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CASE REPORT | PANCREAS

Primary Small Cell Carcinoma of the Pancreas Presenting With Likely Paraneoplastic Features

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Abstract

Primary small cell carcinoma of the pancreas (SCCP) is a rare malignancy, and has been associated with paraneoplastic features in only 2 reported cases. We report a rare and fatal case of SCCP with likely paraneoplastic features in a previously well 67-year-old woman presenting with abdominal pain. She was found to have abnormal biochemical markers (hyperkalaemia and hyponatraemia) with a normal abdominal CT. Emergency laparotomy identified a mass at the head of the pancreas and liver metastases, she died soon after, and diagnosis was confirmed post-mortem.

Introduction

Paraneoplastic syndromes are mediated by altered immune responses or hormones secreted by tumor cells, thus are characterized by the systemic effects of a malignancy that are not a direct consequence of invasion, obstruction or metastases.[1] Most small cell carcinomas (SCC) originate in the lung, with only 2.5–5% being classified as extrapulmonary (EPSCC).[2] EPSCCs appear most commonly within the bladder, prostate, cervix, and gastrointestinal tract.[3] SCC of the pancreas (SCCP) is an extremely aggressive and rare tumor, with fewer than 50 reported cases worldwide.[3,4] While the association between pulmonary SCC and paraneoplastic syndrome is well-described, only 2 cases of SCCP have been associated with paraneoplastic features.[4-6]

Case Report

A 67-year-old woman presented with actue abdominal pain and nausea. She reported a 3-week history of constipation, reduced appetite, and general malaise, without weight loss, diarrhea, or vomiting. Past medical history included chronic obstructive pulmonary disease. She was a heavy smoker and consumed 14 units of alcohol weekly. On examination, her abdomen was significantly distended and tender in the right upper quadrant; however, she was afebrile with normal vital signs. Bowel sounds were inaudible. Both electrocardiogram and chest x-ray were unremarkable. Compared to normal tests 2 months previously, liver and renal functions were acutely abnormal with bilirubin 48 µmol/L, alkaline phosphatase 546 U/L, γ-glutamyl transpeptidase >2100 U/L, alanine aminotransferase 525 U/L, aspartate aminotransferase 673 U/L, amylase 149 U/L, sodium 126 mmol/L, potassium 8.0 mmol/L, urea 17.8 mmol/L, creatinine 261 µmol/L, adjusted calcium 2.3 mmol/L, phosphate 2.3 mmol/L, glucose 4.4 mmol/L, and magnesium 1.1 mmol/L. Coagulation tests demonstrated an international normalized ratio of 1.1. Complete blood panel was unremarkable. Non-contrast abdominal computed tomography (CT) was normal with no evidence of obstruction, malignancy, ascites, biliary duct dilatation, gallbladder distention, or wall thickening (Figure 1). MRI was not available at time of presentation.

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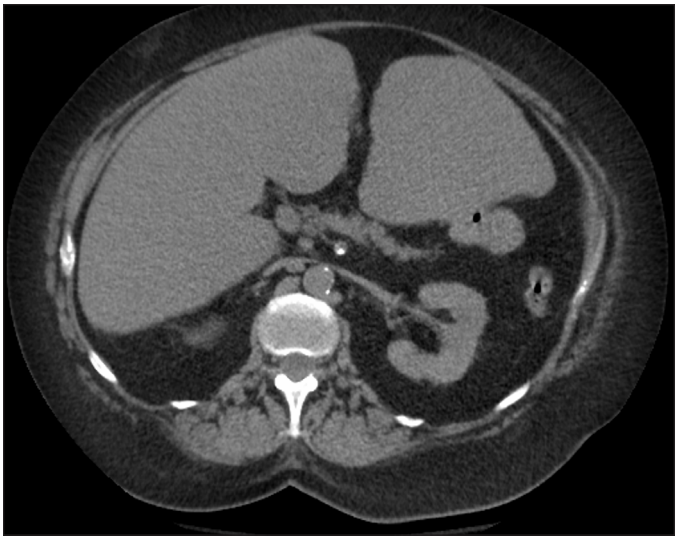

Figure 1. Axial non-contrast abdominal/pelvic CT showing a mildly atrophic pancreas with no demonstrable mass, no obvious intra- or extrahepatic biliary dilatation, no evidence of cholecystitis or ascending cholangitis, and no intrahepatic abnormality.

