Pancreatology xxx (2016) 1–4

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Review article

Primary liposarcoma of the pancreas: A review illustrated by findings from a recent case

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ARTICLE INFO

Article history:
Received 7 April 2016
Received in revised form
8 June 2016
Accepted 6 July 2016
Available online xxx

Keywords:
Pancreatectomy
Pancreatic neoplasms
Dedifferentiated liposarcoma

ABSTRACT

Liposarcoma is the most common soft tissue sarcoma and accounts for 15%–20% of all mesenchymal malignancies. The tumor occurs most frequently in limbs and retroperitoneum, with only rare instances of visceral location reported. Pancreas is a very rare site of primary liposarcoma, with a total of seven cases reported since 1979 and only four of those in the English literature. We review the literature specific for primary liposarcoma of the pancreas and discuss radiological and pathological aspects of this rare tumor type as well as emerging options of treatment. The review is illustrated by findings of a recent case of a dedifferentiated liposarcoma of the pancreas coupled with undifferentiated pleomorphic sarcoma, including the first description of this rare tumor by magnetic resonance imaging. The patient was successfully treated with distal pancreatectomy and splenectomy, followed by adjuvant chemotherapy and radiotherapy. At the 5-year follow-up, the patient showed no signs of recurrence.

1. Introduction

Pancreatic tumors arise from cells of mesenchymal or epithelial origin, or from non-ductal structures and fat. The tumors of epithelial origin, including adenocarcinoma, reportedly account for 85% of all pancreatic tumors [1], while non-ductal tumors account for 5%–15% and mesenchymal tumors account for about 1%. However, the fat-originating tumors, such as focal fatty infiltration of the pancreas, teratoma lipoma, and liposarcoma, are the rarest [1–3].

Liposarcoma is the most common soft tissue sarcoma, and accounts for 15%–20% of all mesenchymal malignancies. The tumor occurs most frequently in limbs and retroperitoneum, with only rare instances of visceral location reported [2,4].

The pancreas is a very rare site of primary liposarcoma. To our knowledge, only seven cases [1,2,5–9] have been reported since 1979, with four of those in the English literature [1,2,8,9]. The first such case reported in the English literature, one of retroperitoneal liposarcoma restricted to the pancreas, was described by Elliott et al. [2] in 1980. Here, we review the English literature specific for liposarcoma of the pancreas and discuss radiological and pathological aspects of this rare tumor as well as emerging options of treatment. The review is illustrated by findings of liposarcoma of the pancreas treated by resection and having no signs of recurrence at the 5-year follow-up. Table 1 summarizes the clinical and pathological aspects and the characteristics of treatment and outcome of patients with liposarcoma of the pancreas reported in English literature.

2. Clinical aspects

In English literature, liposarcoma of the pancreas affected both sex (3 male and 2 female) and occurred in any age (24-year-old to 78-year-old). The patients presented usually abdominal symptoms [2,8,9], like pain and distension, but systemic symptoms occurred,

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http://dx.doi.org/10.1016/j.pan.2016.07.003
1424-3903/

Table 1
Treatment and outcome of patients with liposarcoma of the pancreas published in the English literature.

Author	Age/ Sex	Clinical presentation	Pre-operative diagnosis	Site	Size	Treatment	Liposarcoma subtype	Outcome
Elliott, 1980 [2]	59/F	Abdominal distension	Abdominal mass	Body	16 cm	DPS	Pleomorphic	No recurrence (6 years)
Dodo, 2005 [8]	76/M	Abdominal pain, anorexia and weight loss	Liposarcoma	Body/tail with mesentery metastasis	9 cm	DPS	Well differentiated with area of dedifferentiation	No recurrence (26 months)
Kuramoto, 2013 [9]	24/M	Abdominal distension	Retroperitoneal liposarcoma	Body	25 cm	CP	Myxoid	Recurrence (44 months)
Kim, 2014 [1]	78/F	Asymptomatic	Lipoma/ liposarcoma	Body	NA	Mass excision	Well-differentiated	NA
Present case	42/M	Abdominal pain	NEPMN	Head/Neck	6.8 cm	DPS	Dedifferentiated with high grade components	No recurrence (5 years)

M = male/ F = female/ DPS = distal pancreatectomy and splenectomy/ CP = central pancreatectomy/ NA = not available/ NEPMN = non-epithelial pancreatic malignant neoplasia.

like anorexia and weight loss [8]. Only one patient was asymptomatic [1]. There are no reports of increased tumoral markers.

