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Inflammatory Myofibroblastic Pancreas Tumor: A Case Report

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Abstract Inflammatory myofibroblastic tumor (IMT) is a rare tumor; characterized by a proliferation of myofibroblasts associated with inflammatory reaction cells and which can be observed at the various anatomical sites. The pancreas represents a very rare localization of this tumor. Surgery is the standard treatment, but for inoperable tumors; there is no consensus. We report a case of an inextirpable pancreatic IMT in a 46-years-old woman and we also carry out a literature review.

Keywords: *inflammatory myofibroblastic tumor, pancreas, ALK*

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1. Introduction

The World Health Organization (WHO) has classified inflammatory myofibroblastic tumors (IMT) as low-grade neoplasms composed of myofibroblastic and fibroblastic spindle cells with prominent admixed inflammatory cells, including plasma cells, lymphocytes, and/or eosinophils [1]. These lesions have been reported to show clonal proliferation, invasion, recurrence, and distant metastasis [2]. IMT primarily affects children and young adults, but it has been reported in adult patients of all ages. IMT was detected in the mesentery, omentum, retroperitoneum, pelvis, and abdominal soft tissue in 73% of cases, followed by the lung, mediastinum, and head and neck [3]. Pancreatic location is uncommon and can be confused with malignancy clinically and radiologically and needs to be differentiated from other tumors and chronic pancreatitis.

In this article, we present a new observation of TMI of the pancreas with a literature review.

2. Case Report

A 46-years-old woman operated 3 years ago for a hydatid cyst of the liver, was admitted to hospital with a 3-months history medical of biliary colic type pain without fever or jaundice. All evolving in the context of unencrypted weight loss and apyrexia.

Physical examination shows, in addition to a midline laparotomy scar, a voluminous epigastric mass, with irregular contours, hard and fixed in relation to the deep plane.

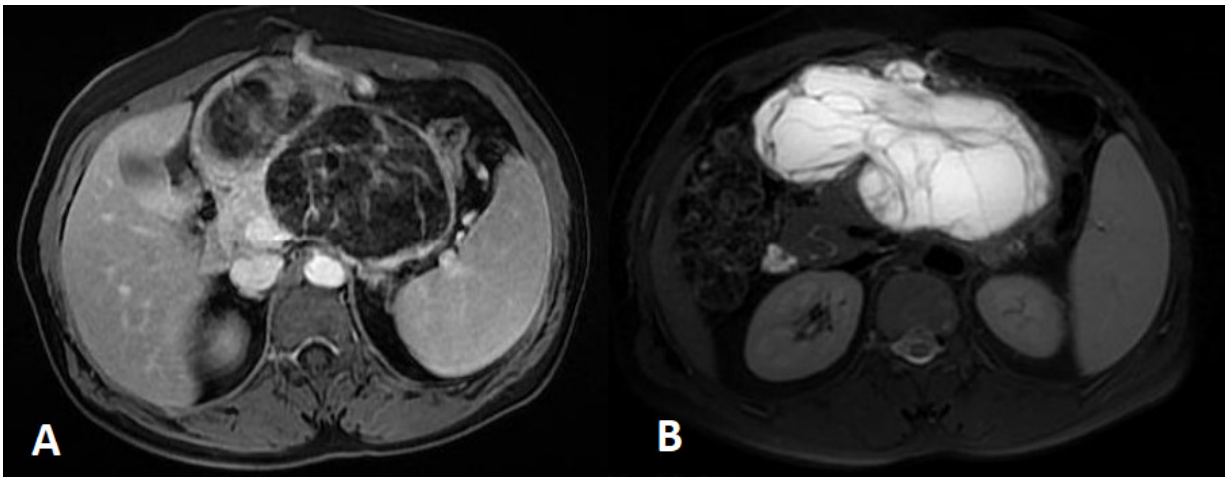

Figure 1. MRI showing a partitioned cystic mass of the body of the pancreas. A: T1-weighted fat-saturated post-gadolinium image, B: T2-weighted fat-saturated image

