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# Inflammatory Myofibroblastic Tumor of the Pancreatic Head: An Unusual Cause of Recurrent Acute Pancreatitis – Case Presentation of a Palliative Approach after Failed Resection and Review of the Literature

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## Key Words

Inflammatory myofibroblastic tumor · Pancreas · Recurrent acute pancreatitis · Chronic obstructive pancreatitis

## Abstract

Inflammatory myofibroblastic tumors (IMTs) are a rare cause of echo-poor pancreatic head enlargement. Histologically, IMTs are characterized by spindle-shaped myofibroblasts or fibroblasts accompanied by a mixed immune cell infiltration. The most common localizations of IMTs have been reported in lung, mesentery and omentum, especially in children and young adults. IMTs show infiltrating growth, multilocular appearance and also metastasis have been reported. Curative resection is the only therapeutic option so far. In the palliative situation, evident data and clear guidelines for this rare tumor entity are missing. We report on a 44-year-old male with an unresectable IMT of the pancreatic head causing recurrent episodes of acute pancreatitis that resulted in a chronic obstructive course of the disease. The patient entered a palliative therapeutic regimen including radiation therapy and antiinflammatory medication. In a regular follow-up of 12 months, he presented with stable disease after initial progression. This case of local progressive IMT of the pancreatic head was managed with a palliative therapeutic regimen and is discussed based on the current literature.

## Introduction

Inflammatory myofibroblastic tumors (IMTs) occur primarily in visceral and soft tissue of children and young adults and occur most frequently in the first two decades of life. The most common localizations of IMTs have been reported in lung, mesentery and omentum [1, 2]. The etiology of IMT is unknown, although infection by Epstein-Barr virus or human herpesvirus-8 and reactive IL-6 production have been observed in a number of cases and discussed as etiological factors [2, 3]. A localization of IMT in the pancreas is very rare and needs differentiation from pancreatic head enlargement due to chronic pancreatitis and pancreatic cancer.

The macroscopic appearance of IMT is usually a well-circumscribed or multinodular, white, firm mass with a whorled fleshy cut surface [2]. Histologically, IMT is composed of spindle-shaped myofibroblasts or fibroblasts accompanied by a mixed inflammatory infiltrate of eosinophils, plasma cells, and lymphocytes [1, 2]. Necrosis, a central scar, osseous metaplasia, and psammomatous calcifications have been described. The symptoms of IMT are determined by the tumor site. If localized in the pancreatic head with obstruction of the main pancreatic duct, it results in acute and finally chronic obstructive pancreatitis. It is a condition that needs to be differentiated from pancreatic head enlargement due to chronic pancreatitis and pancreatic cancer.

Here we present the case of a young male patient with a history of recurrent acute pancreatitis caused by an IMT of the pancreatic head. In contrast to most reported cases, surgical resection was not possible and a palliative therapeutic regimen including radiation therapy as well as antiinflammatory treatment was established with a regular follow-up of 12 months.

## Case Report

A 44-year-old male presented to our outpatients department with a two-year history of recurrent acute pancreatitis of unknown etiology. He complained about recurrent upper abdominal pain, intermittent diarrhea, nausea, recurrent emesis and weight loss of 40 kg in the course of the last year. His family history was negative for any pancreatic or malignant disease.

The patient's past medical history had been inconspicuous until April 2006 when he was admitted to a regional hospital because of recurrent abdominal pain and jaundice. A first ERCP in that hospital revealed a stenosis of the distal common bile duct and a small concrement proximal to the stenosis. After endoscopic papillotomy and concrement extraction an endoprosthesis was inserted. The pancreatic duct was not visualized. In June 2006, the patient was scheduled for an elective surgical procedure because of the common bile duct stenosis of unknown etiology. A cholecystectomy was performed as there was cholecystolithiasis and a biliodigestive anastomosis was created revealing chronic inflammation of the resected common bile duct. The histological specimen of the common bile duct showed chronic granulomatous inflammation with low-grade dysplasia.

