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CASE REPORT

Multifocal Anaplastic Pancreatic Carcinoma Requiring Neoadjuvant Chemotherapy and Total Pancreatectomy: Report of a Case

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ABSTRACT

Context Anaplastic pancreatic carcinoma is a rare tumor with poor survival. Data on surgical and medical therapies are currently limited to case reports and case series with small numbers. **Case report** We describe a case of multifocal anaplastic pancreatic carcinoma treated with neoadjuvant FOLFIRINOX (oxaliplatin, irinotecan, fluorouracil and leucovorin) and total pancreatectomy with subsequent patient disease-free survival currently at 12 months. **Discussion** The goal for anaplastic pancreatic carcinoma treatment should continue to be complete surgical resection. Optimum chemotherapeutic options continue to be investigated.

INTRODUCTION

Anaplastic pancreatic carcinoma is a rare, poorly-differentiated tumor that accounts for 2-7% of exocrine pancreas tumors [1]. Patients frequently present in their 6th to 8th decade of life with vague, non-specific complaints of pain, nausea, vomiting and occasionally jaundice [2]. Overall survival remains poor at a median 5.2 months after diagnosis and just 3% surviving up to 3 years [2, 3].

We report on a patient diagnosed with multifocal anaplastic pancreatic carcinoma treated with neoadjuvant FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin) and total pancreatectomy with vascular reconstruction. To our knowledge, this is the first report to demonstrate prolonged survival after FOLFIRINOX and extensive resection for anaplastic pancreatic carcinoma, demonstrating exciting treatment possibilities for this otherwise devastating disease.

CASE REPORT

A previously healthy, non-diabetic 56-year-old man presented in March 2010 with abdominal pain and nausea to an outside facility. Following an extensive workup, including imaging, he was diagnosed with chronic pancreatitis. Repeat CT, one year later on re-presentation with jaundice, demonstrated an atrophic pancreas and a 3 cm hypodense area in the tail of the pancreas with splenic vein invasion as well as a second mass of 2 cm in the head of the pancreas with invasion of the portosplenic confluence (Figure 1). Endoscopic

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Key words Carcinoma; Neoadjuvant Therapy; Pancreatic Neoplasms

Abbreviations FOLFIRINOX: fluorouracil, leucovorin, irinotecan, oxaliplatin

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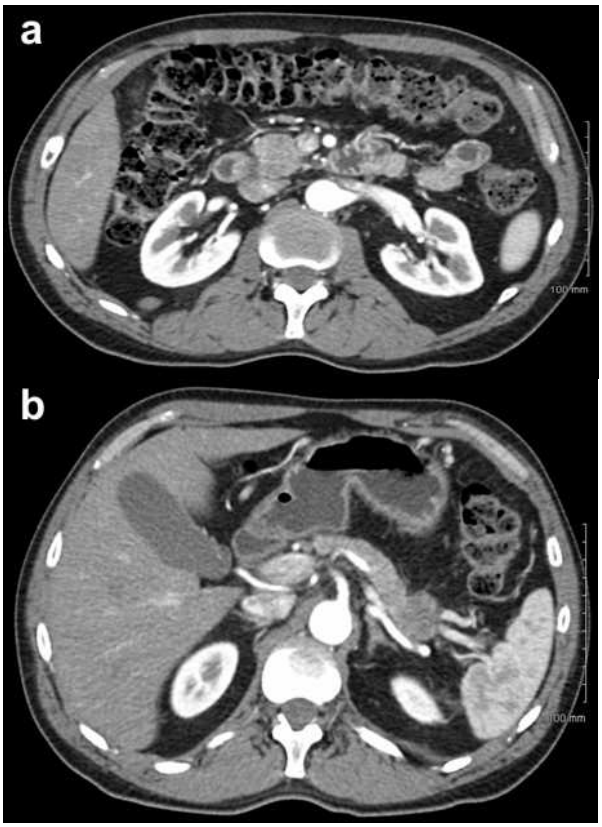

Figure 1. a. Pancreatic head mass. **b.** Pancreatic tail mass.