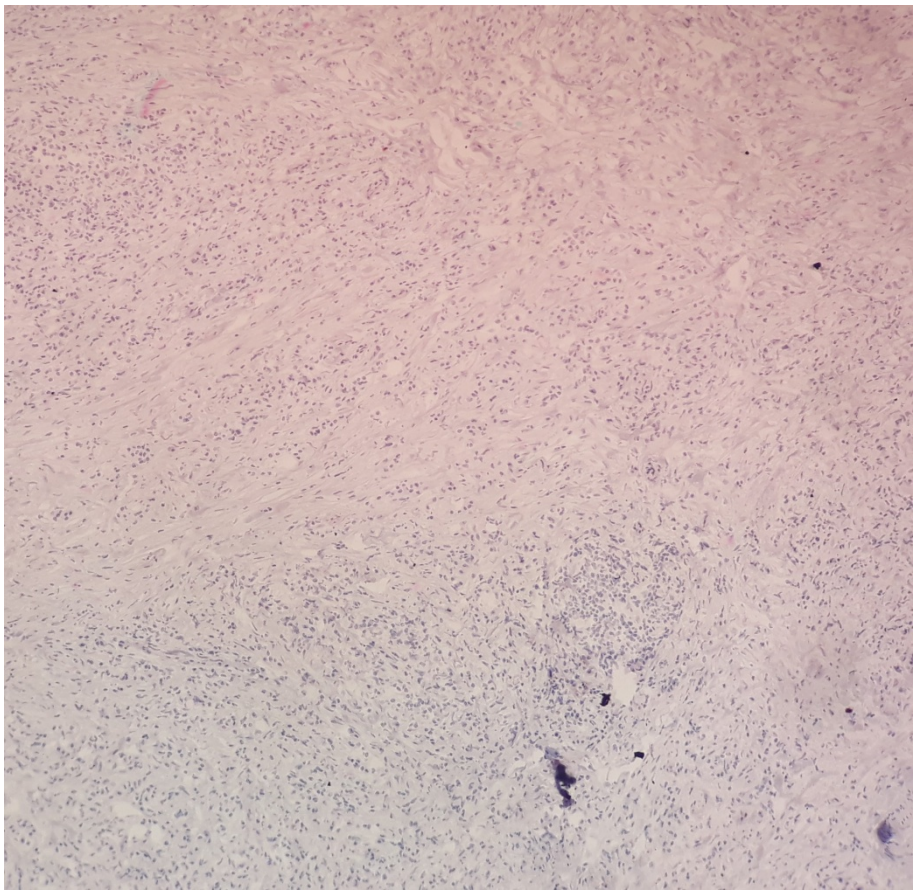

Figure 2. Tumoral proliferation of spindles cells admixed with lymphoplasmacytic infiltrate. (Gx40, HE)

