

CASE REPORT

An Emergent Case of Pancreatic Cancer; Adenosquamous Carcinoma with Sarcomatoid Change

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ABSTRACT

The case describes a 39 year old male that presented with epigastric pain, nausea and constipation. A computed tomography revealed a 2×3 cm lesion in the head of the pancreas. The patient was referred to our institution and a high contrast computed tomography showed the lesion to have grown to 5×5 cm within a period of 15 days. Biopsies were obtained from the pancreatic mass. However, a few days later the patient went into circulatory shock and was transported to the intensive care unit where he was treated for acute onset liver and kidney failure. The patient's condition progressively worsened and despite all efforts of resuscitation, he passed away. Final immunohistochemical analysis revealed a poorly differentiated pancreatic adenosquamous carcinoma with sarcomatoid characteristics. pancreatic adenosquamous carcinoma is a rare exocrine pancreatic tumor demonstrated to have a more aggressive disease course than ductal adenocarcinoma. The additional sarcomatoid component in the tumor may have further promoted cancer cell proliferation and metastatic dissemination. The present case highlights the complex dynamism of pancreatic cancer and that a rapid growth rate of a pancreatic mass should not preclude the suspicion of malignancy.

INTRODUCTION

The poor prognosis of pancreatic cancer is attributed to the absence of symptoms at early stages and aggressive tumor biology [1, 2]. The heterogeneity of the disease accounts for survival ranging from a few months to several years [3]. The majority of pancreatic neoplasms are ductal adenocarcinomas (PDAC). Within the PDAC category, multiple subtypes exist with distinct histologic characteristics. One such subtype is pancreatic adenosquamous carcinoma (PASC), which represents approximately 3-4% of pancreatic malignancies [4]. The prognosis of PASC has been demonstrated to be worse than that of other subtypes of PDAC [5]. It has been shown that the addition of mesenchymal transition or sarcomatoid

change in an adenocarcinoma may further promote cancer cell proliferation and metastatic dissemination [6]. The current report presents a case of a sarcomatoid PASC which underwent such rapid progression that the described patient deteriorated and died within a few weeks of symptom presentation.

CASE REPORT

A formerly healthy 39 year old male from Saudi Arabia presented to his local emergency department with a five day history of epigastric pain, loss of appetite, nausea and constipation. His vital parameters were within normal limits and physical examination revealed mild epigastric guarding and tenderness. Laboratory tests revealed no abnormalities and a CT showed large amounts of fecal matter in the colon. The patient was prescribed laxatives and scheduled to follow up in a few days for a repeat examination.

The patient returned after ten days with worsening abdominal pain despite having had several bowel movements. His vital signs and laboratory values were still within normal limits. However, due to his poor

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general condition he was referred to our institution for further investigation. An ultrasound of the liver was unremarkable and an upper endoscopy showed evidence of inflammation in the descending part of the duodenum. The initial CT examination was reviewed by a senior radiologist who noted a focal 2×3 cm area of inflammation with decreased enhancement in the head of the pancreas **Figure 1a**. The differential diagnosis at this point included focal autoimmune pancreatitis and primary pancreatic malignancy.

This new finding prompted a repeat CT examination according to a specific pancreatic imaging protocol. At this examination the whole pancreatic gland was noted to be inflamed and edematous. The superior mesenteric vein was partially compressed by the inflammatory process and there were numerous peripancreatic lymph nodes with necrosis. Compared to the initial CT investigation 15 days earlier, the lesion in the head had grown from 2×3 to 5×5cm. In addition to this lesion, a cystic collection had formed in the lateral wall of the descending duodenum causing a gastric outlet obstruction **Figure 1b**. Due to the rapid growth, suspicion was raised whether this lesion represented a lymphoma or an infectious process such as tuberculosis. Despite these changes, the patient remained clinically stable. The only notable laboratory parameters at this time were mild elevations of hepatic transaminases. Due to the earlier suspected autoimmune pancreatitis, serum IgG was obtained and found to be within normal limits which decreased the likelihood of the diagnosis.

To better characterize the disease process and obtain a conclusive diagnosis, an endoscopic ultrasound was performed which showed an edematous pancreas with mild dilatation of the main pancreatic duct (4 mm). A core needle biopsy of the lesion was obtained for further analysis. During puncture of the lesion, neither blood nor fluid was aspirated, excluding the diagnosis of a hematoma or pseudocyst. An attempt at ERCP was also made but cannulation of the papilla was unsuccessful due to the extent of inflammation and limited passage through the duodenum. Initial tests for pancreatic tuberculosis were negative on both microscopic assessment and PCR.

