ours is the first description of syphilitic pancreatitis imaged with FDG PET/CT. However, several reports on the use of FDG PET/CT in the imaging of syphilitic pathology have been published. As a primarily granulomatous pathological condition, there is a strong rationale for using FDG PET, both to determine the extent of the tertiary syphilis and to monitor treatment response, as active macrophages are known to avidly accumulate FDG.

**Teaching points**

- Tertiary syphilis is rare, but could be a potential mimicker of various pathological conditions, including, as in our case, primary pancreatic cancer.
- The importance of multidisciplinary involvement in the work-up and management of complex and rare disease entities is emphasised.
• We highlight the potential value of FDG PET/CT to determine the extent of tertiary syphilis, to identify additional biopsy sites and to monitor therapy response.

Declaration. None.

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