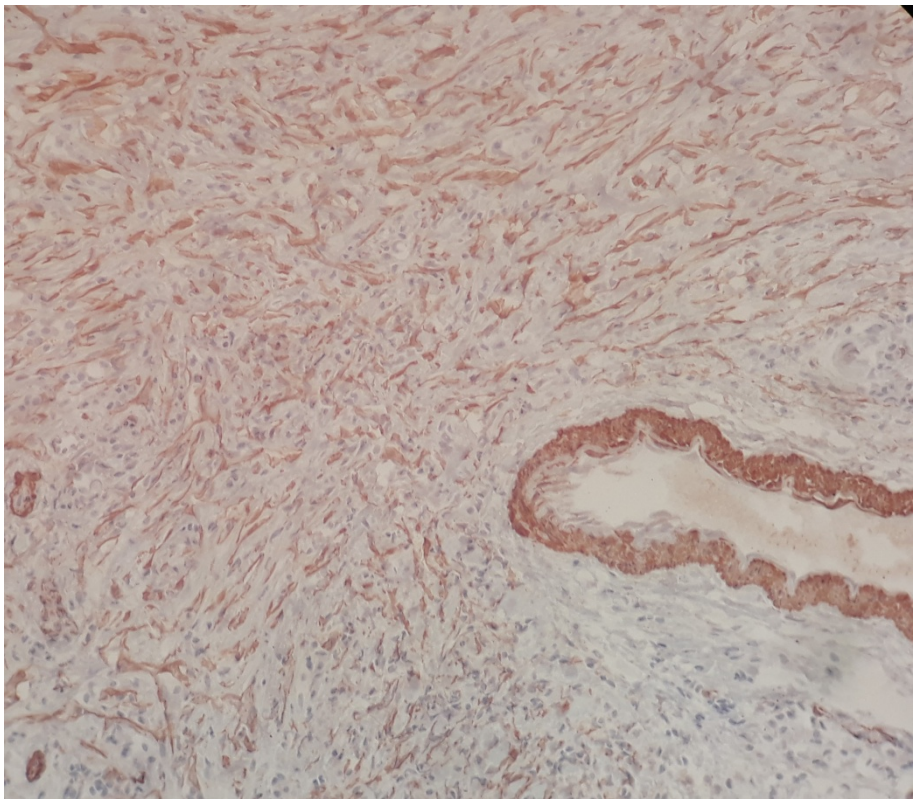

Figure 3. Myofibroblastic cells staining positive for smooth muscle actin. Smooth muscle of blood vessels acted as an internal positive control. (Gx200 HE)

The abdominal ultrasound reveals the presence of a 16 cm long cyst formation, adherent to the pancreas with a mass effect on the neighboring organs. The scanner confirms the pancreatic origin of the mass which develops at the expense of the pancreatic body and compresses the neighboring organs with collateral venous circulation. The MRI returned in favor of a partitioned cystic mass of the body of the pancreas

evoking in the first place a cystic cystadenoma of the pancreas (Figure 1).

Surgical exploration revealed a mass that could not be extirpated, especially by its adhesions relative to the 4th portion of the duodenum and the superior mesenteric artery, therefore a biopsy was performed. The pathology result returned in favor of a myofibroblastic tumor of the pancreas (Figure 2 and Figure 3) with negative anti-ALK antibodies. The patient received 3 months of corticotherapy without clinical or radiological improvement (MRI) then she was referred to the oncology department.

3. Discussion

Various names have been used to describe IMT, such as plasma cell granuloma, plasma cell pseudotumor, inflammatory pseudotumor, inflammatory fibroxanthoma, and histiocytoma [4]. The current WHO classification for this rare tumor entity is a fibroblastic sarcoma or myofibroblastoma, which is a distinctive neoplasm of intermediate biological potential that may be malignant or aggressive [5,6,7].

Although IMT has been seen in various organs, it is extremely rare to be seen in the pancreas. We find only 28 cases of histologically confirmed IMTs of pancreas reported in the English language scientific literature. [8] The average age at diagnosis of all cases was 40.0 years, and a subtle predominance of male gender was evident (17 males and 11 females). The pancreatic mass lesions were mostly located in the pancreas head (20 in the head, two in the body, four in the tail, and two in the body and tail) and had an average size of 4.7 cm. [8]

Abdominal pain or discomfort was the most frequent symptom (56%, 15/27), with jaundice the second most frequent (44%), followed by anorexia or weight loss (26%), and nausea or vomiting (15%). [8]

The radiological features of IMT are nonspecific, and exhibit variable characteristics [9]. Ultrasound and CT examinations reveal a solid, or occasionally cystic‐solid, mass in the pancreas, which is usually sized between 5.0 and 10.0 cm and may be well‐demarcated or metastatic [10].

Due to its nonspecific symptoms and imaging findings, definitive diagnosis of IMT relies on histological evaluations [9]. EUS-FNA demonstrates a fairly high diagnostic ability (nearly 95% sensitivity and specificity) for solid malignant pancreatic lesions [11,12]. The use of thick core biopsy needles [13] and high-negative-pressure aspiration methods [14] has increased the acquisition rate for obtaining core tissue samples. This, in turn, has enabled the determination of the probable nature of the whole pancreatic mass and even the classification of intermediate inflammatory and neoplastic conditions, such as IMTs [8]. The diagnosis of IMT of the pancreas was obtained by EUS-FNA in the only patient in the literature who had this gesture. [8]

The biological marker of IMTs, including histological atypia, ganglion-like cells, TP53 expression, and aneuploidy pattern, have been correlated with more aggressive clinical behavior [15]. Coffin et al. also suggested that ALK (anaplastic lymphoma kinase) expression is another prognostic indicator of IMTs [16]. Approximately half of IMTs carry rearrangements of the anaplastic lymphoma kinase (ALK) gene [16]. ALK is a tyrosine kinase receptor that is normally expressed in the central nervous system. Fusion of the ALK gene with partners such as CLTC, RANBP2, TPM3, TPM4, CARS, ATIC, SEC1L1, ALO17, and PPFIBP [17,18] can cause ALK overexpression and activation of the ALK kinase domain.

