A case of pancreatic acinar cell carcinoma metastatic to skin

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Abstract

We report a rare case of pancreatic acinar cell carcinoma with widespread metastases in a 68-year-old woman who presented with subcutaneous nodules as the initial symptom. Computed tomography showed a pancreatic mass with hepatic tumors and enlarged lymph nodes besides ring-enhanced subcutaneous nodules. Magnetic resonance diffusion-weighted imaging detected the presence of lesions in other organs. Histological analysis of a colonic polypoid lesion revealed carcinoma with endocrine and acinar differentiation compatible with pancreatic origin. Regrettably, she died of a cerebral infarction without any treatment, and autopsy findings confirmed our diagnosis.

Introduction

Acinar cell carcinoma (ACC) of the pancreas is a rare tumor accounting for up to 1% of pancreatic exocrine neoplasms. Half of the patients have advanced disease with metastases or a locally unresectable tumor at the time of diagnosis. We report a 68-year-old female patient with metastatic subcutaneous nodules as the initial presentation of ACC, who had widespread metastases to various organs.

Case Report

A 68-year-old woman presented with a four-week history of anorexia, general fatigue, and multiple subcutaneous nodules on the neck or trunk (Figure 1). These nodules were elastic and hard. Laboratory tests showed mild anemia (hemoglobin 10.1 g/dL), and elevated levels of CA19-9 (355.2 U/mL) and elastase-1 (750 ng/dL). Serum lipase, amylase, and the tumor markers (CEA and AFP) were within the normal ranges. Computed tomography (CT) scan showed ring-enhanced nodules in various subcutaneous sites, including the neck, chest wall, abdominal wall, back and hips (Figure 2C). CT scan also showed a 3-cm mass in the tail of pancreas with multiple hepatic tumors (the largest being 6 cm) and enlargement of the peripancreatic or paraaortic lymph nodes (the largest being 3 cm) (Figure 2A and 2B). Subsequently, magnetic resonance (MR) diffusion-weighted imaging (DWI) confirmed these tumors, and detected high-intensity lesions in the spleen, kidney, adrenal gland, and bone, suggesting possible metastatic tumors (Figure 2D, 2E, and 2F). Colonoscopy showed a polypoid lesion, measuring 7 mm in diameter, with central depression in the transverse colon (Figure 3A). Histological analysis of the biopsy specimen revealed carcinoma with endocrine and acinar differentiation compatible with pancreatic origin (Figure 3B). Taken together, we made a clinical diagnosis of pancreatic ACC with widespread metastases to various organs.

Unexpectedly, she suffered a massive cerebral infarction 4 days after admission, and died 30 days later without receiving any treatment for ACC. We performed an autopsy with the approval of her family. Autopsy revealed a tumor that spread from the body to the tail of pancreas. Macroscopically, the tumor was a solid, well circumscribed, and fleshy lesion with a little haemorrhage (Figure 4A). Microscopically, the tumor was hypercellular, with cords of cytologically uniform cells with granular eosinophilic apical cytoplasm reflecting the accumulation of zymogen granules (Figure 4B). Immunohistochemical staining verified the presence of α-1 antitrypsin (Figure 4C). These findings were consistent with those of ACC. Autopsy also revealed a pathological diagnosis of the subcutaneous nodules as metastatic disease. Moreover, it confirmed the metastases to various other organs including the liver, lymph nodes, spleen, kidneys, adrenal gland, bone, small intestine, colon, and brain.

Discussion

ACC of the pancreas accounts for approximately 1% of all exocrine pancreatic tumors.[1] The adult patients average about 60 years old, and males are more commonly affected.[1-3] Clinical symptoms are usually non-specific, for example anorexia, weight loss, abdominal pain, nausea, and vomiting. ACC may not cause jaundice even when the tumor is located in the head of pancreas.[1,2] ACC occasionally secretes pancreatic enzymes such as trypsin, lipase, chymotrypsin and amylase,[4-6] and some patients develop a distinctive syndrome of subcutaneous fat necrosis and polyarthralgia by over-production of lipase.[7-9] The skin nodules of this syndrome are commonly seen on the lower extremities, and often mistaken for metastatic disease.[2] However, ACC with skin metastases has not been reported. In our patient, serum lipase level was within the normal range, and she had subcutaneous nodules on the neck or trunk, not on the lower extremities. To our knowledge, this is the first report of ACC with skin metastases.