Recurrent attacks of abdominal pain, nausea and emesis in the following months finally led to referral to the department of gastroenterology. Transabdominal ultrasound ([fig. 1](#)) revealed an echo-poor hypovascularized lesion in the pancreatic head, 60 × 40 mm in size, with a dilated main pancreatic duct up to 6 mm in the pancreatic corpus. Additionally, multiple peripancreatic lymph nodes 8–10 mm in diameter were depicted in the peripancreatic mesenterium. Laboratory results showed a 9-fold increase of lipase in combination with elevated markers of cholestasis and slightly elevated transaminases. The concentration of IgG-4 was below the normal range. Blood cell count, coagulation tests and C-reactive protein were within normal ranges. Exocrine pancreatic insufficiency was diagnosed by repeated measurements of pancreatic elastase in the stool and confirmed by <sup>13</sup>C-mixed-triglyceride breath test. Endocrine pancreatic insufficiency was ruled out. Contrast-enhanced

CT scan (fig. 2a) confirmed the findings of the transabdominal ultrasound with inhomogeneous pancreatic parenchyma in the pancreatic head, a hypodense lesion of almost 3 cm in size within the pancreatic head closely adjacent to the neighboring anatomic structures such as the portal vein, and a dilated main pancreatic duct in the pancreatic corpus and tail. Multiple lymph nodes with a maximum size of 24 mm were depicted in close neighborhood of the organ. There were no focal lesions in the hepatic parenchyma and no intrahepatic cholestasis.

With a suspicion of malignant pancreatic head enlargement, the patient underwent surgery. Intraoperatively, the pancreatic head presented as a hard mass. The pancreatic body and tail showed fibrosis but less distinct than within the pancreatic head. Circumscribed necrosis of pancreatic parenchyma was visible. Preparation of the portal vein was not possible due to massive peripancreatic inflammation and multiple adhesions. As resection of the pancreatic head was technically impossible, a pancreaticogastrostomy was performed.

Histological examination (fig. 3) showed an IMT with compact fascicular proliferation of spindled and plump myofibroblasts and fibroblasts. The biopsy contained myxoid, edematous, and collagenized regions as well as a distinctive inflammatory infiltrate of lymphocytes, plasma cells and eosinophils. Spindled cells showed a strong expression of cytoplasmatic vimentin and sm actin whereas immunoreactivity of desmin, S100, cytokeratin, CD117, or ALK was not observed. Necrosis, cellular atypia, mitotic figures, or overexpression of p53 were not evident in the tissue. Histology was consistent with the diagnosis of an IMT. The adjacent pancreatic tissue was partly displaced by proliferating fibroblasts and collagen deposits. More distantly, there were periductular fibrosis and a scattered infiltrate of lymphocytes and histiocytes of the pancreatic tissue, leading to the diagnosis of chronic pancreatitis. No histological evidence of autoimmune pancreatitis was present.

The short-term postoperative course was unremarkable. After a follow-up of 3 months, the patient presented with aggravating abdominal pain and weight loss of 10 kg despite pancreatic enzyme supplementation. CT scan after another 6 months (fig. 2b) revealed a large tumor mass comprising the pancreatic head, liver hilus and mesenteric vessels. Symptomatically, the patient complained about non-infectious diarrhea due to exocrine pancreatic insufficiency and ischemic condition presenting with typical ischemic left colonic lesions and ischemic duodenitis. Lacking evidence-based guidelines, we decided to perform radiation therapy (20/2 Gy) and antiinflammatory medical therapy starting with 60 mg prednisolone per day that was tapered down. After another 3 months, the patient presented well-being in our outpatient department. Pain was symptomatically treated and controlled with novaminsulfon and a low-potent opioid (tramadol), stool frequency was stable and he gained 8 kg of weight. CT scan showed at least a stable tumor mass (fig. 2c) and the patient was scheduled for follow-up.