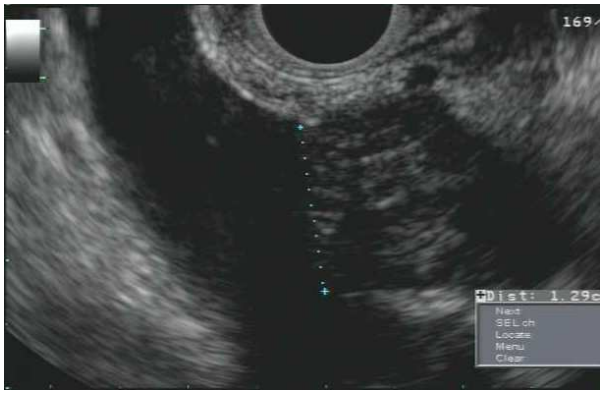

Figure 2. Pancreatic head mass abutting portal vein.

ultrasound with fine-needle aspiration confirmed the presence of both masses with the pancreas head lesion being concerning for invasion into the splenoportal vein confluence (Figure 2). Biopsy of the head mass demonstrated undifferentiated carcinoma with osteoclast-like giant cells. Based on these findings, diffuse involvement of the entire gland with neoplastic process was suspected.

Following a visit to the University of Colorado Multidisciplinary Gastro-Intestinal Tumor Clinic, the patient underwent neo-adjuvant chemotherapy with 3 months of FOLFIRINOX followed by restaging. Repeat pancreas protocol CT scan showed a decrease in the size of the entire pancreas with both masses (head and tail) also decreasing in size. A total pancreatectomy was offered and performed (Figure 3). Segmental superior mesenteric vein resection was also done with an end to end anastomosis, as the tumor came within less than 1 millimeter from the retroperitoneal margin on frozen section. The postoperative course was uncomplicated and the patient was discharged home on day 7. The final pathology demonstrated two discrete tumor masses, 5.0 cm and 4.5 cm, with extensive colonization of the intervening pancreatic duct. On histology, the tumor consisted of sheets of undifferentiated carcinoma cells separated by dense fibrosis. Clusters of multinucleated foreign body-type giant cells, associated with cholesterol clefts and other degenerative features, were present in the stroma adjacent to the tumor cells. These were interpreted as neoadjuvant treatment effect and not as native component of the tumor (Figure 4). All margins, including the superior mesenteric vein segment, were negative for malignancy; three of 28 lymph nodes contained metastatic deposits. Immunohistochemical staining was positive for pancytokeratin AE1:AE3, CA 19-9 and patchy positive for B72.3, negative for chromogranin and synaptophysin and equivocal for CEA. Final pathologic staging was pT3N1M0.

The patient remains without evidence of disease 12 months from the original diagnosis. Following extensive discussion on tumor board, additional 3 months of gemcitabine was administered postoperatively.

DISCUSSION

Anaplastic pancreatic carcinoma remains a rare and deadly disease with limited data on medical and surgical treatment. Presentation is nonspecific, as CEA and CA 19-9 levels are inconsistently elevated [4]. Tumors typically contain solid areas of highly pleomorphic cells and multi-nucleated giant cells and are likely ductal in origin [5, 6]. There are reports that anaplastic pancreatic carcinoma with osteoclast-like giant cells demonstrates better long-term survival; however, overall survival of anaplastic pancreatic carcinoma remains considerably worse than pancreatic adenocarcinoma, based on the very limited data available [4].

