

CASE REPORT

Anaplastic Pancreatic Carcinoma. A Case Report and Review of Literature

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ABSTRACT

Context Anaplastic pancreatic carcinoma is an aggressive neoplasm with survival measurable in weeks. It presents as a large cystic mass with loco-regional and distant spread. Three histological types have been described: pleomorphic, spindle cell and sarcomatoid.

Case report We describe the case of a 74-year-old woman with pleomorphic anaplastic carcinoma of the pancreas diagnosed after laparoscopic biopsy. The patient had a rapid downhill course with progression of the disease and demise within 4 weeks after diagnostic laparoscopy.

Conclusion Due to the rapid spread of the disease, no effective cure exists for these tumors. A brief review of the histological and radiological findings and the possible mechanisms of the pathogenesis of anaplastic tumors is included in the discussion.

INTRODUCTION

Anaplastic cancers of the pancreas (ACP) are rare aggressive tumors and account for 2-7% of all pancreatic cancers [1, 2, 3, 4]. They have been described as pleomorphic carcinomas, pleomorphic giant cell

carcinomas, spindle cell carcinomas, sarcomatoid carcinomas, and anaplastic (undifferentiated) carcinomas [2]. We hereby describe a case of rapidly progressive pleomorphic ACP.

CASE REPORT

A 74-year-old Caucasian female presented with a 6-month history of upper left quadrant pain. Past medical history was significant due to a 50 pack/year smoking background. Her mother had died of colon cancer. Colonoscopy revealed diverticulosis without signs of diverticulitis. She had rapid worsening of the symptoms with increasing pain in a band-like fashion across the mid-abdomen. Computed tomography (CT) of the abdomen and pelvis showed a large lobulated, heterogeneous upper left quadrant mass with focal calcification, which was read as suspicious for 'mucinous cystic tumor' of the tail of the pancreas. The mass invaded the stomach wall and encompassed both the splenic vein and the artery.

After informed consent, a diagnostic laparoscopy was performed to determine the extent of the disease and obtain tissue for diagnostic purposes. A large, multilobulated and indurated tumor mass was identified in the region of the tail of the pancreas, extending to the greater curvature of the stomach and the spleen. Small peritoneal and

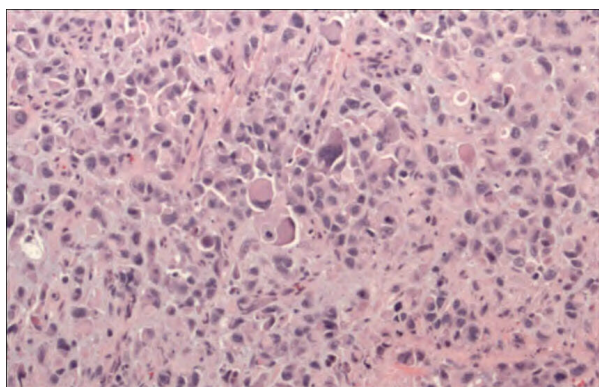


Figure 1. Hematoxylin-eosin staining of the tumor. Note that the tumor cells are non-cohesive and invade in a predominantly single file fashion. There is a marked desmoplastic response to the invasive tumor cells. Cytologically, the tumor cells are pleomorphic with eccentrically placed nuclei and homogeneous eosinophilic cytoplasm. The nuclei are irregular with clumped chromatin and irregular prominent nucleoli.

omental nodules were also identified. At this time, no obvious lesions were visualized in the liver. A biopsy of the pancreatic mass and omental nodules was performed. Histology revealed a marked desmoplastic response to the invasive tumor cells (Figure 1). Pleomorphic tumor cells with eccentrically placed irregular nuclei and a homogeneous eosinophilic cytoplasm were visualized. Immuno-histochemical stains of the tumor cells were positive for cytokeratin and negative for both mucicarmine and alcian blue (pH=2.5/periodic acid-Schiff). The tumor was classified as anaplastic pleomorphic type carcinoma.

One week after laparoscopy, abdominal wall cellulitis extending over the lower left quadrant and flank area was noticed. Interestingly, the ports of entry for the laparoscopy were spared. The cellulitis resolved after a 10-day course of i.v. antibiotics. However, she developed worsening edema of the lower extremities with ischemic changes consistent with vascular and lymphatic obstruction. A restaging CT scan of the chest, abdomen and pelvis carried out 3 weeks after the laparoscopy showed rapid progression of the disease with new lesions in the liver, omentum and left adrenal gland, suggestive of metastasis (Figure 2).

Due to the worsening of her physical condition and the high risk of adverse effects with chemotherapy, the patient and family opted for in-home hospice care. The patient died within 2 weeks.

DISCUSSION

ACPs are more common in older men with an age peak in the seventh-ninth decades of life [3, 4]. Weight loss, fatigue, loss of appetite, abdominal pain, nausea, vomiting and diarrhea are the usual clinical presenting symptoms. Clinical signs include a palpable mass and jaundice. Our patient had some of these clinical symptoms and a palpable mass. Her laboratory findings were within normal limits.