## Discussion

In case of recurrent acute pancreatitis of unknown etiology and echo-poor pancreatic head enlargement, ductal adenocarcinoma is always an important differential diagnosis. Clinically and morphologically, the very rare IMT resembles pancreatic adenocarcinoma as well as inflammatory lesions related to autoimmune pancreatitis or malignant fibrous histiocytoma.

For several decades the term ‘inflammatory pseudotumor’ summarized a wide range of reactive and neoplastic lesions. During the last decade the diagnosis and characterization of IMT has been optimized by distinct pathological and molecular features. The World Health Organization classifies this rare tumor entity as a distinctive neoplasm of intermediate biological potential [4]. Especially the discovery of cytogenetic aberrations in IMT and the recognition of ALK gene rearrangements solidified the concept of IMT as a neoplastic lesion [5]. It most frequently occurs in the lung or the mesenterium of children or young adults and rarely (<5%) metastasizes [5, 6].

In a large study of IMTs by Coffin et al. [2], extrapulmonary IMTs were described to be larger and less well-circumscribed than pulmonary IMTs. Adjacent organs are more often involved, which reduces the opportunity for complete resection and leads to a recurrence rate of approximately 25% related to resectability, multinodularity, and location.

Only 28 cases of pancreatic IMT have been reported so far [7, 8], 60% being located in the pancreatic head (table 1). Histological diagnosis in biopsies or intraoperative frozen sections is difficult and IMTs must be differentiated from inflammatory pseudotumors due to autoimmune pancreatitis [9] or chronic pancreatitis, fibrosarcoma, pancreatic carcinoma and lymphoma [10], as their therapies differ substantially. The low incidence of IMT of the pancreas and the synonymous use of the terms IMT and inflammatory pseudotumor make it even more difficult to give consistent information on epidemiology, clinical presentation and prognosis of this tumor entity.

Here we report the case of a young male with a history of chronic pancreatitis due to recurrent episodes of acute pancreatitis caused by an IMT in the pancreatic head. In contrast to the majority of cases in the literature (table 1), curative resection was impossible. The two-year history of recurrent attacks of acute pancreatitis and of a stenosis of the common bile duct with histopathologic signs of chronic inflammation leads to the assumption that the tumor developed over a longer period of time.

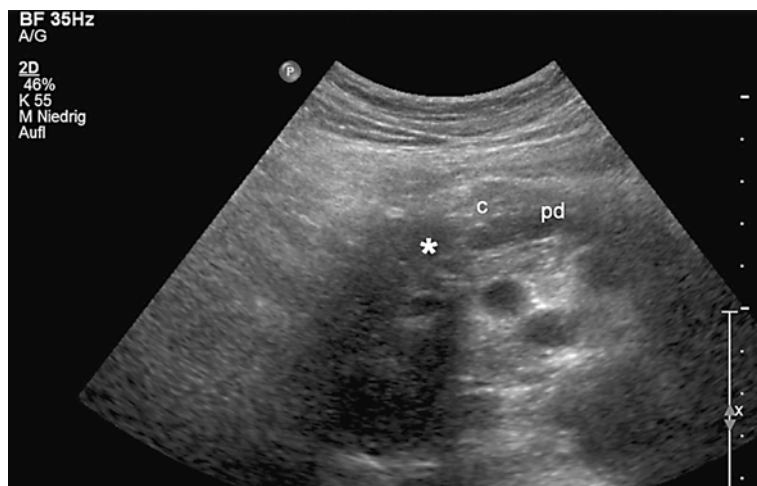
Besides surgical resection, alternative therapeutic regimes are still lacking. While systemic immunosuppressive treatment with steroids has been reported for extrapancreatic IMTs, there is only one reported case of IMT localized in the pancreatic head in a pediatric patient [11] that was treated with a palliative approach. In our patient we decided to perform palliative radiation for local tumor treatment combined with antiinflammatory medical treatment as an individualized approach. The patient has been included in a regular follow-up of 12 months up to now. Radiation therapy and corticoid medication might be discussed for alternative and symptomatic treatment but cannot be recommended as a standard regimen for palliative therapy. Close follow-up and symptomatic therapy are the basic therapeutic modalities that hopefully can be complemented by an effective medical therapy in future.

