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Case Presentation

Calcifying Fibrous Tumor Mimicking Pancreatic Cancer

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2. Key words

Calcifying fibrous tumor; Malignancy; Pancreatectomy; Differential diagnosis

1. Abstract

We report a case of a 75-year-old male incidentally diagnosed with pancreatic mass. A laparoscopic radical antegrade posterior modular pancreatosplenectomy was performed. An unexpected diagnostic of calcifying fibrous tumor (CFT) was revealed. CFT can mimic malignancy due to its imaging characteristics, location and growth and it should be taken into consideration in the differential diagnosis when pancreatic malignancy is suspected. Most of them are asymptomatic tumors discovered in imaging performed for other reasons. In some cases, it presents non-specific symptoms. It can also debut with systemic symptoms. The radiological characteristics of this tumor are unspecific and usually do not provide a definitive diagnosis. Usually, the definitive diagnosis is given by histopathology, where immunohistochemistry techniques are very useful. No deaths have been reported from this cause, however, there are a few cases of local recurrence described in the literature. Although the optimal follow-up time for the CFT is not known, if free margins are achieved, no lymph nodes or metastasis are expected to appear in the follow-up.

3. Introduction

Calcifying Fibrous Tumor (CFT) is a recently described rare benign mesenchymal tumor. It was originally described in 1988 by Rosenthal as "childhood fibrous pseudotumor with psammoma bodies" [1] and posteriorly named as "calcifying fibrous pseudotumors" as an abnormal reaction in the healing process of tissues [2]. Histologically, is composed of dense well-circumscribed hyalinized collagen with lymphoplasmatic infiltrate, spindle cells, lymphoid aggregates, psammomatous or dystrophic calcifications and variably prominent mononuclear inflammatory infiltrate [3-5]. The real incidence of this tumor is not fully known. It seems to be more frequent in females and in a recent systematic review the male: female ratio was 1:1, 27 [3]. Most cases occur in people under 30 years old, especially in children. Although some cases present with non-specific symptoms, most are asymptomatic. The cause of CFT is thought to be related to previous infection, history of trauma, and surgical intervention; however, the certain mechanism or causes have not been confirmed. The major diagnostic challenge is to determine the benign or malignant character of the tumor in the preoperative stage. Although there are some cases of coexisting pancreatic cancer and CFT in the literature [6], a pancreatectomy because of a CFT had not been reported before.

4. Case Presentation

We present the case of a 75-year-old male with a history of type 2 diabetes. He was admitted to the outpatient clinic for non-irradiated low back pain of 4 months of evolution. He did not associate any other symptomatology. Physical examination was normal. An MRI of the spine was requested, which incidentally revealed a poorly defined pancreatic tail mass. An extension study with body Computed Tomography (CT) was performed confirming the presence of 51 x 21 centimeters isointense pancreatic tail tumor with subcentimetric gross calcifications. The adrenal gland and splenic hilum were infiltrated causing splenic vessels thrombosis with collateral circulation (Figure 1). No evidence of distant metastatic disease was found. The echoendoscopy showed a permeable celiac trunk and no suggestive of malignancy adenopathies. The patient presented no analytical alterations and the tumoral markers (alfa-fetoprotein, Carcino-Embryogenic Antigen (CEA), carbohydrate antigen 19-9 (CA 19.9) and cancer antigen 125 (CA 125) were normal.

With the suspected diagnosis of a malignant tumor of the pan-

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creas tail, it was decided to perform a laparoscopic radical antegrade posterior modular pancreatosplenectomy. During surgery the CT findings were confirmed, however, the left renal hilum also seemed to be infiltrated by tumor, and since the initial suspicion was pancreatic carcinoma, we decided to include the left kidney in the surgical specimen in order to achieve a free posterior resection margin.

The patient spent 2 days in the intensive care unit. In the postoperative period, he developed a paralytic ileus with oral intolerance that required insertion of a nasogastric tube, an intra-abdominal hematoma that required percutaneous drainage and a grade "B" pancreatic fistula [7] that required antibiotic therapy and percutaneous repositioning of the drainage tube. After 32 days the patient was discharged.

