Case Report 1
Metastatic Pancreatic Cancer

Simon Micallef & Sarah Vella
Reviewed by: Dr. Norbert Vella MD FRCP (London)

Case Summary:
A 69-year-old Caucasian woman who had recently been diagnosed with pancreatic cancer presented with severe low back pain associated with weakness and paresthesiae in her lower extremities. She had also developed urinary retention. She was diagnosed with spinal cord compression at T10-11 secondary to vertebral and epidural metastasis. In view of the poor prognosis, the patient was referred for palliative care.
This case documents spinal cord compression secondary to bone metastasis, a rare complication of pancreatic cancer.

Presenting Complaint:
A 69-year-old woman with known pancreatic cancer was admitted to hospital with severe low back pain as well as weakness and sensory disturbance in her lower limbs.
History of Presenting Complaint:
The patient developed the lower lumbar back pain about two weeks earlier but it became so severe that it was waking her up at night. Movement exacerbated the pain which would sometimes also radiate from her back to her legs.
Two days prior to her admission she began experiencing weakness and numbness in her lower extremities such that she began finding it hard to bear her own weight. She was also finding it increasingly difficult to completely void her urinary bladder.

Past Medical and Surgical History:
The patient suffers from Type II diabetes mellitus, hypertension and congestive heart failure (CHF). At 57 years of age she underwent spinal surgery for a herniated disc.
Two months prior to her last hospital admission she presented with epigastric pain, nausea and vomiting, melaena, loss of appetite and weight loss. A CT scan revealed a mass causing gastric outlet obstruction which was later shown to be a pancreatic tumour whilst the patient was undergoing a gastrojejunostomy. There is no documented adverse reaction to anaesthesia.

Drug History:
On admission to hospital, the patient was on the following medications:
- Glucophage and Glibenclamide for her diabetes
- Omeprazole and Metoclopramide to control the gastric symptoms
- Lisinopril and Carvedilol for her hypertension and CHF
- Pancrelipase (Creon) as a substitute for pancreatic digestive enzymes
- Protifar as a high protein feed supplement
- Ketoprofen for her back pain
- Palliative chemotherapy

She has no known drug allergies.

Family History:
Her sister had breast cancer.

Social History:
The patient never smoked, and has no past history of alcohol or drug abuse.

Systemic Enquiry:
Non-contributory.

Current Therapy:
Soon after being admitted to hospital the patient was put on oral Dexamethasone in an effort to decrease the oedema surrounding the metastatic lesion and thus protect the spinal cord from further injury. She was also on oral Etoricoxib (Arcoxia) to try and relieve her back pain, but its effect was minimal.

Physical Examination & Discussion of Results:
On admission to hospital, the patient had a Glasgow Coma Scale of 15. She was afebrile but appeared pale and dehydrated. There was no sign of jaundice, clubbing or dependant oedema. Her pulse rate was 72 beats per minute and regular, the blood pressure was 119/58 mmHg, and her heart sounds were normal. Chest auscultation elicited a few sparse wheezes over the left lung apex associated with decreased air entry.
Inspection of the abdomen revealed a supraumbilical midline laparotomy scar. On palpation the abdomen was soft but there was mild tenderness in the left iliac fossa. There was dullness to percussion over the suprapubic region which turned out to be a distended urinary bladder. No costo-vertebral tenderness was elicited. The bowel sounds were normal. Digital rectal examination revealed the presence of haemorrhoids.
On examination of the musculoskeletal system, the patient had normal tone and power in her upper extremities, but was found to be weak in both her lower limbs, proximally 2/5 and distally 5/5. There was also evidence of sensory impairment in both legs. Straight leg raising was limited by pain to 10° bilaterally.
The back pain along with the weakness and decreased sensation in the lower extremities and the urinary retention, were highly suggestive of spinal cord compression.

