CASE REPORT

Inflammatory Myofibroblastic Tumor Presenting as a Pancreatic Mass: A Case Report and Review of the Literature

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ABSTRACT

Context Inflammatory myofibroblastic tumor is a distinctive lesion of unknown etiology. It has generally been considered a rare benign pseudosarcomatous lesion of admixed inflammatory infiltrates with myofibroblastic spindle cells. Although original case descriptions focused on the pulmonary system, it is now recognized that virtually any anatomic location can be involved. However, an inflammatory myofibroblastic tumor located in the pancreas is rare.

Case report We report a case of an asymptomatic 70-year-old Caucasian man with a 3.8 cm inflammatory myofibroblastic tumor located in the tail of the pancreas which was discovered incidentally on a computed tomography scan of the abdomen. Endoscopic ultrasonography with fine needle aspiration was negative for malignancy. However, because of worrisome radiographic features, a distal pancreatectomy with splenectomy was performed. The pathology revealed an inflammatory myofibroblastic tumor with focal extension into the peripancreatic soft tissues, but with negative surgical margins. The patient has been followed for 10 months without evidence of recurrence.

Conclusions To date, there have been only 25 cases of inflammatory myofibroblastic tumor located in the pancreas reported in the English language scientific literature. Even with multimodal pre-surgical investigation, it can be extremely difficult to differentiate inflammatory myofibroblastic tumor from pancreatic malignancies. Most cases require surgical exploration and complete resection to obtain an accurate diagnosis. A review of published case reports is also presented.

INTRODUCTION

Inflammatory myofibroblastic tumor (IMT) is a relatively new histopathologic term describing an entity previously known as an inflammatory pseudotumor. It has generally been considered a rare benign pseudosarcomatous inflammatory lesion which develops in the soft tissues. It was initially described in the pulmonary system but it was subsequently recognized that virtually any anatomic location can be involved. However, IMT located in the pancreas remained a rare condition. We report a case of an asymptomatic 70-year-old Caucasian man with an IMT found in the tail of the pancreas presenting as a pancreatic mass, incidentally identified by a CT scan of the abdomen. Thus far, there have only been 25 cases reported in the literature due to its rarity. Most cases require surgical exploration and complete resection in order to obtain an accurate diagnosis. Even with multimodal pre-surgical investigation, it remains...
challenging to differentiate IMT from pancreatic malignancies.

CASE REPORT

A 70-year-old Caucasian man with a significant past medical history of hypertension, coronary artery disease and abdominal aortic aneurysm presented to our gastroenterology clinic for evaluation of a pancreatic mass. Initially, the patient underwent a computed tomography (CT) scan of the abdomen for follow-up of an abdominal aortic aneurysm. A mass measuring 3.5x2.4 cm, which was not present on a previous CT scan performed 15 months previously, was discovered incidentally in the tail of the pancreas (Figure 1). No regional lymphadenopathy or liver lesions to suggest metastases were identified. The patient was asymptomatic with unremarkable physical examination. Systematic reviews failed to demonstrate any significant presenting symptoms including abdominal pain, unintentional weight loss, anemia, jaundice, fever or any other systemic symptoms. Basic laboratory examinations of hemoglobin, white blood cell count, platelet count, electrolytes including calcium, magnesium, phosphorus, blood urea nitrogen, and creatinine were all normal. Serum amylase, lipase, and liver chemistry were also within normal limits. The patient had smoked 30 packs of cigarettes a year and had had a history of heavy alcohol consumption up to 20 years before presentation. The patient indicated that there was no family history of pancreatic malignancies or disorders. With an elevated probability of a malignant pancreatic neoplasm, the patient underwent further evaluation using endoscopic ultrasononography (EUS) with a radial echoendoscope (GF UM-130, 7.5 MHz; Olympus, Melville, New York, USA) to further evaluate and stage the mass. The EUS demonstrated parenchymal changes such as hyperechogenic foci and strands, lobularity and hyperechogenic borders of the pancreas suggestive of early chronic pancreatitis. A 36x25 mm hypoechoic mass with well-defined margins at the tail of the pancreas was confirmed (Figure 2). Fine needle aspiration was performed (GF UC-30P echoendoscope; Olympus, Melville, New York, USA) using a 22-gauge needle (Wilson-Cook Co., Winston Salem, North Carolina, USA). Cytopathology showed chronic inflammatory cells, benign columnar cells and scant stromal cells with no evidence of malignancy. Since imaging findings could not exclude malignancy and the mass appeared resectable, the patient underwent a distal pancreatectomy with splenectomy. The operation was performed successfully without

Figure 1. CT scan of the pancreas shows a low density mass in the tail region (arrow).