ACC is a highly aggressive tumor. Half of the patients have evidence of metastatic disease at presentation, and an additional 23% subsequently developed metastases to the regional lymph nodes and liver.[1] Several clinical studies have reported that the lungs, spleen, and adrenal gland are other potential sites.[4,10,11] Our patient proved to have widespread metastases to various organs including the skin, kidneys, bone, small intestine, colon, and brain, in addition to the sites mentioned above. This finding indicates that ACC can target these organs as metastatic sites, and that ACC may be so indolent that some patients present without specific symptoms even in advanced stage.

With regard to the treatment of ACC, surgical resection remains the best therapy for those patients with local, resectable disease. Recently, resection has been actively performed and improved survival.[2,3,12] Kitagami *et al.* reported a 5-year survival rate of 43.9% in the case of total resection.[12] Holen *et al.* reported a median actuarial survival rate of 36 months for those patients initially treated by operative resection.[2] Unfortunately, more than 70% the patients who undergo surgical resection are eventually confirmed to show recur-

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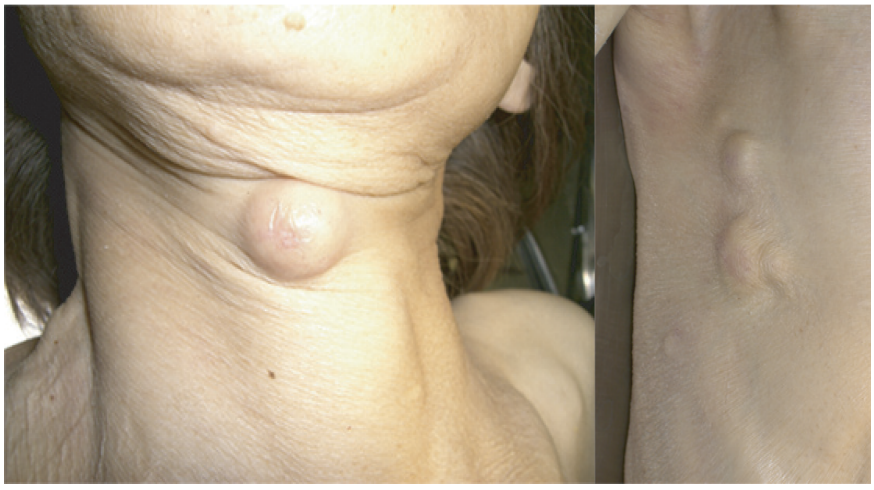

Figure 1. Subcutaneous nodules on the neck or trunk.

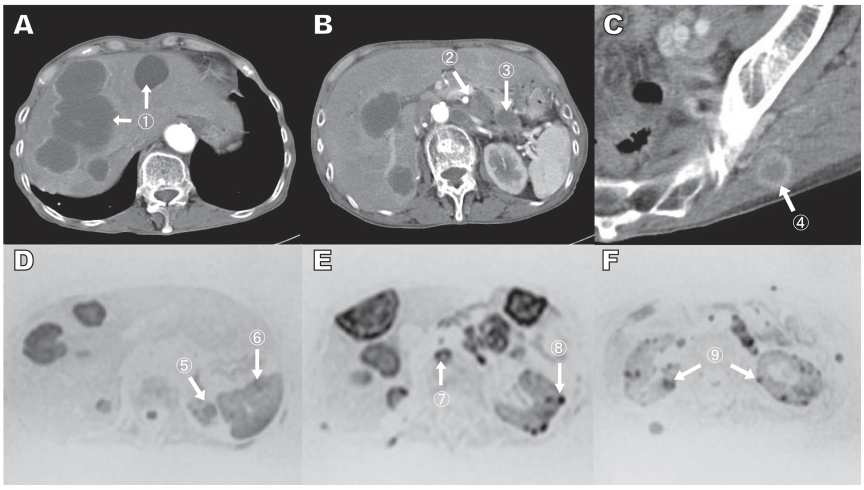

Figure 2. Computed tomography showing a pancreatic mass (B-3) with multiple hepatic tumors (A-1), enlarged lymph nodes (B-2), and ring-enhanced subcutaneous nodules (C-4). Magnetic resonance diffusion-weighted imaging showing high-intensity lesions in the adrenal gland (D-5), spleen (D-6), bone (D-7), and kidney (E-8, F-9).