Three days after the endoscopic ultrasound, the patient's general condition acutely worsened over a period of hours. He became confused and disoriented. A systolic blood pressure drop to 60 mm Hg was noted. The patient was transferred to the intensive care unit where rapid fluid infusion and inotropic agents were administered. At this point blood work showed a worsening of kidney and liver function. A repeat CT examination demonstrated now an increase in the size of the pancreatic mass to 10×7 cm; a further 100% increase in 10 days (**Figure 1c**). The pancreatic mass also caused necrosis of the surrounding tissues which radiologically resembled necrotizing pancreatitis. Additional findings included portal vein

thrombosis, multiple hypo-dense lesions in the liver, large amounts of ascites and edematous small bowels **Figure 1c**. The sudden drop in blood pressure was therefore attributed to septic complications from the peripancreatic necrosis together with an acute onset of liver failure.

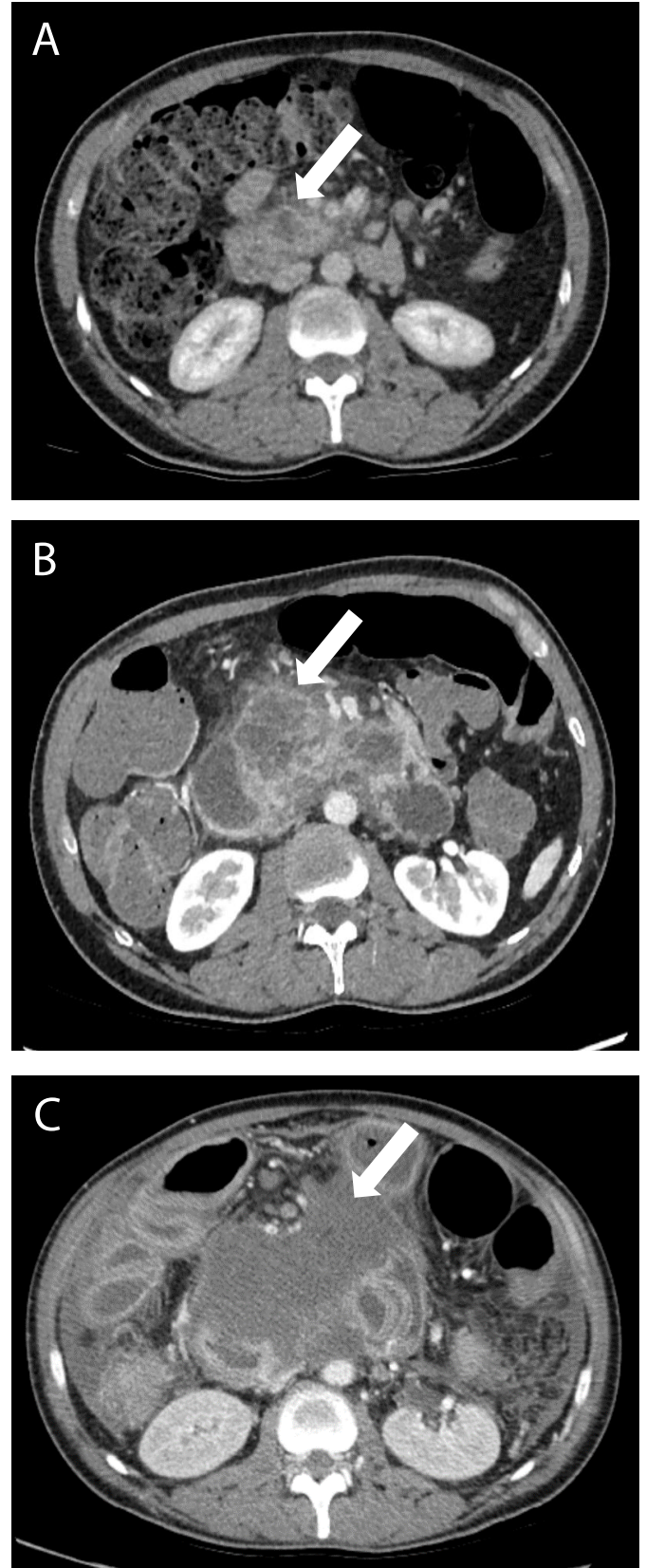


Figure 1. CT examination with the pancreatic mass at (a.). the time of symptom presentation, (b.). 15 days following symptom presentation and (c.). 25 days following symptom presentation.