#### Disclosure Statement

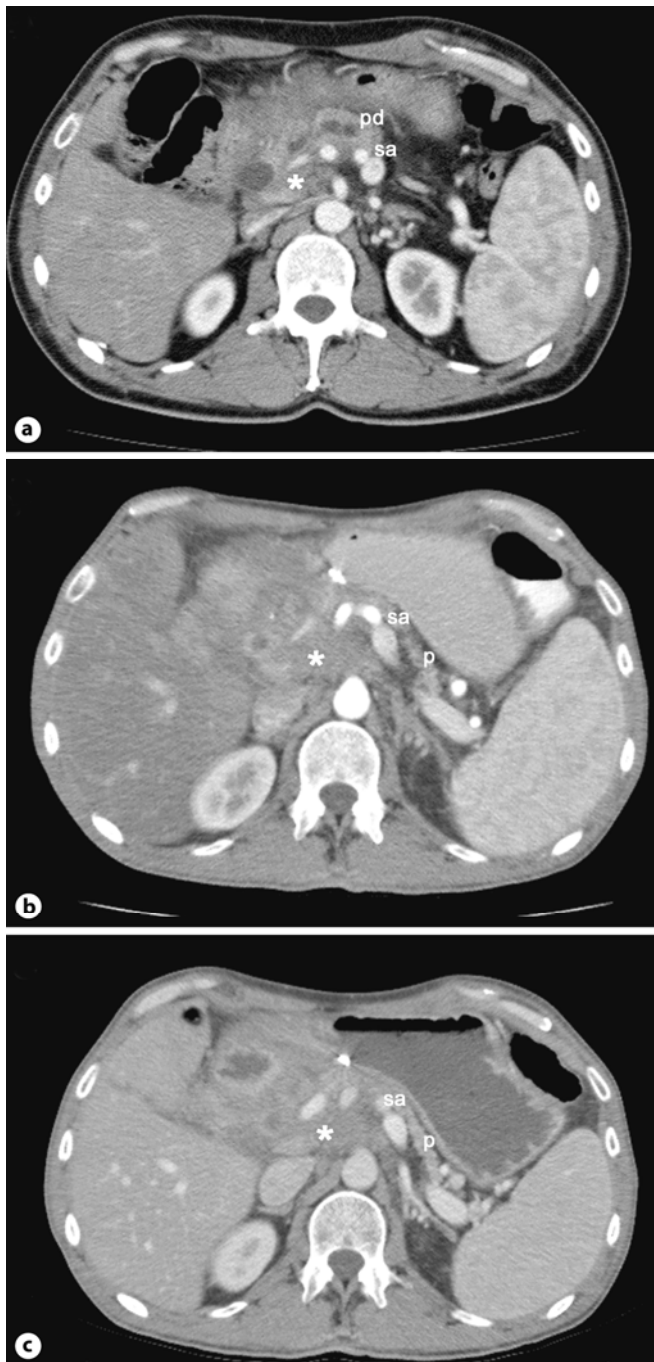
The authors have no competing interests to declare.

**Table 1.** Case reports of pancreatic IMT displaying age at time of diagnosis, gender, tumor size and localization, therapy and follow-up