Due to this typically late presentation, there was a question of whether surgical resection had any impact on overall survival [7]. Strobel *et al*. demonstrated a 5-month survival benefit after an R0/R1 resection compared to palliative surgery [4]. Recently, Clark *et al*. reviewed all patients diagnosed with anaplastic pancreatic carcinoma un the 17 registries from the Surveillance, Epidemiology and End Results (SEER) database (http://seer.cancer.gov/resources/) between 1988 and 2008, resulting in the largest data group to

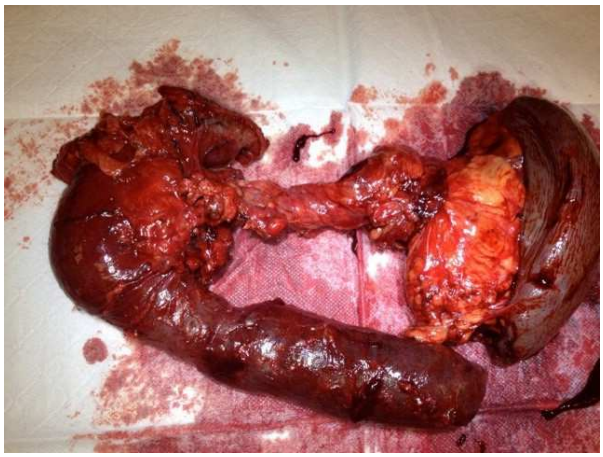

Figure 3. Total pancreatectomy/splenectomy specimen.

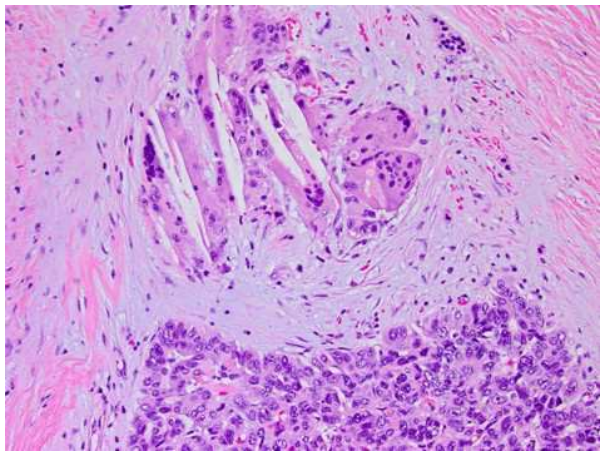

Figure 4. Foreign body giant cells.

date of 353 patients [8]. While overall survival of patients diagnosed with anaplastic pancreatic carcinoma was significantly worse than patients with pancreatic adenocarcinoma, patients who underwent resection had comparable survival to patients with pancreatic ductal adenocarcinoma.

To our knowledge, this case is the first report on the management of multifocal anaplastic pancreatic carcinomas with neoadjuvant therapy and total pancreatectomy with vascular resection. Aggressive surgical management is an important option and goal, considering almost 20% of anaplastic pancreatic carcinoma can be multifocal upon presentation [3].

Chemotherapeutic options also remain poorly studied with various responses in submitted case reports. In general, there is possible survival benefit for anaplastic pancreatic carcinoma from adjuvant/neoadjuvant therapy [9, 10, 11]. Improved survival in metastatic pancreatic adenocarcinoma with FOLFIRINOX has been published and was chosen for this patient [12]. This significantly improved response rates to FOLFIRINOX in metastatic disease suggests that this regimen be further investigated for neoadjuvant treatment in locally advanced anaplastic pancreatic carcinoma as well [13].

In conclusion, aggressive surgical management to achieve an R0/R1 resection should remain the goal in the treatment for anaplastic pancreatic carcinoma even with multifocal disease. Secondary to the rarity of disease, therapeutic options remain poorly studied; however, neoadjuvant therapy followed by aggressive surgical resection may be considered in appropriately selected candidates. Tumors containing osteoclast-like giant cells may follow a less aggressive course; however this case demonstrates successful treatment of a case of anaplastic pancreatic carcinoma despite unfavorable histology.

Conflict of interests The authors have no potential conflict of interests

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