CASE REPORT

Metastatic pancreatic cancer: abdominal pain in a 22-year-old woman

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SUMMARY

Pancreatic cancer remains fourth among cancer-related deaths. Its diagnosis is often missed, owing to its vague abdominal symptoms, leading to a diagnosis of stage IV pancreatic cancer. FOLFIRINOX chemotherapy was administered to the patient in this report, resulting in significant improvement based on tests of biological markers as well as radiographic resolution of the metastatic disease. A keen awareness of this condition along with appropriate diagnostic tests can allow for an earlier diagnosis and may impact its high mortality.

BACKGROUND

Pancreatic cancer is one of the leading causes of cancer deaths due to its rapid spread and difficulty in detection at an early stage.¹ Findings of metastatic pancreatic cancer in our very young patient should create a more keen awareness in the broader differential diagnosis of unexplained abdominal pain, allowing for early appropriate diagnostic tests that may impact its high mortality, as evident in our patient.

CASE PRESENTATION

A 22-year-old non-obese Asian woman, with no pertinent medical history, first developed reflux-type symptoms, and had several episodes of mid-back and abdominal pain beginning in July 2013. She had no history of pancreatitis or prior history of hospital admissions for abdominal pain. She did not drink alcohol and was a non-smoker. The remainder of the review of systems was not significant. The family history was negative for gastrointestinal malignancy. Physical examination showed mild epigastric tenderness. The patient was initially empirically treated with a proton pump inhibitor, showing marginal improvement. Despite the treatment, she had persistent progressive pain, which led to further diagnostic evaluation including endoscopy and computerised axial tomography (CT) of the abdomen, revealing an abnormality in the head of the pancreas.

INVESTIGATIONS

Diagnostic evaluation included an oesophagogastroduodenoscopy (16 August 2013), which showed only mild gastritis and reflux oesophagitis; an abdominal ultrasound (27 September 2013) was notable for a prominent pancreatic duct with no definitive mass. An abdominal computerised axial tomography with contrast (3 October 2013) showed a lobular-appearing low-density lesion, 1.1×0.6 cm, in the uncinate process of the

pancreas (figure 1), and multiple small low-density lesions scattered throughout the liver (figure 2).

MRI performed on 6 December 2013 showed pancreatic ductal dilation secondary to a 15 mm ill-defined mass in the pancreatic head. Additionally, at least 2 hepatic lesions were seen, mildly T2 hyperintense and hypovascular, measuring 6 and 13 mm, respectively. An endoscopic ultrasound (9 January 2014) showed a heterogeneous, hypoechoic, ill-defined mass, measuring 21.2×20.5 mm, in the pancreatic neck. This was seen obstructing the pancreatic duct, with upstream dilation to 6.3 mm in the neck of the pancreas and 4.1 mm in the body and tail of the pancreas. Endoscopic ultrasound findings of chronic pancreatitis were seen in the body and tail, including lobulation, stranding, atrophy and focal calcifications. The bile duct was not obstructed by the mass, and no pericoeliac or other worrisome lymph nodes were seen.

Subsequently, the patient underwent an axial CT-positron emission tomography (CT-PET) scan (16 January 2014) confirming a hypermetabolic, mildly low-density lesion, measuring 27×13 mm, within the pancreatic neck, with maximal standardised uptake value of 8.1. The pancreatic duct was dilated up to 7 mm, and vascular involvement with abutment of the narrowed superior mesenteric artery was seen. The CT-PET scan confirmed occlusion of the portal vein near the portal venous confluence. The CT-PET scan also confirmed multiple low-density liver lesions with peripheral

Figure 1 Axial CT image of lobular-appearing low-density lesion in the uncinate process of the pancreas pretreatment on 3 October 2013.

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Figure 2 Axial CT image of multiple small low-density lesions in the liver pretreatment on 3 October 2013.

enhancement, including the largest measuring 10 mm with maximal standardised uptake value of 4.5, and at least seven other subcentimetre hypodense lesions present. These liver lesions were strongly indicative of metastatic disease. There was no hypermetabolic lymphadenopathy.

Relevant diagnostic studies (8 November 2013) revealed a normal complete blood count: white cell count of $7.4 \times 10^9/L$, haematocrit of 39.5% and platelet count of $157 \times 10^9/L$. The comprehensive metabolic panel revealed normal liver function tests. The patient underwent an endoscopic ultrasound with biopsy (9 January 2014), which revealed a mucin-producing adenocarcinoma, consistent with pancreatic ductal origin (figure 3). The CA19-9 level was 3840 U/mL (21 January 2014).

TREATMENT

On the basis of the patient's age, performance status and comorbid conditions, she was an appropriate candidate for the FOLFIRINOX regimen, the most aggressive option to treat her stage IV pancreatic cancer.

Figure 3 Adenocarcinoma, consistent with pancreatic ductal origin. Biopsy obtained via endoscopic ultrasound on 9 January 2014.