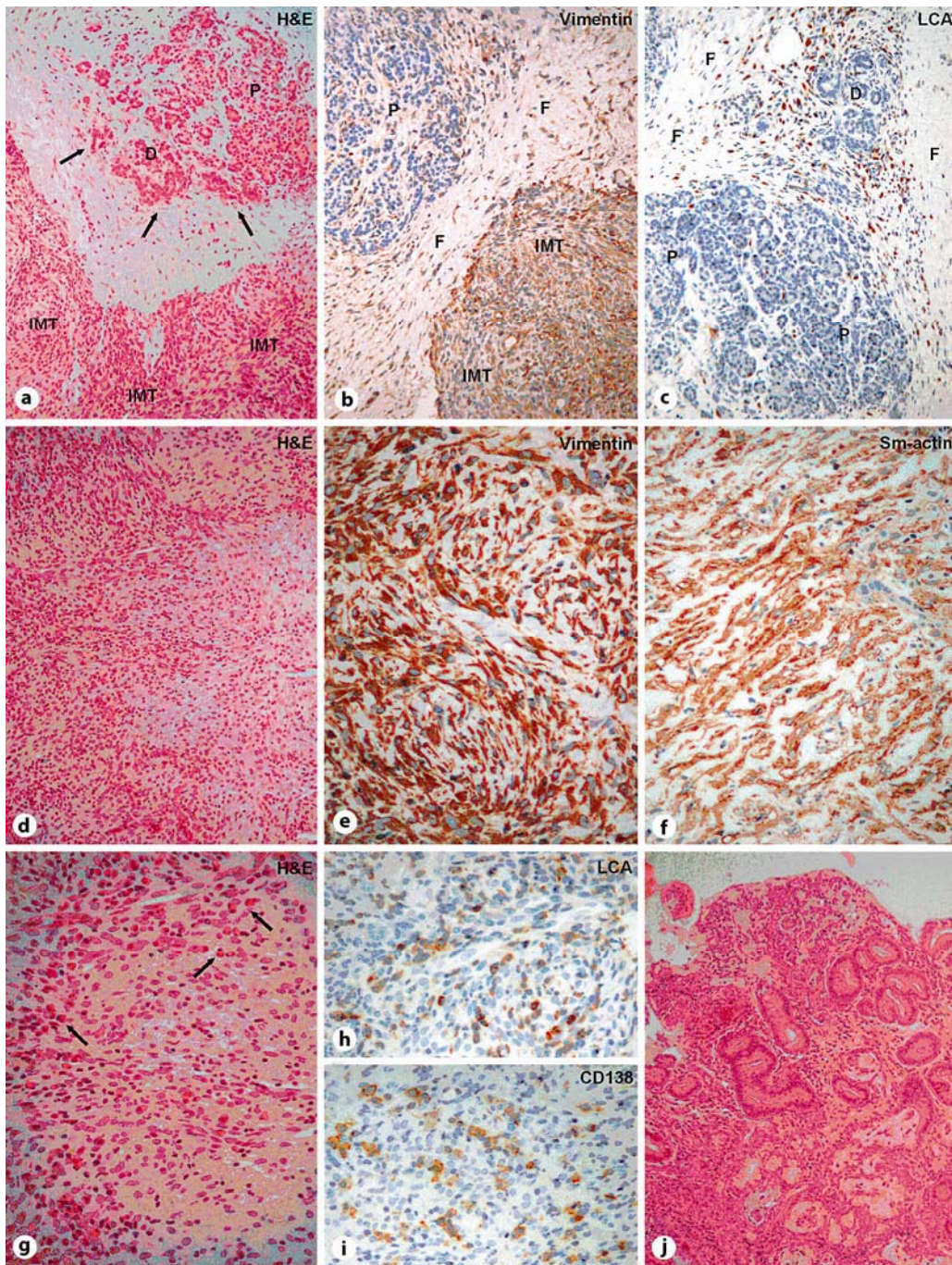
Reference	Age (years)	Gender	Tumor size (CT/US)	Localization	Therapy	Follow-up
Johnson et al. [12]	29	F	10 cm	pancreatic head	resection	relapse after 8 months
Abrebanel et al. [13]	12	F	12 cm	pancreatic body	resection	2 years, curative
Scott et al. [14]	2.5	F	13 cm	pancreatic body	resection	6 years, curative
Palazzo and Chang [15]	52	F	3 cm	pancreatic tail	resection	6 months, curative
Uzoaru et al. [16]	8	F	3 cm	pancreatic head	resection	4.5 years, curative
Kroft et al. [17]	39	F	7 cm	pancreatic body	resection	6 months, curative
Qanadli et al. [18]	29	M	12 cm	pancreatic tail	resection	5 months, curative
Shankar et al. [19]	8	F	10.7 cm	pancreatic body and tail	resection	2 years, curative
Petter et al. [20]	64	M	5 cm	pancreatic head	resection	4 years, curative
Morris-Stiff et al. [21]	11	M	10 cm	pancreatic body and tail	resection	3 years, curative
McClain et al. [22]	11	F	3.4 cm	pancreatic head	resection	not available
Liu and Consorti [23]	54	F	5 cm	pancreatic head	resection	2 years, curative
Walsh et al. [24]	35	M	5 cm	pancreatic head	resection	relapse with lung metastasis after 6 years
Zanger et al. [25]	62	F	4.5 cm	pancreatic head	resection	6 months, curative
Yamamoto et al. [26]	55	M	1.5 cm	pancreatic head	resection	28 months, curative
Slavotinek et al. [27]	4	F	3 cm	pancreatic head	resection	4 years, curative
Esposito et al. [28]	69	M	tumor mass	pancreatic body and tail	resection	7 months <sup>†</sup>
Pungpapong et al. [7]	70	M	3.8 cm	pancreatic tail	resection	10 months, curative
Wreesman et al. [29]	62	M	3 cm	pancreatic head	resection	6 years, curative
	56	M	not available	pancreatic head	resection	5 years, curative
	50	M	5 cm	pancreatic head	resection	4 years, curative
	57	F	not available	pancreatic head	resection	3 years, curative
	45	M	no mass lesion identified	pancreatic head	resection	10 years, curative
	32	F	2.5 cm	pancreatic head	resection	12 years, curative
Stringer et al. [30]	5	F	7 cm	pancreatic body	resection	9 months, curative