Over the following 24 hours the patient developed respiratory and circulatory failure requiring endotracheal intubation, mechanical ventilation and high doses of noradrenalin for blood pressure maintenance. More than 10 liter of ascites was drained from the abdomen and blood work indicated fulminant liver failure. The patient's condition progressively worsened and despite all efforts of resuscitation and life-sustaining treatment, he passed away. An autopsy was not conducted in accordance with the family's wishes.

The pathologist's initial impression of the EUS-guided pancreatic biopsy was that of a poorly differentiated

adenocarcinoma, without signs of lymphoma. Cytological analysis of the ascites fluid identified adenocarcinomatous cells. Final immunohistochemical analysis revealed a poorly differentiated adenosquamous pancreatic cancer with sarcomatoid characteristics.

DISCUSSION

The current report describes a case of a healthy young male with a rapidly progressive pancreatic cancer. Cancer-related symptoms progressed from the initial complaint of abdominal pain to fulminant multi-organ failure in

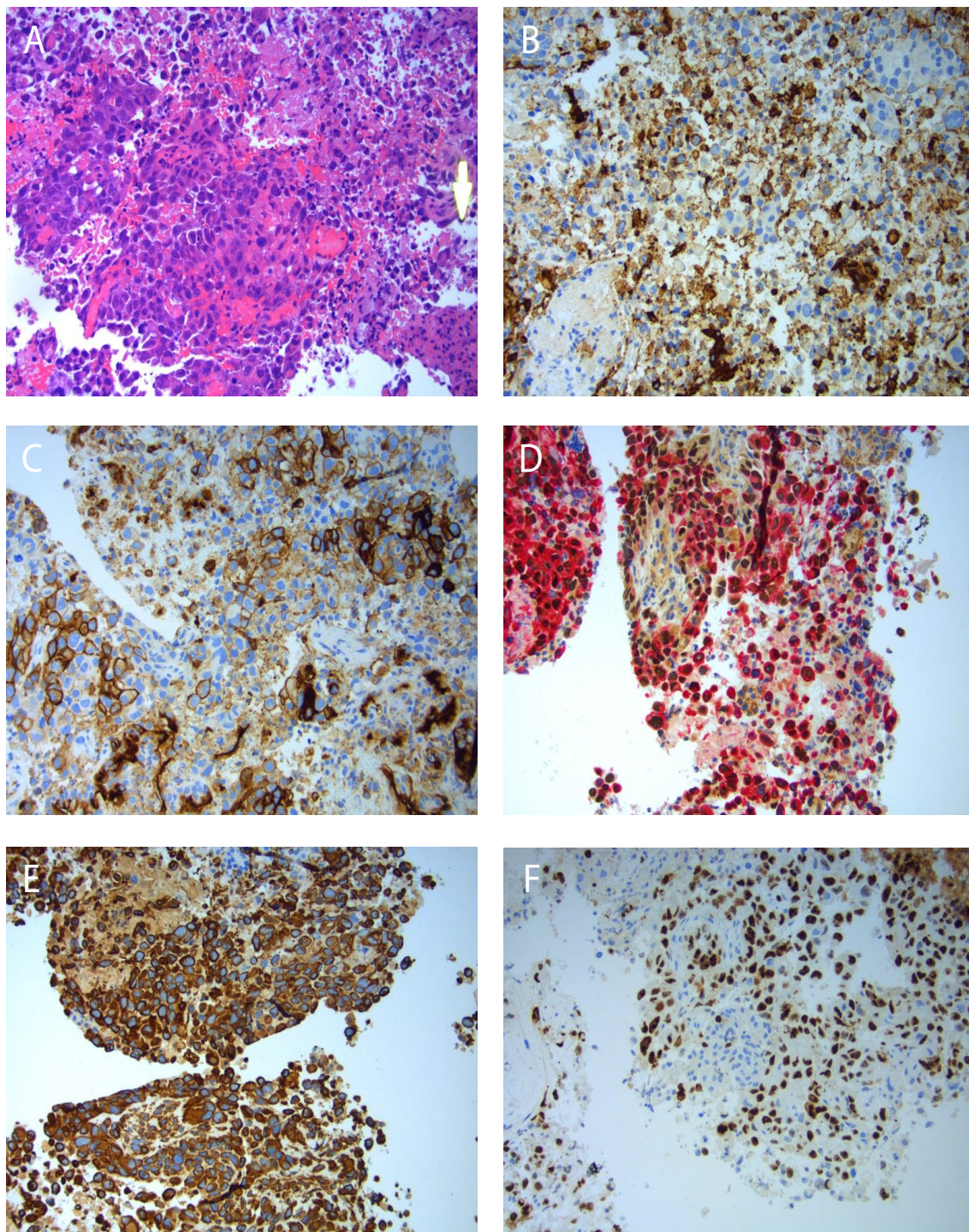


Figure 2. Histology of the pancreatic biopsy **(a.)**, stained with hematoxylin och eosin, **(b.)**, positive for CA19-9, **(c.)**, positive for Muc1, **(d.)**, positive for p40 (brown)/CK5 (red), **(e.)**, positive for vimentin, **(f.)**, an 80% proliferation index of Ki67. These markers indicate a highly proliferating adenosquamous carcinoma of pancreatic origin with sarcomatoid change.

less than one month. Radiological imaging demonstrated a growth of the pancreatic mass from an initial 2x3cm to 5x5cm in 15 days and then subsequently to 7x10cm within the next 10 days. The final pathological report identified the mass as a pancreatic adenosquamous carcinoma with signs of sarcomatoid change.

Despite its rarity, adenosquamous carcinoma of the pancreas has been well documented in the literature [7, 8]. The rapid progression in the present case has to our knowledge never been described and a subtype with sarcomatoid change has previously been described only once [9]. In this report, the patient, a 58 year old woman presented with epigastric pain without signs of jaundice, vomiting or weight loss similar to the current patient's initial presentation. Laboratory tests however showed increased serum levels of C-reactive protein and leukocytosis and initial imaging revealed a significantly bigger mass of 12x10 cm. In contrast to the present case, the patient underwent surgical resection of the mass with development of liver metastasis five months thereafter.