Figure 2. EUS shows a hypoechoic well-defined mass in the tail of the pancreas without invasion.
complications. Macroscopic pathology revealed an irregular white firm area of fibrosis measuring 3.8 cm in the tail of the pancreas with focally infiltrating borders. Microscopic pathology showed predominantly bland spindle and stellate-shaped cells in a loose fibrous background surrounding the residual benign pancreatic parenchyma. Focally, the proliferation extended into the peripancreatic soft tissues, and scattered, loosely formed lymphoid aggregates were present (Figure 3). There was a prominent admixed lymphoplasmacytic infiltrate (Figure 4). Paraffin section immunohistochemistry demonstrated strong diffuse positivity for smooth muscle actin with patchy positivity for CD68 (KP-1) and no staining for c-kit (CD117) (Figure 5). CD3 and CD20 stains showed a normal mixture and distribution of T and B cell lymphocytes. Kappa and lambda light chain stains showed a polyclonal plasma cell population. In-situ hybridization testing for Epstein-Barr virus RNA was negative. The proximal surgical margin and radial margins were uninvolved. The patient has been followed for 10 months without clinical or radiographic evidence of recurrence.

DISCUSSION

The term inflammatory myofibroblastic tumor, commonly referred to as inflammatory pseudotumor in the earlier literature, was initially proposed in 1990 in the study of inflammatory lesions of the pulmonary system [1]. Various names have been used to describe this entity, such as plasma cell granuloma, plasma cell pseudotumor, inflammatory fibroxanthoma, inflammatory pseudotumor and histiocytoma [2]. IMT has generally been considered a benign tumefaction having a possibly reactive nature due to its occasional occurrence after surgery or trauma, or in association with another malignancy [3]. Despite the distinctive inflammatory component, concurrent
infection is usually not documented, although some researchers suggest the role of cytokines, particularly interleukin-6, in its pathogenesis [3]. Some clinical and pathological aspects of IMT suggest the possibility that this lesion is more similar to a neoplasm than a post-inflammatory process, such as reports of cytogenetic clonality and recurrent involvement of chromosomal region 2p23 [3, 4]. Other investigators, however, argue that IMT may, in fact, be a true sarcoma and prefer the designation inflammatory fibrosarcoma [5]. Case reports of inflammatory fibrosarcoma which had characteristics of aggressive local behavior and potential metastases resulting in some deaths have been described. [5]. It still remains controversial whether IMT and inflammatory fibrosarcoma are actually the same tumor or distinct entities. Currently, it is generally accepted that IMT is indeed a true neoplasm with a wide spectrum of biological behavior, varying from the more frequent benign lesions to the rare tumors which are multifocal and prone to recurrence [3].

Inflammatory fibrosarcoma has become recognized as part of a spectrum of inflammatory myofibroblastic proliferations, which has the potential for local aggressive behavior and occurs predominantly in the mesentery of children and young adults [6]. IMT is a rare mass-like lesion composed of a variety of inflammatory or other mesenchymal cells [7]. Although it occurs more frequently in the pulmonary system, similar lesions have been reported in a wide variety of organs [8]. In a large series comprising 84 cases of extrapulmonary IMT, the sites of involvement were the mesentery and/or the omentum in 36 cases (42.9%), other intra-abdominal sites in 13 cases (15.5%), genitourinary tract in 8 cases (9.5%), upper respiratory tract in 9 cases (10.7%), pelvis and retroperitoneum in 4 cases (4.8%), trunk in 8 cases (9.5%), extremities in 3 cases (3.6%), and head and neck in 3 cases (3.6%) [9, 10, 11]. Moreover, IMT has also been described in other specific sites, including the orbit [12], the salivary glands (Kuttner tumor) [13], the spleen [14], the liver [15, 16], the urinary bladder and the soft tissues [17]. Sclerosing mediastinitis, retroperitoneal fibrosis (Ormond’s disease) and Riedel’s disease of the thyroid region also share many of the features of IMT and should perhaps be included in the list of extrapulmonary IMTs [8].

IMT is characterized histologically by paucicellular to moderately cellular spindle to stellate-shaped cells with an admixed inflammatory infiltrate of varying density [7]. The histological features of this tumor vary slightly from site to site, which may, at least in part, be related to differences in the phase of the lesion’s development at the time the lesion becomes symptomatic or detectable by radiographic imaging. Key features include the presence of a myofibroblastic proliferation, often with a vaguely storiform architecture, and a varying degree of inflammatory infiltrates, mainly consisting of lymphocytes, histiocytes and plasma cells [8]. Focally, there is lymphoid follicle formation with germinal centers. Mitotic figures are variable, but not atypical. Although there are only scattered eosinophils in many cases of IMT, in some instances eosinophils can be present as a prominent feature [8, 18]. A few case reports of patients who underwent a Whipple resection for what proved to be an IMT in the head of the pancreas demonstrated a predominant eosinophilic inflammatory component, making them difficult to differentiate from the rare condition of true eosinophilic pancreatitis [18, 19]. Histologically, eosinophils did not only involve the lesion itself, but also infiltrated adjacent structures including the duodenum, the distal common bile duct and the ampulla. However, peripheral eosinophilia was not present.