The patient rapidly deteriorated, becoming unresponsive, pale, and bradycardic. Cardiac monitoring showed widened QRS complexes and complete heart block consistent with hyperkalemia. Arterial blood gas demonstrated metabolic lactic acidosis. Following successful resuscitation with intravenous fluids, insulin, and calcium gluconate, potassium stabilized at 5.2 mmol/L. Due to concerns for ischemic bowel, she underwent emergency laparotomy, which demonstrated no evidence of ischemic gut, bowel obstruction, or intraperitoneal free fluid or gas. However, an indurated area at the pancreas head and multiple liver lesions consistent with metastases were noted. Postoperatively, she remained intubated, and despite supportive therapy including mechanical ventilation, fluids, inotropes, insulin, and glucose, her condition deteriorated with worsening hyperkalemia and hyponatraemia. She died 10 hours later with the cause of death remaining uncertain.

Autopsy examination revealed a multi-nodular pancreatic head mass measuring 25 x 10 x 10 mm with adjacent nodal metastases. The pancreatic body and tail were normal. Histological exam showed poorly organized small to intermediate-sized tumor cells with a high nuclear to cytoplasmic ratio and dense ovoid nuclei with prominent nucleoli, consistent with a diagnosis of SCCP. Immunoperoxidase staining was positive for neuron-specific enolase (NSE) and thyroid transcription factor-1 (TTF-1). The liver was enlarged with multiple metastases, and further metastases were noted in the local, porta hepatis, deep mediastinal, and subclavian lymph nodes, as well as the vertebral body bone marrow. All lesions exhibited similar histological appearance. There was no evidence of pleural, pulmonary, or cerebral primary malignancies or metastases. The biliary system and pituitary, thyroid, parathyroid, and adrenal glands were all normal.

Discussion

Accounting for less than 1% of primary pancreatic neoplasms, SCCPs most commonly arise in the head of the pancreas.[3,7] As poorly differentiated tumors, SCCs are composed of small to intermediate-sized cells often associated with endocrine features.[3] Although SCC cells generally stain positive for TTF-1, which distinguishes them from other neuroendocrine tumors, TTF-1 does not reliably differentiate between pulmonary and extrapulmonary SCCs.[8] Histological autopsy findings consistent with SCC and positive TTF-1 staining in the absence of primary pulmonary disease helped confirm our SCCP diagnosis. Furthermore, positive immunoperoxidase staining for NSE suggests a neuroendocrine differentiation of the tumor cells and may explain this patient's paraneoplastic features.[9]

The association between pulmonary SCC and paraneoplastic features is well recognized.[4] However, it is not well documented in SCCPs, despite evidence demonstrating that such tumors have the potential to cause paraneoplastic syndromes through production of endocrine compounds.[7] Indeed, there are only 2 reported cases of SCCP associated with paraneoplastic features.[5,6] One patient had elevated ectopic adrenocorticotropic hormone (ACTH), irregular periods, and hirsutism, while the second presented with hypercalcemia, possibly due to the presence of parathyroid hormone-like peptide. SCCP carries a poor prognosis with median survival between 3 and 20 months.[3,4] However, as with the previously reported 2 patients, who both died within 6 weeks, our patient died soon after presentation, suggesting that paraneoplastic features in the setting of SCCP carries an extremely poor prognosis.

Biochemical abnormalities in our patient most notably included hyponatremia with marked hyperkalemia. Our patient was clinically euvolemic and on no diuretic medications. These biochemical abnormalities may represent syndrome of inappropriate anti-diuretic hormone (SiADH), although we cannot be certain without definitive osmolality testing. SiADH is associated with pulmonary SCC and has been reported in EPSCC of the cervix and gallbladder, but not SCCP.[1,2,10]

Although our case cannot be linked definitively to a specific paraneoplastic pattern, the patient's grossly abnormal electrolytes and fluctuating clinical state are likely to reflect the paraneoplastic nature of this SCCP. Furthermore, postmortem findings of positive immunoperoxidase staining for NSE confirms the neuroendocrine nature of this SCCP and potential paraneoplastic syndrome, via excretion of SiADH.

We recommend awareness of possible paraneoplastic syndrome secondary to SCCP in a rapidly deteriorating patient, in which no other cause for the symptoms has been identified.

Disclosures

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