**Fig. 1.** Transabdominal ultrasound (Philips, 2D 35 Hz) revealing an echo-poor pancreatic head enlargement (\*) and consecutive dilatation of the pancreatic duct (pd). The pancreatic tail presented with unsuspecting parenchyma, whereas small calcifications (c) were visible in the pancreatic head.



**Fig. 2.** CT scan images documenting tumor size and spread (\*) at diagnosis (a), 6 months after diagnosis (b) and another 3 months after radiation and corticoid therapy (c). At diagnosis, consecutive dilatation of the pancreatic duct (pd) was visible secondary to the pancreatic head enlargement. CT scan did not reveal typical morphological signs of advanced chronic pancreatitis [pancreatic parenchyma (p) and splenic artery and vein (sa)]. Follow-up after 3 months (b) presented a diffuse tumor mass comprising the pancreatic head, liver and mesenteric arteries. After radiation and corticoid therapy (c), a partial response of the tumor mass was visible. No metastases were detected.



**Fig. 3.** Panels of H&E staining (**a**) and immunohistochemical staining of vimentin (**b**) and LCA (leukocytic common antigen; CD45) (**c**) demonstrating replacement of the pancreatic tissue (P) by IMT with compression of the ductuli (D, →), fibrosis (F) and sparse infiltration of lymphocytes. High magnification showed a compact spindle proliferation with fascicular and storiform pattern (**d**) and a polymorphous inflammatory infiltrate with predominant eosinophils (**g**, →), lymphocytes (**h**), and plasma cells (**i**). Biopsy of the duodenum showed ischemic changes with irregularity, atrophy and regenerative atypies of the epithelium (**j**). Spindle cells showed diffuse cytoplasmatic immunoreactivity of vimentin (**b**, **e**) and sm actin (**f**) (microscope: Zeiss Axioscope 50, camera: Nikon coolpix 990; magnification:  $\times 200$ ,  $\times 400$ ).

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The presentation of this case was approved and secured by the local ethics committee of our institution (Ethikkommission Otto von Guericke University Magdeburg, Faculty of Medicine) and conducted according to the Declaration of Helsinki.