Differential Diagnosis:
- Vertebral metastasis from the pancreatic tumour
- Osteoarthritis
- Rheumatoid arthritis (usually affects cervical and not lumbar spine)
- Paget's disease of bone
- Psoriatic arthritis
- Ankylosing spondylitis (unlikely as first symptoms usually appear during one's twenties)

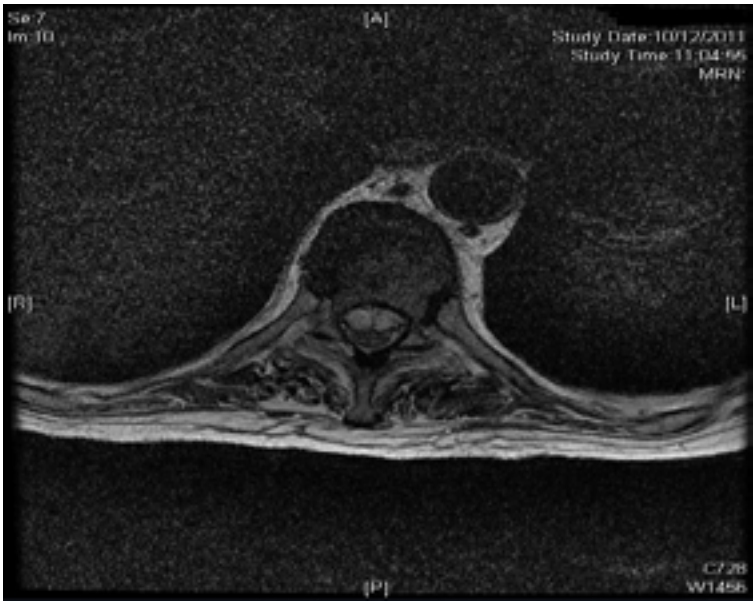
A diagnosis consisting solely of referred pain to the back due to the pancreatic tumour was unlikely considering the patient's other symptoms which included weakness and numbness in the lower limbs.

Diagnostic Procedures:
a) Laboratory tests:
The white cell count was high at 14.3x109/L with 13.3x109neutrophils/L. The lymphocyte count was low at 0.46x109/L as was the red cell count at 3.2x1012/L. This blood picture could be explained by the recent chemotherapy. It was also found that the patient had low levels of amylase (24u/l), calcium (1.91mmol/L) and sodium (132mmol/L). Random blood glucose was also taken as patients with pancreatic cancer may sometimes suffer from hyperglycaemic episodes but the result came back normal (8.03mmol/L). In conclusion, these blood test results, especially the anaemia with a haemoglobin level of 8.6g/dL, were suggestive of bone metastasis. Moreover, although not a very sensitive marker for bone secondaries, the alkaline phosphatase level was high at 223U/L.

b) Imaging Studies:
Plain radiograph of the lumbar spine showed severe degenerative changes.

The thoracic spine MRI revealed an epidural mass, 5 x 1cm, extending from the rostral aspect of the T10 vertebra down to the caudal aspect of T11. The spinal cord appeared to be displaced at the level of these 2 vertebrae, and the vertebral marrow signal was altered suggesting infiltration by neoplastic tissue. There were no signs of vertebral collapse or of intervertebral disc protrusions.
MRI of the cervical spine showed severe stenosis due to the degeneration of the intervertebral discs and the presence of osteophytes. A change in the intensity of the cord signal at the level of the C3 and C4 vertebrae indicated possible myelomalacia.

The patient's brain CT was normal.



Diagnosis:
The patient was diagnosed with spinal cord compression at the level of the T10 and T11 vertebrae, secondary to vertebral and extradural metastases from a previously diagnosed pancreatic tumour. Prognosis for this patient was poor with an average life expectancy of less than six months.

Further Management:
Following discussions with the patient, her immediate relatives, the neurosurgeons and the oncologists, it was decided that the patient could only be offered palliative care, including radiotherapy to her spine, for pain control.

Case Discussion:
Pancreatic cancer is the fourth leading cause of cancer-related deaths in North America. The most likely reason for this is that once patients present to their physician they are often already in the advanced stages of the disease rendering it virtually impossible to cure. Pancreatic cancer is more likely to affect men than women. The most common type is adenocarcinoma of the pancreas which affects the organ's exocrine glands. The endocrine part of the pancreas gives rise to a completely different type of cancer which is referred to as pancreatic neuroendocrine carcinoma or islet cell tumour.