Treatment of FOLFIRINOX chemotherapy began on 28 January 2014 (figure 4). The regimen comprised of calcium folinate 350 mg, oxaliplatin 85 mg/m², irinotecan 180 mg/m², 5-fluorouracil 400 mg/m² and 5-fluorouracil 2400 mg/m² intravenous infusion over 46 h. She underwent 12 cycles of FOLFIRINOX followed by maintenance capecitabine. Chemotherapy was tolerated well. She did develop transient thrombocytopenia with mild transaminitis, which warranted a dose reduction. She also developed mild transient peripheral sensory neuropathy, alopecia, mouth dryness and fatigue. Suspected seizures were reported without any structural or metabolic sources found. Neutropenia was not an issue, but she did receive primary prophylaxis with Neupogen after each treatment cycle. Owing to her young age and the potential for future infertility with use of chemotherapy, she was referred to the reproductive endocrine fertility department to consider egg harvesting or ovarian suppression.

OUTCOME AND FOLLOW-UP

At the 12-month follow-up after beginning treatment, previously visualised hepatic metastases were not visualised. The patient had both clinical and radiographic resolution of her symptoms and her biomarkers were, at writing, within normal range (CA-19-9 is 31 U/mL). Figures 5 and 6 show post-treatment improvements in the pancreas and liver, respectively. To evaluate vascular involvement, follow-up axial CT of the abdomen after completion of chemotherapy showed no change from pre-chemotherapy, with stable short segment occlusion of the superior mesenteric vein (SMV) and portal vein.

DISCUSSION

FOLFIRINOX worked well for this patient, as it is the most active combination chemotherapy regimen for the management of pancreatic cancer and it has a higher response rate than gemcitabine monotherapy. Both oxaliplatin and irinotecan are important ingredients of the regimen.

Our patient had no risk factors for pancreatic cancer. Persistent unexplained abdominal pain led to further diagnostic work up revealing the pancreatic cancer. No major medical organisations have recommended routine screening of patients who are not at increased risk for pancreatic cancer. However, recent data show that exosomes containing the surface protein glypican-1 (GPC-1) may be available to screen individuals at risk for pancreatic cancer. The role of this screening in average-risk patients is yet to be determined but it could help in earlier diagnosis with improved prognosis.²

We believe our patient responded very well due to her young age and tolerability of aggressive chemotherapy without significant need for delay in treatment or significant dose reductions. She continues to remain under close monitoring.

Pancreatic cancer remains the fourth leading cause of cancer deaths in the USA, with 43 920 new cases in the year 2012 alone.³ The incidence increases with age and the majority of cases occur in patients over the age of 60 years. It was found, from research in the UK, that <0.4% of cases have been reported to occur in ages <34 years.⁴ Highest incidences have occurred in Europe and North America, and the lowest in Asia and Africa, with African-Americans and women having an increased risk.⁵

Pancreatic cancer can be classified based on its origin: cancer formed in the pancreatic ducts accounts for more than 90% of cases and is known as adenocarcinoma; cancer formed in the hormone-producing cells accounts for 10% of cases and is known as endocrine cancer.³

Figure 4 Cancer Antigen 19-9 levels before treatment (shown with black line) and after treatment (shown in red line). FOLFIRINOX worked well for this patient as it is the most active combination chemotherapy regimen in management of pancreatic cancer and it has a higher response rate than gemcitabine monotherapy.

Mild risk factors include alcohol use (more than 4 drinks/day), obesity (body mass index $>30 \text{ kg/m}^2$), having Breast Cancer-1 (BRCA1) gene carrier, polycyclic or chlorinated hydrocarbon exposure, type II diabetes mellitus (for more than 5 years), familial adenomatous polyposis, familial non-polyposis (Lynch syndrome), having a first-degree relative with pancreatic cancer and tobacco use or exposure (25–30% of pancreatic cancer cases).³

Moderate risk factors include having Breast Cancer-2 (BRCA2) gene carrier, chronic pancreatitis, cystic fibrosis and having two first-degree relatives with pancreatic cancer.³

Severe risk factors (more than a 10-fold increased risk) include familial atypical multiple mole melanoma, having three first-degree, second-degree or third-degree relatives with

pancreatic cancer, hereditary pancreatitis and having Peutz-Jeghers syndrome.³

Pancreatic tumours can often grow for some time without any symptoms. Symptoms when developed, may include: unexplained weight loss, nausea and vomiting, loss of appetite, early satiety, jaundice, abdominal pain, indigestion, back pain, depression, new onset of type II diabetes mellitus (in patients over 50 years of age), recurring thrombophlebitis, dark urine with pale stools (with involvement of the head of the pancreas), left supraclavicular lymphadenopathy and subcutaneous nodules of fats (pancreatic panniculitis).³

Pancreatic cancer can be identified by general markers or tumour markers. General markers include alkaline phosphatase and conjugated serum bilirubin. Tumour markers include

Figure 5 Axial CT image showing pancreas post-treatment on 16 September 2014.