The absence of ALK expression in IMT was associated with a higher age of the patients [19]. All six of the observed metastases developed in 59 IMTs that were negative for ALK expression, and they developed before 20 years of age (mean age: 13.2 years), indicating a metastatic potential for ALK-negative IMTs in the younger subset [19]. Therefore, ALK expression as a clinical indicator in IMTs in older patients needs further evaluation [8].

IMTs show spontaneous regression in a minor fraction of patients. Although the actual incidence is not clear due to surgical procedures and asymptomatic and/or undetected cases, 16 cases of IMT with spontaneous regression, all sites combined, have been reported to date [8,20,21] including 2 cases of spontaneous regression reported for the pancreas: the first case of spontaneous regression in 2 months of an IMT of 5cm in an 82-year-old Japanese woman and the second case of regression after 8 weeks of corticosteroid therapy in a 10-year-old child [8,10]. Corticosteroids and/or nonsteroidal anti-inflammatory drugs were used in 5 spontaneous regression patients with extra-pancreatic location [8]. Our patient received 3 months of corticotherapy without clinical or radiological improvement.

Surgery with complete excision remains the primary therapeutic option for IMT, although no real consensus regarding the treatment of IMT exists [10,22]. The low risk of malignant transformation or metastasis has been described in previous cases of IMT, but if the excision is incomplete, the risk increases from <5 to 25% [5]. Due to the possibility of malignancy and relapse, many authors have reported that a simple tumor excision is uncertain [23] and that radical resection may be appropriate if the patient's physical condition is adequate [10,22].

For unresectable, metastatic or recurrent lesions, several medical treatments, including chemotherapy, radiotherapy, nonsteroidal anti-inflammatory drugs, corticosteroids, antitumor necrosis factor‐binding antibodies and ALK inhibitors, have been previously administered to palliate or shrink these IMTs to a resectable size and configuration [9,10,23]. Ogata has grouped 7 cases from the literature for which crizotinib, an ALK inhibitor, has been used for tumors harboring ALK mutations. The patients were young and the locations of the tumors were varied. In the majority of cases, crizotinib initially provided a partial or very good response; but the end result was different [24]. A dramatic response to alectinib in inflammatory myofibroblastic tumor with ALK fusion gene with renal metastasis has also been reported [25].

According to a retrospective analysis of the value of chemotherapy in the treatment of IMT, in 38 patients under the age of 21, all locations combined, chemotherapy with alkylator-based regimens seems to be justified to attempt to reduce tumor size in unresectable cases to enable tumor resection [26]. The combination of methotrexate and vinorelbine allowed a partial response to

a recurrence of an inoperable IMT of the gallbladder in a 62-year-old patient [27].

Rituximab, an anti-CD20 antibody, was used in 2 cases of IMT; one of the mandible and the other of the central nervous system. A long-term response has been obtained [28].

Recently, a clinical study showed a high degree of PD-1/PDL-1 expression in the TMIs [29]. This could imply immune-mediated dysfunction in the development of IMT [19,30,31]. On the other hand, the expression of PD-1/PD-L1 could predict the effectiveness of immunotherapy in the future. the PD-L1 status appears to be independent of ALK status, suggesting that it could be particularly useful clinically in ALK-negative IMT or those resistant to tyrosine kinase inhibitor therapy. [29]

4. Conclusion

For unresectable, metastatic or recurrent IMD lesions, medical treatment remains poorly defined given the lack of strong statistical evidence. The choice between chemotherapy, ALK inhibitors and immunotherapy is difficult and requires further study of predictive factors for a therapeutic response like ALK expression and PD1/PD-L1 expression. We also point out the need for the use of TNM classification and objective therapeutic response criteria in future studies.

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