Besides the aforementioned extrapulmonary sites, IMT occurring in the pancreas is rare [2, 8]. Thus far, there have been only 25 patients with IMT arising in the pancreas reported in the English language scientific literature [2, 7, 8, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35]. Table 1 presents a summary of these case reports (including our case) in terms of patient demographics (age
and gender), tumor characteristics (size and location), and pre-surgical diagnostic investigations. IMT of the pancreas may develop at any age (reported range: 2.5-70 years; average: 36 years). Ten of the 25 patients (40.0%) were younger than 30 years of age, and the age distribution resembled that of IMT in pulmonary sites [1, 2, 9]. Slightly more than half of the patients (56.0%) were female. The most common clinical presentation of IMT located in the pancreas is a mass discovered incidentally by radiographic investigations for other reasons [1, 2, 9]. Table 2 lists a summary of presenting symptoms and signs of pancreatic IMT including abdominal pain or discomfort (64.0%), unintentional weight loss (44.0%), jaundice (40.0%), palpable abdominal mass (28.0%), and anemia (20.0%). In addition, fatigue, fever, anorexia, nausea and vomiting were also described as associated clinical presentations. Ten of the 15 patients with IMT found in the head of the pancreas (66.7%) presented with jaundice and pruritus from the mass causing extrahepatic biliary obstruction. Interestingly, one patient with IMT located in the body and the tail of the pancreas developed splenic vein thrombosis resulting in splenomegaly, thrombocytopenia and upper gastrointestinal hemorrhage from isolated gastric varices [24]. IMT of the pancreas has a tendency to be a larger mass than that in the pulmonary system at the time of diagnosis [2, 9]. Tumor size ranged from 1.5 to 13 cm with an average of 6 cm and 12 of 20 patients (60%) had masses of 5 cm or more. The tumor was located in the head of the pancreas in 15 patients (60.0%), whereas it was found in the body and the tail of the pancreas in 10 patients (40.0%).

Table 1. Summary of case reports of IMT arising from the pancreas.

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Gender</th>
<th>Tumor size</th>
<th>Tumor location</th>
<th>Investigation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson [20]</td>
<td>29</td>
<td>F</td>
<td>10 cm</td>
<td>Head</td>
<td>Endoscopy</td>
</tr>
<tr>
<td>Abrebanel [21]</td>
<td>12</td>
<td>F</td>
<td>12 cm</td>
<td>Body</td>
<td>US</td>
</tr>
<tr>
<td>Scott [22]</td>
<td>2.5</td>
<td>F</td>
<td>13 cm</td>
<td>Body</td>
<td>US</td>
</tr>
<tr>
<td>Stringer [23]</td>
<td>5</td>
<td>F</td>
<td>7 cm</td>
<td>Head</td>
<td>US</td>
</tr>
<tr>
<td>Dudiak [24]</td>
<td>45</td>
<td>M</td>
<td>Unknown</td>
<td>Body and tail</td>
<td>CT</td>
</tr>
<tr>
<td>Palazzo [25]</td>
<td>52</td>
<td>F</td>
<td>3 cm</td>
<td>Tail</td>
<td>CT, MRI</td>
</tr>
<tr>
<td>Uzoaru [26]</td>
<td>8</td>
<td>F</td>
<td>3 cm</td>
<td>Head</td>
<td>CT</td>
</tr>
<tr>
<td>Kroft [27]</td>
<td>42</td>
<td>F</td>
<td>7 cm</td>
<td>Body</td>
<td>CT</td>
</tr>
<tr>
<td>Qanadli [28]</td>
<td>29</td>
<td>M</td>
<td>12 cm</td>
<td>Tail</td>
<td>US, CT</td>
</tr>
<tr>
<td>Shankar [29]</td>
<td>8</td>
<td>F</td>
<td>10.7 cm</td>
<td>Body and tail</td>
<td>US, CT</td>
</tr>
<tr>
<td>Petter [30]</td>
<td>64</td>
<td>M</td>
<td>5 cm</td>
<td>Head</td>
<td>CT</td>
</tr>
<tr>
<td>Morris-Stift [31]</td>
<td>11</td>
<td>M</td>
<td>10 cm</td>
<td>Body and tail</td>
<td>US, CT</td>
</tr>
<tr>
<td>McClain [32]</td>
<td>11</td>
<td>F</td>
<td>3.4 cm</td>
<td>Head</td>
<td>US, MRI</td>
</tr>
<tr>
<td>Liu [33]</td>
<td>54</td>
<td>F</td>
<td>5 cm</td>
<td>Head</td>
<td>CT</td>
</tr>
<tr>
<td>Slavotinek [34]</td>
<td>4</td>
<td>F</td>
<td>3 cm</td>
<td>Head</td>
<td>US, CT</td>
</tr>
<tr>
<td>Wreesman [8]</td>
<td>62</td>
<td>M</td>
<td>3 cm</td>
<td>Head</td>
<td>US, CT</td>
</tr>
<tr>
<td></td>
<td>56</td>
<td>F</td>
<td>Unknown</td>
<td>Head</td>
<td>US, CT</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>M</td>
<td>5 cm</td>
<td>Head</td>
<td>US, CT</td>
</tr>
<tr>
<td></td>
<td>57</td>
<td>F</td>
<td>Unknown</td>
<td>Head</td>
<td>US, CT</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>M</td>
<td>No definite mass lesion</td>
<td>Head</td>
<td>US, CT</td>
</tr>
<tr>
<td></td>
<td>32</td>
<td>F</td>
<td>2.5 cm</td>
<td>Head</td>
<td>US, CT</td>
</tr>
<tr>
<td>Yamamoto [2]</td>
<td>55</td>
<td>M</td>
<td>1.5 cm</td>
<td>Head</td>
<td>US, CT</td>
</tr>
<tr>
<td>Walsh [7]</td>
<td>35</td>
<td>M</td>
<td>5 cm</td>
<td>Head</td>
<td>CT</td>
</tr>
<tr>
<td>Esposito [35]</td>
<td>69</td>
<td>M</td>
<td>Unknown</td>
<td>Body and tail</td>
<td>CT</td>
</tr>
<tr>
<td>Present study</td>
<td>70</td>
<td>M</td>
<td>3.8 cm</td>
<td>Tail</td>
<td>CT, EUS</td>
</tr>
</tbody>
</table>