Figure 6 Axial CT image showing liver post-treatment on 16 September 2014.

Table 1 Staging and prognosis of pancreatic cancer based on Tumours, Nodes, Metastasis⁷

Stage	Tumour grade	Node status	Distant metastases	5-Year survival, %	Characteristics
IA	T1	N0	M0	14	Tumour <2 cm
IB	T2	N0	M0	12	Tumour >2 cm
IIA	T3	N0	M0	7	Tumour extends beyond pancreas but no involvement of the coeliac or superior mesenteric artery
IIB	T1-T3	N1	M0	5	Regional lymph node metastasis
III	T4	N0-N1	M0	3	Tumour involves the coeliac and mesenteric artery
IV	T1-T4	N0-N1	M1	1	Distant metastases

Cancer Antigen 19-9 (used for diagnosis and prognosis, not screening), β -human chorionic gonadotropin (a prognostic indicator) and Cancer Antigen 72-4 (a prognostic indicator).

Pancreatic cancer can be staged by Tumour, Nodes, Metastasis (TNM) staging (table 1) and clinical staging based on resectability with four main stages: resectable disease, borderline resectable disease, locally advanced unresectable disease and metastatic disease.⁵ Resectable disease is based on the absence of extrapancreatic disease without evidence of direct invasion of the SMV or the coeliac axis. Borderline resectable disease is characterised by the absence of extrapancreatic disease with some superior mesenteric artery encasement and short segment SMV occlusion. Locally advanced and unresectable disease is based on the absence of extrapancreatic disease, unreconstructable SMV and portal vein occlusion, and lymph node involvement beyond field of resection. Metastatic disease is classified as any disease involving distant metastasis.

Treatment of pancreatic cancer involves surgical options and chemotherapy. Surgical options include Whipple procedure, distal pancreatectomy, total pancreatectomy or palliative surgery.⁷ The Whipple procedure is used for cancer contained in the head of the pancreas. The procedure involves resection of the head of the pancreas, the duodenum, the gall bladder and a portion of the bile duct. A distal pancreatectomy involves the removal of the tail and the body of the pancreas, and a possible splenectomy. A total pancreatectomy involves the removal of the entire pancreas. Palliative surgery is performed when pancreatic cancer is in its advanced stages and cannot be removed surgically; it is used to alleviate symptoms.

Pancreatic cancer may also be treated by a chemotherapy regimen comprised of oxaliplatin, irinotecan, fluorouracil and leucovorin (FOLFIRINOX) or gemcitabine as first-line therapy in patients with metastatic pancreatic cancer as opposed to other alternative treatments such as gemcitabine/nab-paclitaxel or gemcitabine monotherapy. FOLFIRINOX was shown in a phase III French cooperative group trial to be superior to gemcitabine monotherapy for patients with metastatic pancreatic cancer.⁸ Objective response rate was 31.6% in the FOLFIRINOX group versus 9.4% in the gemcitabine group in the study. FOLFIRINOX has been shown in recent studies to have a survival advantage compared to other chemotherapy treatments.⁸ Other therapeutic options include a combination of nab-paclitaxel plus gemcitabine and erlotinib plus gemcitabine. The median overall survival was 11.1 months in the FOLFIRINOX group as compared with 6.8 months in the gemcitabine group. Median progression-free survival was 6.4 months in the FOLFIRINOX group and 3.3 months in the gemcitabine group.⁸

The overall median survival for pancreatic cancer can range from 24.1 months for stage IA to 4.5 months for stage IV.¹

Despite advances in the understanding of the disease process with improved diagnostics, the overall 5-year survival rate remains at <5%, mostly due to its vague non-specific symptoms. For such reasons, palliative care frequently becomes a challenge as the disease process continues, with increased focus directed on alleviating pain and managing the complications of tumour progression. With pancreatic head tumours, 75% of patients develop jaundice. These patients may warrant endoscopic placements of either Teflon or metal stents. The relief offered may enhance overall quality of life even when survival is limited. Most worrisome to patients and to their families is the aspect of pain, with 44% of patients experiencing severe pain.⁹ Most patients will require opioids around the clock. Percutaneous coeliac plexus block and intraspinal drug delivery (intrathecal or epidural) may be effective in select patients. Patients may develop intestinal obstruction that may need nasogastric suctioning, total parenteral nutrition and, occasionally, expandable metal stents in non-surgical candidates, as palliative measures.

Learning points

- ▶ Pancreatic cancer is one of the leading causes of cancer deaths, due to its rapid spread and difficulty in detection at an early stage.
- ▶ Screening of high-risk persons, with imaging methods and measurements of serum biomarkers, could allow for an early diagnosis.
- ▶ Many of the symptoms of pancreatic cancer can overlap with other medical conditions. A greater awareness of pancreatic cancer in the differential diagnosis of abdominal pain remains imperative for early diagnosis and intervention even in patients of young age. More cases are likely to be discovered and diagnosed with increased cognisance.

Competing interests None declared.

Patient consent Obtained.

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