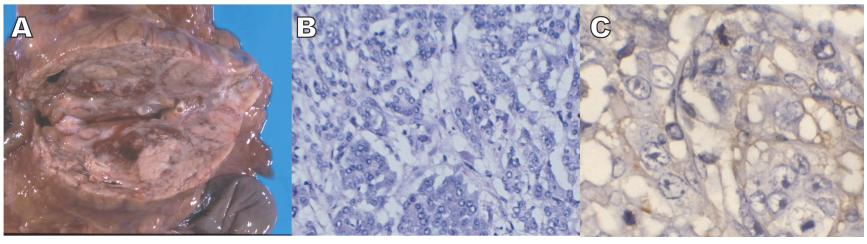

Figure 4. Autopsy findings. Macroscopic finding: pancreatic tumor (A). Histological analysis: hematoxylin and eosin staining (B), immunohistochemical staining for -1 antitrypsin (C).

rent disease.[2] Chemotherapy and radiotherapy are other therapeutic options when ACC is unresectable or recurs after resection, but no effective treatment strategies have been established. Although various chemotherapies have been performed, their results have been unsatisfied. Holen *et al.* reviewed 22 chemotherapy regimens administered to 18 different patients, and reported that there were no complete response, only 2 PRs and 7 SDs.[2] Recently, only a few case reports have shown the efficiency of neoadjuvant or adjuvant treatment with chemotherapy or radiation.[13,14] Seth et al. reported four patients underwent surgical resection after successful neoadjuvant chemoradiation using 5-fluorouracil, gemcitabine, cisplatin and adriamycin.[13] Lee *et al.* reported two PR cases of locally advanced ACC treated by capecitabine and concurrent radiotherapy.[14]

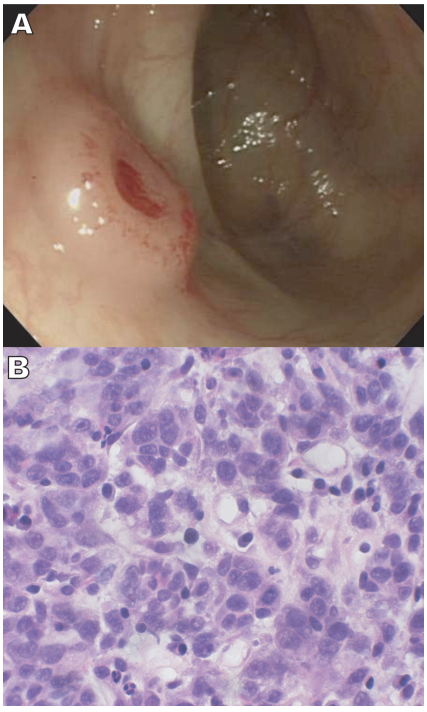

Figure 3. Colonoscopy showing a polypoid lesion (A). Histological analysis: hematoxylin and eosin staining (B).

Chemoradiation may be the best option for the patients with unresectable yet locally confined disease.[2] Therefore, it is important to know the accurate extent of disease in determining appropriate therapies. In our case, MR DWI detected not only original pancreatic tumor, but also metastatic lesions in the spleen, kidney, and adrenal gland, which CT scan failed to show clearly. This indicates that MR DWI can be a helpful imaging modality in the choice of treatment or the early detection of recurrence in ACC patients.

Our patient died of a massive cerebral infarction without receiving any treatment for ACC. Stroke is a frequent complication in patients with cancer. The principal mechanisms of stroke pathogenesis have been reported to be nonbacterial thrombotic endocarditis (NBTE), diffuse intravascular coagulation, and atherosclerosis.[15] NBTE is characterized by the presence of relatively acellular aggregates of fibrin and platelets attached to normal heart valves, and is often the cause of cerebral infarction.[15,16] In our patient, the autopsy revealed not the progression of metastases in the brain, but cerebral infarction with occlusive thrombus in the right posterior cere-

bral artery and NBTE with vegetation on the mitral valve. Therefore, we considered that she died of stroke induced by the cancer-related hypercoagulable state.

In conclusion, we have reported a case of pancreatic ACC with widespread metastases to various organs. This is the first report of ACC with skin metastases. Recent studies have clarified the characteristics of ACC, but ACC has not been fully understood. Future studies of more patients are needed.

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