Radiological findings of ACPs are non-specific. CT scan findings in our patient were consistent with a diagnosis of mucinous cystadenoma/cystic neoplasm of the pancreas. Interestingly, Ichikawa *et al.* also reported that all cases of anaplastic carcinoma in their series were interpreted incorrectly the first time [2]. Usual CT findings include a large, heterogeneous, moderately enhancing, exophytic and lobulated lesion with an area of necrosis. Incremental bolus dynamic CT is the

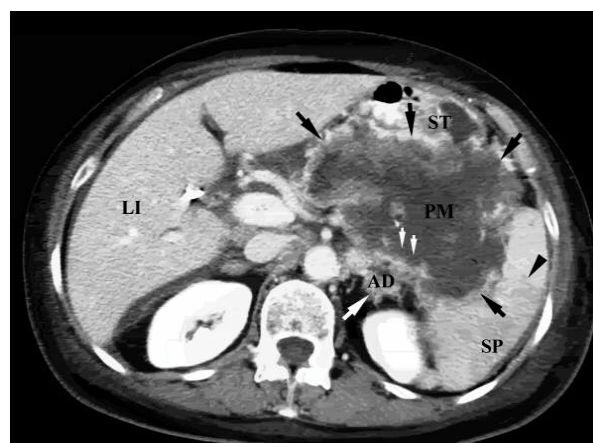


Figure 2. CT scan image of the abdomen at the L1 vertebral level showing the pancreatic mass (PM), invading the stomach wall (ST) and spleen (SP) as indicated by the black arrows. Splenic ischemic change (black arrow head) is secondary to the invasion of the splenic vessels by the mass (double white arrows). Left adrenal (AD) metastasis is noted (white arrow). Liver (LI) metastasis are not visualized in this section.

optimal technique for evaluating the pancreas with visualization during the early arterial and portal venous phases. In contrast to adenocarcinoma, ACPs show marked enhancement after contrast administration [5]. On pathological examination, these tumors are large, exophytic, heterogeneous, cystic masses with areas of necrosis or hemorrhage. The predominant site of origin (head, body and tail) is variable [5]. ACPs can be further subclassified since they show marked heterogeneity on microscopic examination. ACPs are subdivided into three basic histological subtypes: spindle cell carcinoma, pleomorphic carcinoma and round cell carcinoma depending on the predominant cell type.

Immunohistochemical staining is the key to determining the origin of tumor cells and distinguishing them from metastatic carcinoma, malignant melanoma, rhabdomyosarcoma, choriocarcinoma, anaplastic large cell lymphoma, epithelioid sarcomas, and malignant fibrous histiocytoma. ACPs are epithelial in origin and are reactive to epithelial markers (CK7, EMA or pancytokeratin).

Yonemasu *et al.* found that E-cadherin expression was completely lost in 87.5% cases of ACPs in their series [6]. Also, impaired alpha- and beta-catenin expression was documented in ACP cases [6]. The altered expression of adhesion molecules is probably correlated to dedifferentiated change and is contributory to the aggressive biological behavior of these tumors. ACPs exhibit a significantly higher incidence of K-ras mutations, which possibly accounts for their aggressive behavior [3]. Mutations in p53 have also been related to a poor prognosis [3].

ACPs tend to have an aggressive nature with rapid local and distant spread. In our case, there was direct locoregional spread to the surrounding soft tissues, stomach, spleen and peritoneum, similar to that reported in the previous literature [3, 7] Tumors of the body and the tail are more likely to give pulmonary rather than hepatic metastasis [8]. Kamisawa *et al.* reported a higher incidence of

pulmonary metastasis in ACPs [9]. Our patient had hepatic metastasis from a tumor arising from the tail of the pancreas but no pulmonary lesions. Our findings concur with those of Paal *et al.* [3]. Tumor size does not appear to be a reliable indicator of prognosis in this malignancy. Paal *et al.* found pleomorphic tumors to have a better prognosis than spindle cell types [3]; however, poor survival was seen in our patient.

Irrespective of the type, ACPs are associated with poorer survival when compared to invasive ductal adenocarcinomas having only 3% 3-year survival [3, 10]. There are limited data available on treatment options for these tumors. Curative resection is usually not successful due to extensive disease at presentation and the aggressive nature of disease with rapid recurrence [11, 12]. A few case reports exist where local radiation therapy for the tumors has been used, but they had no success [13]. Patients tend to have a rapid deterioration of physical condition; as a result, they are not good candidates for chemotherapy.

Anaplastic pancreatic cancers are among the most aggressive solid tumors of the pancreas. Histological confirmation should be sought in cystic neoplasms which, on radiology, appear to be regionally invasive. Treatment options for this disease remain to be defined.

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Keywords Biopsy; Histology; Laparoscopy; Pancreatic Neoplasms; Tomography, X-Ray Computed

Abbreviations ACP: Anaplastic cancer of pancreas

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