MRI: magnetic resonance imaging
US: trans-abdominal ultrasonography
the patients (24 of 25 patients) underwent exploratory laparotomy and surgical resection. However, correct diagnoses were not made in any of these patients before pancreatic resection, even with an intraoperative frozen section biopsy. Preoperative or intraoperative diagnoses included pancreatic carcinoma in 14 patients, benign tumor of pancreas in 3 patients, pancreaticoblastoma in 1 patient, and neuroblastoma in 1 patient.

The prognosis of IMT is generally considered to be favorable, with only a rare incidence of malignant transformation and remote metastasis [36]. The only known effective treatment for IMT is complete surgical resection [22, 37, 38]. In most cases, further aggressive measures, including chemotherapy and radiation therapy, are avoided due to the generally benign clinical course and the seemingly limited biologic potential of these tumors [36]. However, in one study, a significant recurrence rate of 25% was demonstrated, likely related to factors precluding complete surgical resection, such as adherence to vital structures and multifocality [9]. IMT occurring in the abdomen or retroperitoneum has a propensity for more aggressive behavior with multiple recurrences, invasion into adjacent structures and metastases [36]. Some studies suggest that a combination of atypia, ganglion-like cells, aneuploidy and p53 expression may indicate more aggressive behavior [38, 39].

Histologically, malignant transformation is demonstrated by transition from uniform spindle cells to atypical polygonal cells or plump cells with vesicular nuclei, prominent nucleoli, increased proliferative activity and tumor necrosis [9, 37]. These lesions are very difficult to differentiate from inflammatory fibrosarcoma, and may at times be indistinguishable due to a high degree of morphological and clinical overlap [36]. Little data is available regarding the management of aggressive IMT or inflammatory fibrosarcoma due to the rarity of these tumors [36]. Some modalities reported to have some benefit in the treatment of incompletely resected or invasive IMT include radiation therapy [5, 40, 41], immunosuppressive therapy with corticosteroids and nonsteroidal inflammatory agents [42], and chemotherapy with or without combined radiation therapy [9, 36]. Although specific management is not clearly defined, the potential role of cisplatin, doxorubicin, and methotrexate as an adjunct to surgical resection has been proposed, especially for locally recurrent malignant tumors not amenable to complete resection [36].

This case emphasizes the difficulty in pre-surgical differentiation of IMT from pancreatic malignancies, even with multimodal investigation. As previously mentioned, the pre-surgical diagnosis is often incorrect and most patients usually require surgical exploration and resection to establish an accurate diagnosis. In our patient, the pre-surgical differential diagnosis included pseudotumor pancreatitis, non-functioning islet cell tumor and pancreatic adenocarcinoma. Because of a higher recurrence rate, approaching 25% in extrapulmonary IMT, our patient has been closely followed with no clinical or radiographic evidence of recurrence 10 months following surgery.

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Abbreviations  IMT:  inflammatory myofibroblastic tumor;  MRI:  magnetic resonance imaging;  US:  trans-abdominal ultrasonography

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