Case report

Adenosquamous pancreatic cancer producing parathyroid hormone-related protein

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An autopsy case of adenosquamous pancreatic cancer in a 61-year-old male patient with an elevated serum level of parathyroid hormone-related protein (PTH-rP) is reported. He was admitted to our hospital with a 1-month-long history of abdominal discomfort and progressive abdominal fullness. A computed tomography (CT) scan of the abdomen showed a retroperitoneal mass, approximately 10 cm in diameter, involving the pancreas, with round enhancement on contrast examination. Histological examination of a specimen taken by CT-guided needle biopsy suggested squamous cell carcinoma or transitional cell carcinoma. Laboratory data on admission revealed a high serum calcium level and high PTH-rP level. The calcium level initially responded to intravenous hydration, furosemide, calcitonin, and bisphosphonates, decreasing from 15.0 to 9.0 mg/dl. However, the hypercalcemia recurred after 10 days. The patient developed carcinomatous peritonitis and acute renal failure, and died on the 25th hospital day. Autopsy revealed a mass in the pancreatic body to tail, invading the retroperitoneum, with progressive carcinomatous peritonitis. Histological examination of the mass revealed infiltrating carcinoma, showing squamous differentiation with focal intracytoplasmic lumina formation, consistent with pancreatic adenosquamous carcinoma. Immunohistological examination showed positive staining for PTH-rP. Adenosquamous carcinoma of the pancreas is relatively rare; only a few cases associated with hypercalcemia and for which PTH-rP has been identified as a causative factor have been reported. This is the first case in which immunohistochemistry proved localized PTH-rP in adenosquamous pancreatic cancer cells, associated with persistent hypercalcemia.

Key words: adenosquamous cell carcinoma of the pancreas, hypercalcemia, parathyroid hormone-related protein (PTH-rP)

Introduction

Adenosquamous carcinoma is a relatively rare form of pancreatic cancer, accounting for 1%–4% of cases. Humoral hypercalcemia of malignancy (HHM) is defined by the biochemical features of hypercalcemia without bone metastasis. The plasma concentration of parathyroid hormone-related protein (PTH-rP) is increased in more than 90% of hypercalcemic patients with various malignancies, such as those with squamous cell carcinoma of the head, neck, lung, and esophagus. However, HHM is rarely associated with exocrine pancreatic cancer. To our knowledge, adenosquamous carcinoma of the pancreas has been rarely observed; only seven cases of exocrine pancreatic cancer have been reported associated with hypercalcemia caused by an elevation of PTH-rP. We report an autopsy case of adenosquamous carcinoma associated with hypercalcemia due to PTH-rP, which was identified in the tumor cells by immunohistochemical examination.

Case report

A 61-year-old man with a 1-month-long history of abdominal discomfort was referred to our hospital because of progressive abdominal fullness, appetite loss, and a body weight loss of 4.3 kg within 2 weeks. On admission, his temperature was 35.5 °C, pulse was 78/min, and blood pressure was 130/70 mmHg. Physical examination showed slight abdominal distension, however, tumor was not palpable. Initial laboratory studies were as follows: white blood cell count was 8400/μl (nor-
mal range, 4000–8000/µl), amylase was 70IU/l (normal range, 50–200IU/l), lipase was 6.8U/l (normal range, 5–60U/l), calcium was 11.8mg/dl (normal range, 8.8–11.0mg/dl), inorganic phosphorus was 3.3mg/dl (normal range, 2.3–4.5mg/dl), blood urea nitrogen (BUN) was 13mg/dl (normal range, 8–20mg/dl), creatinine (Cr) was 0.92mg/dl (normal range, 0.7–1.3mg/dl), carcinoembryonic antigen (CEA) was 3.2ng/ml (normal, <5.3ng/ml), carbohydrate antigen 19-9 (CA19-9) was 5U/ml (normal, <37U/ml), neuron-specific enolase (NSE) was 58ng/ml (normal, <10ng/ml), squamous cell carcinoma antigen (SCC) was 2.0ng/ml (normal, <1.5ng/ml), fragment of cytokeratin subunit 19 (CYFRA) was 1490ng/ml (normal range, <3.5ng/ml), high-sensitivity PTH (HS-PTH) was 140pg/ml (normal range, 160–520pg/ml), and PTH-rP was 9.4pmol/l (normal, <0.6pmol/l).

Abdominal computed tomography (CT) scans revealed a low-density mass approximately 10cm in diameter, that was circumferentially irregular, located in the retroperitoneum, involving the pancreatic body. Contrast CT showed round enhancement (Fig. 1). Magnetic resonance imaging (MRI) showed low signal intensity on a T1-weighted image, and slightly high signal intensity on a T2-weighted image (Fig. 2). Histological examination of a biopsy specimen taken by CT-guided needle biopsy suggested squamous cell carcinoma or transitional cell carcinoma (Fig. 3).

After admission, the patient’s abdominal fullness and appetite loss were rapidly progressive. The serum calcium level increased to 15.0mg/dl. Although parenteral hydration combined with furosemide, followed by treatment with synthetic calcitonin and bisphosphonate, temporarily normalized the serum calcium level to 9.0mg/dl, once, the hypercalcemia recurred and subsequently did not respond to treatment. Finally the serum calcium level increased to 17.4mg/dl. The patient developed renal failure and died of progressive disease on the 25th hospital day.

Autopsy revealed extensive peritoneal dissemination of cancer, the main tumor mass was located in the pancreatic body to tail, and measured 7.0 × 6.5 × 4.0cm, with a 2.4-cm-sized pseudocyst. The pancreatic duct and the biliary duct were not obstructed, and the pancreatic duct appeared to be not connected to the pseudocyst. Cancer cells also involved the peripancreatic, perigastric, mediastinal, and perithyroid lymph nodes. The cancer was histologically characterized by infiltrating sheets of polygonal cells containing keratin pearls and foci of clear cells (Fig. 4). A small number of cancer cells showed intracytoplasmic lumina, a distinct finding for glandular differentiation. Excluding the pancreas, no large mass had formed, and this finding suggested that the primary lesion was in the pancreas. Therefore we diagnosed this case as adenosquamous carcinoma of the pancreas. Immunohistochemical stainings of tumor cells for cytokeratin and epithelial membrane antigen (EMA) were positive. In particular, immunohistochemical staining for PTH-rP, with mouse monoclonal antibody PTH-rP (clone Ab-1; Oncogene Research Products, Boston, MA, USA) was also positive in the tumor cells of squamous cell carcinoma (Fig. 5). No bone metastasis was found, but an increase in the number of osteoclasts around the trabecular bones was revealed. None of the four parathyroid glands showed pathological changes.

Discussion

Adenosquamous carcinoma is a relatively rare form of carcinoma of the pancreas; several reports have cited an incidence of about 1%–4%. Histological findings of