The histological study showed the presence of a proliferative lesion in the splenic hilum with focal infiltration of the spleen and the pancreatic tail without kidney infiltration. The splenic vessels were surrounded by the lesion, but there was not vascular infiltration. It was composed of a low cellular density, hyalinized, fibrous stroma with small, oval nucleus, and scarce eosinophilic fusiform cytoplasm fibroblastic cells. Small calcifications and little lymphocytic inflammatory infiltration were observed. No histological signs of malignancy such as cellular atypia, mitosis, or necrosis were observed. Immunohisto chemical techniques revealed positive staining for vimentin, CD34 and, XIIIa factor and negative expression for β-catenin, ruling out possible fibromatosis and establishing the diagnosis of calcifying fibrous tumor (Figure 2).

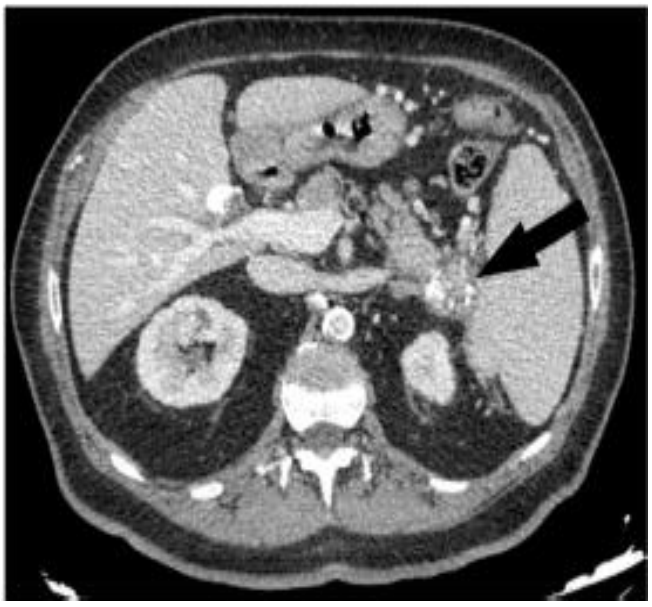

Figure 1: Preoperative CT scan, axial plane. A pancreatic tail mass with calcifications in close contact with the splenic hilum is observed.

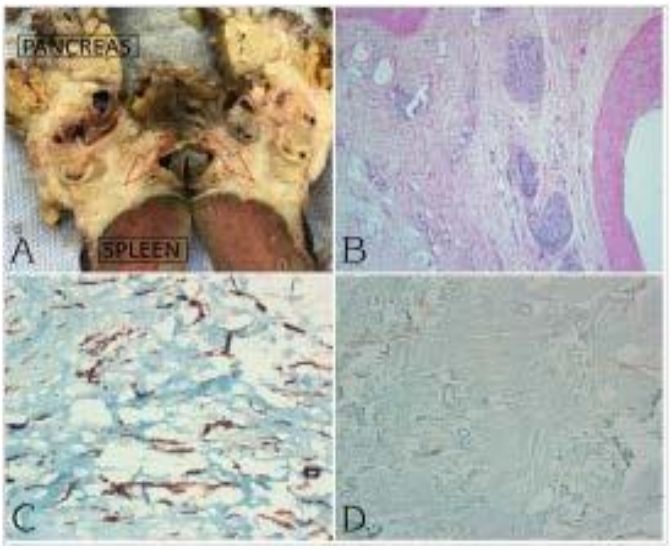

Figure 2: A. Surgical specimen. Splenic vessels (*) surrounded by tumor (red arrows). B. Hematoxylin & Eosin stain (40x) of tumoral tissue showed low cellular density stroma. C. Vimentin (200x) positive expression in tumoral tissue. D. β-catenin (100x) negative inmunoexpression in tumoral tissue.

5. Discussion

The real incidence of this tumor is not well known, with less than two hundred cases reported since it was described [3]. The pathogenesis of this tumor is not fully known, although some pathogenic theories have been established. The first one proposes that CFT derives from the sclerosis of an Inflammatory Myofribroblastic Tumor (IMT) [8,9]. It has also been suggested that it could be reactive to trauma process or intestinal suffering [5,10]. In fact, Fetch et al. [2] described a series of 10 cases of what they called "calcifying fibrous pseudotumour", as they considered its origin to be inflammatory. Although it appears to be an acquired disease, Chen et al [11]. described the case of two sisters with multifocal peritoneal calcifying fibrous tumor, so we cannot exclude a genetic component as part of the pathogenesis of this tumor.