A limitation of the present case was the absence of an autopsy and a complete macro and microscopic examination to fully characterize the cancer. The final diagnosis was confirmed on immunohistochemistry from the EUS guided core needle biopsy. Tumor cells stained positive for CA19-9 and MUC1 indicating an adenocarcinoma of pancreaticobiliary origin [10, 11]. P40/CK5 positivity was indicative of squamous epithelial differentiation [12]. Positive staining for Vimentin showed that the cancer cells had undergone sarcomatoid change [13]. The proliferation index of Ki-67 was around 80%, which corresponds with the fulminant clinical course and further highlights the aggressive biology of this cancer [14]. The positivity of the described markers is illustrated in **Figure 2**. This immunohistochemical pattern is similar to that of the previously reported case [9].

Adenosquamous pancreatic carcinoma in general has a worse prognosis than other subtypes of PDAC [8]. The prognosis of pancreatic adenosquamous carcinoma with sarcomatoid change has not been sufficiently described due to its rarity. The present case was extensively analyzed at the institutional morbidity and mortality review board. The reason for initially suspecting lymphoma or an infectious process was because of the rapid growth of the pancreatic mass which was considered atypical for malignancy. Intraparenchymal bleeding or pancreatitis could possibly have explain the rapid tumor growth, but neither were supported by the CT examination and endoscopic ultrasound. Earlier transfer to the intensive care unit was not warranted as all vital signs and laboratory parameters were within normal limits until the patient went into circulatory shock. The drastic increase in pancreatic size resulted in only mild elevation of the C-reactive protein and white blood count. Points of criticism were the missed pancreatic mass on the initial radiological report of the first CT scan, and that serum CA19-9 levels were not obtained when the pancreatic changes were first noticed.

Considering the patient's age, acute presentation and unremarkable laboratory work, a pancreatic tumor was low on the list of differential diagnoses. Even if the diagnosis had been established earlier, it is unlikely that this would have led to a surgical resection before the patient's clinical deterioration; however, if this was the case, it is difficult to predict what the clinical outcomes of a resection could have been. In the previously reported case by Lu BC et al, a multi-visceral organ resection was performed [9]. Their patient did not receive adjuvant chemotherapy and subsequently developed liver metastases 5 months postoperatively.

To conclude, certain forms of exocrine pancreatic cancer can grow at rapid rates which underscore the heterogeneous nature of this aggressive disease. Due to limited available data on adenosquamous cancer with sarcomatoid elements an appropriate treatment protocol is yet to be established. This case however highlights the complex dynamism of pancreatic cancer and that a rapid growth rate of a pancreatic mass should not preclude the suspicion of malignancy.

Conflicts of Interest

The authors have no conflicts of interest to declare. This work did not receive any support or funding and was conducted in accordance with the Declaration of Helsinki (2003).

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