The exact aetiology of pancreatic carcinoma is unknown but it has been found that the risk is higher in people who smoke, drink large amounts of alcohol or coffee, or ingest a lot of dietary fats. Also, recent studies have shown that there is a relationship between mutation of the BRCA2 gene and the incidence of pancreatic cancer as well as that of breast cancer. In our case, one could speculate that there could have been a common BRCA2 gene mutation between the patient and her sister who had suffered from breast cancer.

The clinical features of pancreatic cancer depend on the part of the pancreas that is affected. Tumours of the head of the pancreas usually present with painless jaundice which could also be associated with pruritus and anorexia. Jaundice occurs as a result of compression of the common bile duct in its course through the head of the pancreas. This type of obstructive jaundice can be distinguished from jaundice resulting from gallstone disease because the latter presents with a history of typical biliary colic. Moreover, Courvoisier's law states that, in the presence of gallstones, chronic inflammation and fibrosis prevent distension of the gall bladder such that it is not palpable. On the other hand, cancer of the head of the pancreas often distends the gall bladder rendering it easily palpable. Cancer affecting the body or tail of the pancreas presents with epigastric pain which often radiates to the back as well as loss of appetite and weight loss. The patient may also complain of nausea which could be the result of intestinal obstruction by the tumour. Diabetes mellitus and clinical depression are two conditions that can be associated with pancreatic carcinoma, either antedating it or occurring as a result of the cancer. Cases of patients diagnosed with either of these two conditions, and months or even years later developing pancreatic cancer, are currently being studied. The association with diabetes is due to the tumour affecting the insulin-producing β-cells of the pancreas resulting in hyperglycaemia. In our case, the patient was a long-time sufferer of type II diabetes mellitus but her blood glucose was well controlled with two oral hypoglycaemic agents. The relationship between pancreatic cancer and clinical depression is as yet unknown.

Like many other tumours, pancreatic cancer can spread directly to contiguous tissues or else metastasize via the blood or lymphatic systems. Direct spread may involve the common bile duct. Haematogenously, cancer cells may spread to the liver and, in rare cases, from the liver to the lungs. Lymphatic spread commonly reaches the regional lymph nodes, namely, the nodes in the paraduodenal peritoneum as well as the nodes of the celiac axis, porta hepatis, lesser and greater curvatures of the stomach, and the hilum of spleen.

It is rare for pancreatic cancer to spread to bone so much so that in patients diagnosed with pancreatic cancer and bone metastasis one may have to look for another primary tumour. Bone metastasis is not only diagnosed through the use of imaging but also by looking at blood test results for signs of anaemia or hypercalcaemia. The latter normally occurs as calcium is released from the bone into the bloodstream. If untreated, malignant hypercalcaemia may cause encephalopathy, coma and death. In bone metastasis, the uncoupling of the regulation of osteoclasts and osteoblasts leads to bone malformation. This, along with the lowering of the pH that occurs in the extracellular matrix surrounding the osteoclasts, activates nociceptors (pain receptors) in the bone and surrounding tissue, thus giving rise to the dull, chronic pain that these patients often complain of.

If spinal cord compression secondary to neoplastic disease is not reversed, the patient is likely to end up with irreversible paraplegia. In our case, the patient had not yet reached the point of complete compression of the spinal cord but there was evidence of cord damage at the level of the vertebral and epidural metastasis. This included weakness and numbness in the lower limbs, below the level of cord compression, and difficulty in emptying the urinary bladder completely.

In advanced cases of pancreatic carcinoma, where there has been extension to other nearby organs and involvement of the retroperitoneal nerves, the patient experiences severe pain. In fact, severe and continuous pain is one of the clinical features of end-stage pancreatic cancer, and is usually described as being 'deep' and 'gnawing'. There have even been recorded cases of suicide due to the excruciating pain. The pain tends to be more severe on lying down, and is poorly relieved by analgesics. However, it may be lessened by leaning forward in a sitting position.