Cases of very different locations have been described, especially in the abdominal (stomach 18%, and small intestine 8.7%) and thoracic cavity (pleura 9.9%). The majority of cases correspond to single tumors, although a few cases make their debut with two or more tumors in the same or different locations [8, 12, 13].

It is a benign and normally well circumscribed tumor, although it presents some local aggressiveness, being able to infiltrate neighboring structures and organs. Normally, the diagnosis, as in our case, is casual by an imaging test requested for another reason, however, occasionally peripheral tumors may be visible or palpable. When there are symptoms, they can be divided on a practical level into chronic or acute. The symptomatology depends on the

location, so in superficial tumors, it is possible to see a slow-growing mass that presents increasing pain. As for intrathoracic or intraabdominal tumors, the symptomatology is more varied and is usually related to compression and/or infiltration of adjacent structures such as dyspnea, halitosis, nausea, vomiting, rectal bleeding or gastrointestinal ulcers. Intestinal perforation with peritonitis and intussusception have been described as acute symptoms [3]. More non-specific symptoms such as fever, anorexia and weight loss have also been described, but these are more difficult to associate directly with CFT.

Ultrasound shows well-delimited heterogeneous masses with posterior echo attenuation [14, 15]. In Computed Tomography (CT) and MRI we can see hypointense, hyperintense or isointense images with ill-defined edges, spicules or calcifications [16]. Those characteristics are the reason why it is sometimes not possible to rule out malignancy with imaging tests. Our patient's mass had poorly defined edges in MRI and TC, and vascular thrombosis, so it was highly suggestive of pancreatic tail cancer. Laboratory tests are not useful, so biopsy provides the diagnosis in all cases.

Even anatomopathological diagnosis of CFTs is challenging, requiring the use of immunohistochemical techniques. Vimentin and XIIIa factor and less frequently CD34 or CD68 are molecular markers that are expressed in the fibroblasts of CFTs. Others such as desmin, actin, Smooth Muscle Actin (SMA), Epithelial Membrane Antigen (EMA) or β-catenin are not expressed. The most important differential diagnosis is with the ITM, where immunohistochemistry plays an essential role. The ITM presents immunoexpression of actin, desmin and, pathognomonically, anaplastic lymphoma kinase (ALK-1). The ITM affects a younger age group and is more commonly associated with systemic symptoms than CFT [3, 17].

While most pancreatic neoplasms are pancreatic ductal adenocarcinomas, the differential diagnosis include neuroendocrine tumors and cystic neoplasms, solid pseudopapillary tumors, acinar cell carcinoma, lymphoplasmacytic sclerosing pancreatitis and primary pancreatic lymphoma. Although there are several etiologies of a pancreatic mass, some of them benign, approximately 7 % of patients undergoing pancreatoduodenectomy for suspected malignancy are ultimately diagnosed with benign disease [18]. Biopsy for suspected resectable adenocarcinoma is not normally necessary [19], but if it is required, should not delay the surgical treatment. The main reason is that when there is a high suspicion of malignancy, the positive predictive value of a negative biopsy for malignancy is lower than 20% [20].

There is not enough evidence about the optimal follow-up time. Local recurrences have been described in a few patients and they are probably in relation with a positive resection margin [3]. Therefore, we can establish that surgical excision is curative in the great majority of reported cases.

6. Conclusion

CFT is a rare benign tumor with a very difficult differential diagnosis. With non-specific clinic and radiology, immunohistochemistry plays a fundamental role in the diagnostic process. Due to its low incidence, there is no consensus on optimal treatment. However, it seems that surgical excision with free margins is the most widely used treatment and the one that can prevent recurrences.

We have described the first case of an isolated CFT that required a pancreatectomy for its treatment because of the high suspicion of malignancy. Despite the increased accuracy of the complementary tests, the combination of many of them and the availability of molecular markers, the percentage of pancreatectomies with benign result has not been significantly decreased due to de difficulty of the differential diagnosis. Therefore, it seems logical to indicate surgery when there is high suspicion of malignancy, assuming a small percentage of false positives.

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