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CASE REPORT

Unresectable pancreatic tumour? The issue is tissue

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ABSTRACT

The majority of tumours in the pancreas are adenocarcinomas for which therapeutic options are limited and which are associated with an unsatisfactory prognosis. However, alternative diagnoses may result in other therapeutic approaches with often a more favourable outcome. Hence, it is crucial to obtain a histological diagnosis before a definitive therapeutic plan can be devised. In this manuscript, a small series of pancreatic tumours other than adenocarcinoma are described.

KEYWORDS

Adenocarcinoma, histology, pancreatic cancer

What was known on this topic?
In rare cases, well treatable malignancies may present as an unresectable pancreatic adenocarcinoma. Tumour markers may help monitoring response to therapy but should not be used to confirm a diagnosis.

What does this add?
This article emphasises the importance of pathological confirmation of one's diagnosis in the case of an unresectable pancreatic tumour.

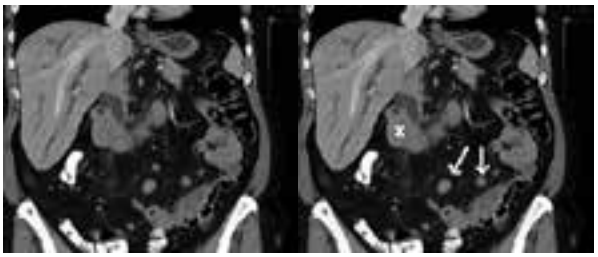
INTRODUCTION

Patients presenting with obstructive jaundice are often diagnosed with a tumour in the pancreas. Unresectable pancreatic adenocarcinoma can not be cured and has a dismal prognosis. In daily practice, the typical combination of clinical features and radiological findings, together with the lack of curative options, may result in refraining from pathological confirmation.
We describe three patients with similar complaints of obstructive jaundice and an unresectable pancreatic tumour who, after pathological examination, turned out to have a more favourable prognosis with therapeutic options.

CASE REPORTS

A 65-year-old woman presented with weight loss, fatigue, dark-coloured urine and itching. Laboratory results showed a total bilirubin of 164 µmol/l (normal 2-20) and conjugated bilirubin of 106 µmol/l (normal <5), an alkaline phosphatase level of 381 U/l (normal <120), and a γGT of 600 U/l (normal <38). The tumour marker CA 19.9 was high: 655 U/l (normal <37). An abdominal computed tomography (CT) scan revealed a tumour in the pancreatic head (3 x 3.7 cm) together with dilated intra- and extrahepatic bile ducts and locoregional lymphadenopathy. There were no signs of distant metastasis (*figure 1*).
An ultrasound-guided lymph node biopsy was carried out which revealed no metastasis. We referred our patient to an academic centre to investigate possible resection of the tumour. However, because of the enlarged lymph nodes the tumour was considered to be unresectable. To treat the obstructive jaundice a wall stent was placed during endoscopic retrograde cholangiopancreatography (ERCP). Of notice, a cytological examination of a bile duct brush revealed a low-grade B-cell non-Hodgkin lymphoma. This diagnosis was confirmed after external revision of the lymph node biopsy. A bone marrow aspiration revealed no localisation of the lymphoma.
Chemotherapy was started to treat a stage III follicular lymphoma using rituximab, cyclophosphamide, vincristin and prednisone (R-CVP). However, during the first course

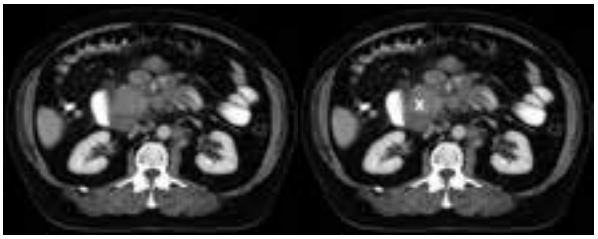
Figure 1. *Abdominal CT scan showing the tumour in the pancreatic head (marked by X in figure 1a), dilated intra- and extrahepatic bile ducts as well as loco regional lymphadenopathy (marked by arrows in figure 1a)*



the patient noticed a lump in her right breast (which in retrospect could not be seen on the CT scan), which turned out to be a diffuse large B-cell non-Hodgkin lymphoma.
To treat this transformed high-grade lymphoma chemotherapy was continued using R-CVP plus doxorubicin (R-CHOP). After three courses a PET/CT scan showed complete remission of the lymphoma.
After a total of six courses, because transformed lymphomas have a high chance of recidivating after just R-CHOP therapy, the lymphoma is currently consolidated with an autologous stem cell transplantation after 90Y-ibritumomab tiuxetan (Zevalin®) and carmustine, etoposide, cytarabine and melphalan (BEAM) chemotherapy and the patient is doing well.

