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# Medullary Carcinoma of the Pancreas: Case Reports and Literature Review

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## ABSTRACT

This two-case report of medullary carcinoma of the pancreas adds to the limited experience published in the literature. Both patients initially presented with epigastric pain with an unremarkable physical exam. After an extensive diagnostic workup, they were both submitted to surgical resection. The histopathological report revealed a distinct entity with a medullary pattern, for which no current guidelines exist. However, this entity is known to have a better prognosis than pancreatic adenocarcinoma. (J CANCEROL. 2015;2:80-3)
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## INTRODUCTION

Medullary carcinoma of the pancreas is somewhat of a new entity. It has been previously identified as a poorly differentiated subset of the pancreatic ductal adenocarcinoma[1,2]. However, medullary carcinomas are histologically distinct entities, characterized by expanding borders, a prominent syncytial growth pattern, and extensive necrosis[3,4]. There are only a small number of cases published in the literature, and therefore limited experience in diagnosis and treatment. Currently, there are no guidelines regarding this particular diagnosis, and hence, the most common algorithm used in clinical practice is that of the pancreatic adenocarcinoma.

## CASE REPORT

Herein we present a case of a 58-year-old female patient with past medical history of arterial hypertension, hypercholesterolemia, and papillary thyroid cancer treated with thyroidectomy in 1982 and 30 radiotherapy sessions.

In May 2008, during a routine abdominal ultrasound (US), she was diagnosed with a solid mass on the pancreatic tail. Afterwards, an abdominal computed tomography (CT) scan further characterized the pancreatic tumor as a 1 cm diameter hypodense mass without contrast enhancement and without invasion to adjacent structures. The CA-19-9 levels were within normal range. Chemotherapy with gemcitabine was given on the 9th and 16th of January 2009; 10 days later, a new abdominal CT showed a 3.7 × 3.2 cm lesion that grew in cephalic direction and reached the lesser curvature of the stomach. Due to these findings, she was referred to our institution.

Upon arrival she manifested mild epigastric pain that exacerbated with meals, abdominal fullness, and 2 kg weight loss due to anxiety hyporexia. The physical examination was unremarkable. In mid February 2009, she underwent distal pancreatectomy with splenectomy and total gastrectomy with a esophagojejunal anastomosis reconstruction. She was discharged 11 days later without complications.

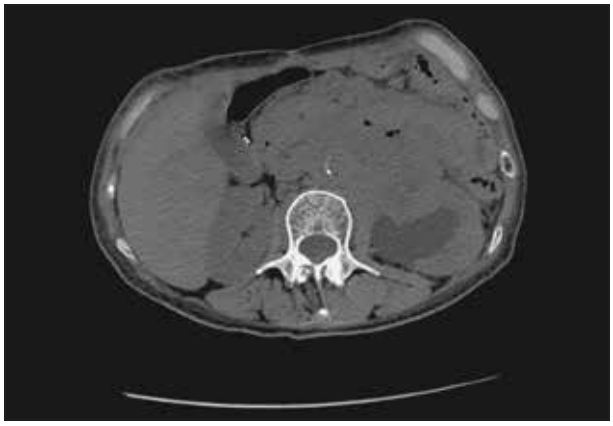

**Figure 1.** Case 1: Computed tomography scan, simple phase showing recurrence of the disease, with a retroperitoneal lymphatic conglomerate which invades left kidney and left ureter.

The histological examination showed a poorly differentiated medullary carcinoma of the pancreas with peripancreatic tissue invasion and positive border margin within the pancreas. The tumor showed microsomal stability and lack of infectious evidence for Epstein Barr virus.

Later on, she received adjuvant chemotherapy with gemcitabine for a total of six cycles, which ended in mid October 2009. Follow-up was performed with serial abdominal CT scans every six months during the first year, and afterwards every year during the next two years, without evidence of disease recurrence. However, during the following 11 months she lost 10 kg, and in January 2012, a follow-up CT scan revealed a retroperitoneal lymphatic conglomerate of 15 × 8.5 × 8 cm that involved the left adrenal gland, left kidney and ureter, as well as the celiac trunk, superior mesenteric artery, the duodenum, and the proximal small intestine. There were also two 5 mm hypodense lesions found in the liver segment 6 and 8, with prominence of the internal bile ducts (Fig. 1 and 2). She was diagnosed with recurrence of the disease and was not considered candidate for either surgical or medical treatment.