Pancreatic cancer patients usually present with non-specific symptoms so a number of investigations may be necessary before rendering a diagnosis. An abdominal ultrasound detects a pancreatic abnormality in 75% of cases. If an anomaly is suspected on ultrasound, one would proceed to an abdominal CT scan. A pancreatic mass, which can be easily missed on physical examination, can be picked up on CT. A biopsy would often be taken to confirm that the mass is malignant. Apart from these radiological studies, suspicion of pancreatic cancer may arise due to elevation of the CA 19-9 tumour marker in the blood. However, CA 19-9 is not specific for pancreatic carcinoma as a number of other cancers can also raise it. CA 19-9 also has a low sensitivity for detecting pancreatic cancer. There have been several documented cases of pancreatic cancer whose CA 19-9 remained within the normal range. However, its level may help in monitoring treatment response as a progressive increase in the CA19-9 level may suggest that the administered treatment is not having the desired effect.

Pancreatic cancer is relatively resistant to medical treatment and the only potentially curative treatment is surgical. Once diagnosed, the cancer is 'staged' with stage I being the earliest stage of the disease and stage IV being the most advanced with evidence of metastatic disease. Patients with pancreatic cancer are also grouped into three classes. Class I includes those patients with local disease (equivalent to stage I or II), class II patients have locally advanced unresectable disease (stage III), and those with metastatic disease are included in class III (equivalent to stage IV). Patients with stage III and stage IV cancer have little to no chance of being cured.

Resectable pancreatic cancer is cured surgically. The surgical procedure most commonly performed is a Whipple procedure (pancreatico-duodenectomy). This involves removing the distal half of the stomach, the entire duodenal loop, the head and body of the pancreas and the lower end of the common bile duct. The tail of the pancreas, the hepatic duct and the remainder of the stomach are then anastamosed to the jejunum. This procedure is preferred to total pancreatectomy as this would result in the patient suffering from brittle diabetes for the rest of his/her life. Following this procedure, patients are started on chemotherapy for six months to lower the risk of recurrence.

In locally advanced unresectable disease, the cancer would have already invaded important local structures such that it cannot be resected surgically. However, since the cancer would have not yet metastasized, other forms of treatment are still available, although the chances of the patient being cured at this stage are minimal. Treatment may include low dose chemotherapy to decrease the probability of metastasis together with radiotherapy to the pancreas and surrounding tissues to minimize further local progression and thereby decrease the patient's symptoms. In metastatic disease, chemotherapy is used as a form of palliative care so as to enhance the patient's quality of life.

References:

Jimenez-Andrade, J.M.; Mantyh, W.G.; Bloom, A.P.; Ferng, A.S.; Geffre, C.P. & Mantyh, P.W. (2010)
Bone Cancer Pain.
Ann NY Acad Sci 1198:173-181. doi:10.1111/j.1749-6632.2009.05429.x

Julius, B; & Basbaum, A.I. (2001)
Molecular mechanisms of nociception.
Nature 413:203-210. doi:10.1038/35093019

Teitelbaum SL. (2007)
Osteoclasts: What do they do and how do they do it?
Am J Pathol. 2007 170(2):427-35. doi:10.2353/ajpath.2007.060834

http://www.cancer.org/
Learn About Cancer
Available from: http://www.cancer.org/Cancer/BoneMetastasis/DetailedGuide/bone-metastasis-diagnosis
Cited: 6th February, 2012

http://www.medicinenet.com Pancreatic Cancer
MedicineNet.com
Available from: http://www.medicinenet.com/pancreatic_cancer/article.htm
Cited: 6th February, 2012

http://www.emedicinehealth.com/ Pancreatic Cancer
emedicinehealth experts for everday emergencies
Availale from: http://www.emedicinehealth.com/pancreatic_cancer/article_em.htm
Cited: 6th February, 2012

Burkitt, H.G.; Quick, C.R.G.; Reed, J.B. & Deakin, P.J. (2007)
Essential Surgery Problems, Diagnosis & Management, 4th Edition Churchill Livingstone Publishers
ISBN: 9780443103452

Kumar, P. & Clark, M. (2009)
Kumar & Clark's Clinical Medicine, 7thEdition Elsevier Inc., Spain
ISBN: 9780702029936

Longmore, M.; Wilkinson, I.B.; Davidson, E.H.; Foulkes, A. &Mafi, A.R. (2010)
Oxford Handbook of Clinical Medicine, 8th Edition Oxford University Press Inc., New York

ISBN: 9780199232178