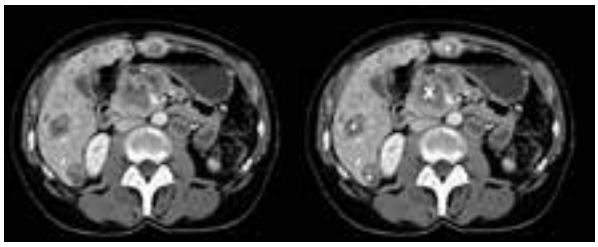
A 59-year-old man presented with abdominal pain, dark-coloured urine and light coloured stools. Laboratory results showed a total bilirubin of 67 µmol/l (normal 2-20) and conjugated bilirubin of 45 µmol/l (normal <5). An abdominal CT scan showed an unresectable pancreatic tumour invading the surrounding tissues (*figure 2*).
Histology of ultrasound-guided biopsies of the tumour revealed a small-cell neuroendocrine carcinoma. Serum chromogranin A, a marker for neuroendocrine tumours, was slightly elevated: 130 ng/l (<100). After six courses of etoposide/cisplatin a control CT scan showed complete remission. After a follow-up of five years the patient is still doing well.

Figure 2. *Abdominal CT scan showing the pancreatic tumour invading surrounding tissues (marked by X in figure 2a)*



A 56-year-old woman presented with abdominal pain and weight loss. On physical examination the liver was enlarged with an irregular surface. The tumour marker CA 19.9 was elevated: 81 U/l (<37).
An abdominal CT scan showed a tumour in the pancreatic head with liver metastases and peripheral lymphadenopathy (*figure 3*).

Figure 3. *Abdominal CT scan showing the tumour in the pancreatic head (marked by X in figure 3a) and liver metastases (marked by * in figure 3a)*



Histological examination of a liver biopsy showed a large cell carcinoma with neuroendocrine differentiation, suggesting an atypical carcinoid. This diagnosis was confirmed by high uptake on an octreotide scan together with an elevated serum level of chromogranin A: 354 ng/l (<100).
We referred our patient to an academic centre where she was treated with radioactive labelled octreotide (Lutetium-177-ocreotate). A control CT scan after four courses showed regression and the patient is doing well after a follow-up of almost two years.

DISCUSSION

Pancreatic adenocarcinoma is diagnosed in over 90% of all pancreatic malignancies. Unresectable pancreatic adenocarcinoma is a diagnosis with few therapeutic options and a very poor prognosis, with a median survival of only 3 to 6 months.[1,2]
However, not all unresectable malignant pancreatic tumours prove to be adenocarcinoma. A pancreatic tumour may be the first presentation of a malignant lymphoma.[3,4]
A tumour size of more than 6 cm at presentation, as well as peripheral lymphadenopathy, are clues that may lead to this diagnosis.[3,5]
In 1-2% of all cases the tumour appears to be a neuroendocrine tumour.[6,7] Pancreatic neuroendocrine tumours (PNETs) are rare and have different treatment options and a longer median survival.[6,8] The incidence of these tumours seems to be increasing, possibly due to improving radiological and pathological techniques such as endoscopic ultrasound fine-needle aspiration (EUS-FNA).[1,9]

Rarely, the tumour appears to be benign, for example concerning (IgG4-mediated) autoimmune pancreatitis.[10]

These cases show that both laboratory and radiological findings may be misleading in the case of an unresectable pancreatic tumour. An elevated CA 19.9 does not exclude a diagnosis other than pancreatic adenocarcinoma, and sometimes an unresectable pancreatic tumour may be well treatable. Given the fact that other, benign conditions such as cirrhosis and cholangitis may also lead to elevated levels, the diagnostic use of CA 19.9 will lead to a high rate of false-positive results. It may provide valuable information on response to therapy but, with a sensitivity of only 80% in symptomatic individuals, should not be used as a diagnostic tool.[11,12]

In order to establish a diagnosis, EUS-FNA has become an important tool. The new guideline 'pancreatic carcinoma' by the Comprehensive Cancer Centre the Netherlands (IKNL) states that, in the case of an unresectable pancreatic tumour, EUS-FNA is superior to ultrasound or CT-guided biopsy.[13] Additionally, in patients with suspected pancreatic malignancy in whom a CT scan is negative or inconclusive, EUS-FNA should be considered to establish a diagnosis, doing so in 88% of cases in a recent case series.[14]

We think that all patients diagnosed with an unresectable pancreatic tumour should have this diagnosis confirmed by pathological examination, ideally by histological biopsy but otherwise by EUS-FNA or ERCP-acquired cytology. This is in line with the IKNL guideline 'pancreatic carcinoma' version 2.0.[13]

CONCLUSION

An unresectable pancreatic tumour is not always an unresectable adenocarcinoma with an infaust prognosis. Pathological confirmation of the diagnosis is always indicated and may be lifesaving.

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