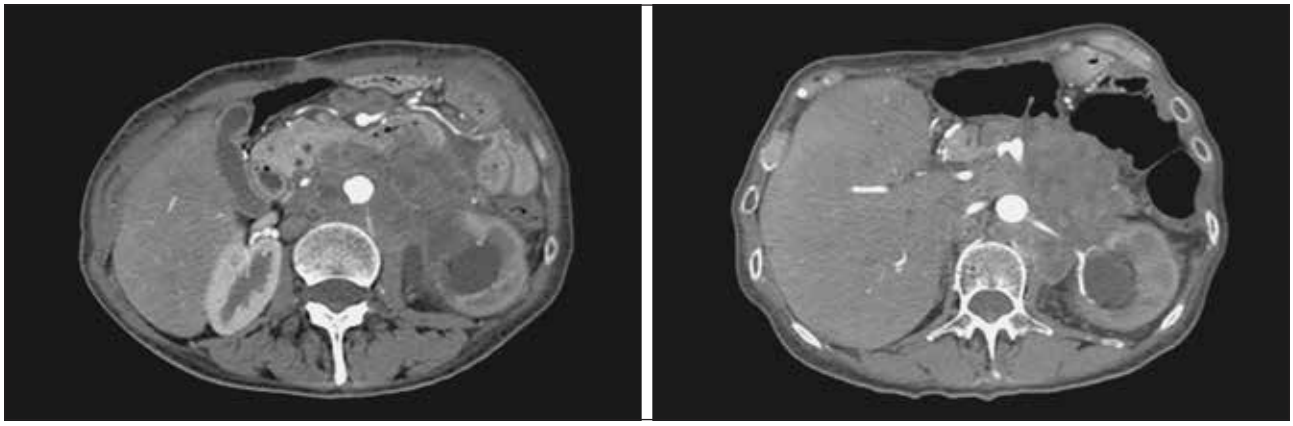

**Figure 2.** Case 1: Computed tomography scan in an arterial contrast phase, showing invasion of the celiac axis, the left renal artery, and adjacent structures.

**Figure 3.** A 7 × 6 cm irregular tumor of the body and tail of the pancreas.

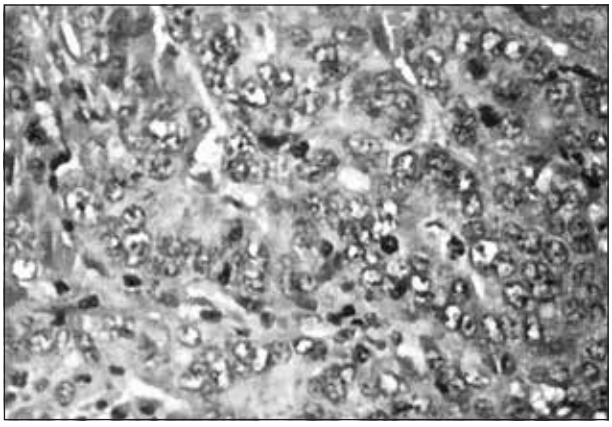

**Figure 4.** Poorly differentiated carcinoma with a syncytial growth pattern, expansive borders, and necrosis.

The second case is a 34-year-old female patient with no past medical history and a positive family history for cervical cancer and a non-specified gastrointestinal cancer in first-degree relatives. She presented with a history of six-month, mild-to-moderate, oppressive epigastric pain. The rest of the history and physical examination was unremarkable. Upon initial evaluation, an abdominal US showed evidence of a pancreatic tumor, which was further characterized with an abdominal CT and magnetic resonance imaging (MRI) as a heterogeneous 7 cm pancreatic tumor that originated from the body and tail of the gland without vascular infiltration. She underwent subtotal pancreatectomy, splenectomy, and portomesenteric confluence reconstruction in November 2011. The histological examination revealed a 7 × 6 cm infiltrative tumor with undefined margins and necrotic areas, further characterized as a medullary pancreatic carcinoma with tumor-free surgical margins and seven out of 18 positive lymph nodes (Fig. 3 and 4). The tumor was found to have microsatellite instability.

She was discharged six days later without any complications. Afterwards, she received adjuvant chemotherapy with gemcitabine and is currently on follow-up with an annual MRI. Her last image showed no signs of recurrence of the disease.

## DISCUSSION

In 1998, Goggins, et al. found and described a medullary histologic pattern in three out of 82 screened carcinomas of the pancreas. Typical pancreatic ductal adenocarcinomas contain a mutant K-ras gene; however, all three of the medullary carcinomas expressed a wild-type K-ras[3]. In a more recent publication, Wilentz, et al. described performance of an analysis of 450 randomly chosen pancreatic cancers and found 18 medullary carcinomas, of which 67% had a wild-type K-ras gene ($p < 0.0001$) and 22% had microsatellite instability ($p = 0.001$), whereas only 5.6% of the 72 conventional ductal adenocarcinomas had wild-type k-ras gene[4]. An association ($p = 0.0004$) between a family history of any cancer in a first-degree relative, especially breast, lung, melanoma, prostate, and pancreatic cancer in a descending fashion (except for basal cell and squamous cell of the skin), has been described[4].

All of these findings suggest that medullary carcinoma of the pancreas can be either an inherited or acquired mutation, similar to the hereditary nonpolyposis colorectal carcinoma syndrome (HNPCC), which is also characterized by microsatellite instability[5,6]. On the other hand, colorectal adenocarcinomas associated with HNPCC express medullary features.

In 2006, Banville, et al. described the association between HNPCC and other types of carcinomas such as endometrial, colorectal, and pancreatic tumors[5]. In his paper, he reported the second case of medullary carcinoma of the pancreas occurring in a man with HNPCC who presented with mild gastrointestinal discomfort, flatulence and satiety, after years of surgical treatment for rectal adenocarcinoma and metachronous cecal adenocarcinoma[5].

## CONCLUSION

Medullary carcinoma of the pancreas can only be diagnosed after histological examination by complying with the description performed by Goggins, et al. in 1998[3]. This disease presents as nonspecific gastrointestinal discomfort, with no associated body weight loss. However, as mentioned before, only a handful of cases have been reported, and therefore the need for proper identification and case reports is essential for further knowledge of the disease's diagnosis, treatment, and response. Due to the genetic properties of this disease, family members may benefit from genetic counseling, screening, and thus early detection and treatment, which will provide a better prognosis if related to microsatellite instability[6].

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