We discuss a case of a 42-year-old male patient who was referred to our hospital with complaint of abdominal pain that had persisted for 3 months, without other symptoms. The patient's medical history included myocardial infarction 7 years previous and diabetes mellitus, systemic arterial hypertension and smoking that were ongoing. The patient self-reported a family history of cancer, including prostate cancer (grandfather) and breast cancer (sister). Physical examination was normal, but laboratory tests showed hyperglycemia and slightly elevated Ca-19-9, probably related to obstruction of the main pancreatic duct.

3. Radiological aspects

Unfortunately, there is no pattern described for primary liposarcoma of the pancreas, due to few reports in literature. There are two case reports [8,9] describing computed tomography findings of these lesions and both were heterogeneous masses in pancreatic tail, one of them with areas of low density consistent with fat.

In our case, magnetic resonance imaging (MRI) demonstrated a multilobulated, well-demarcated and heterogeneous mass within pancreatic head-neck interface, with thick wall and septations, measuring 6.0 cm (Fig. 1C), without involve the common bile duct. Pattern of enhancement was marked hypovascular and signal predominantly hyperintense in T2 weighted sequences (Fig. 1A and B). There was dilation of the main pancreatic duct up to 0.7 cm and displacement of common hepatic artery and portal vein, but without signs of vascular invasion. There were no signs of extrapancreatic extension or distant metastasis. Analysis of fat suppression sequences did not demonstrated presence of lipid elements (Fig. 1D). This is the first description of pancreatic liposarcoma by MRI.

On MRI examination, lipomatous components usually can be clearly demonstrated in well-differentiated and myxoid liposarcoma, however pleomorphic liposarcoma less frequently contains adipose tissue. This feature makes the imaging diagnosis more challenging. Our case had marked high signal intensity with T2 weighed images corresponding to the abundant myxoid component and areas of necrosis and hemorrhage were related to heterogeneity seen in this lesion [10].

Moreover, our case fit with the presence of thick septations for liposarcoma of the pancreas, but not with the presence of internal calcifications within the tumor, which can be helpful in the differentiation of liposarcoma from lipoma [3].

These imaging and clinical findings are non-specific for a ductal adenocarcinoma that accounts for 85–95% of all pancreatic malignancies [1]. Therefore, pancreatic solid lesions more rare such as acinar cell carcinomas, adenosquamous carcinoma or anaplastic carcinoma must be considered as part of the differential diagnosis. According to these findings, surgical treatment was indicated (distal pancreatectomy with splenectomy and regional lymphadenectomy).

4. Pathological aspects

There are four histological subtypes of liposarcomas according to their morphologic features and cytogenetic aberrations: well-differentiated, dedifferentiated, myxoid/round cell, and pleomorphic [14]. The well-differentiated and myxoid/round cell forms are tumors with a low grade malignancy, slow growth, low metastatic potential and progressive destruction of normal pancreatic tissue, associated with a more favorable prognosis. The undifferentiated and pleomorphic type are neoplasms with high-grade malignancy, remarkable biological aggressiveness and higher metastatic potential. Pleomorphic liposarcoma is very rare (less than 5% of all liposarcomas), much more aggressive, and with a higher (30–50%) frequency of distant metastasis, including lung, bone and liver [4,11]. The reports of these tumors also indicate a highly resistant phenotype to all current treatment modalities [11].

Dedifferentiation occurs in up to 10% of well-differentiated liposarcomas and approximately 90% of dedifferentiated liposarcoma cases are *de novo*, whereas 10% develop as recurrences of previous cancers [12]. The dedifferentiated component may also be morphologically low grade, generally consisting of non-lipogenic cellular spindle cell areas with a vaguely fascicular growth pattern. No difference in outcome has been noted between the low-grade and high-grade dedifferentiated lesions, and both are associated with a 5-year metastatic risk of only 20%–25% [13,14].

Amplification and overexpression of MDM2 is characteristic of well-differentiated and dedifferentiated liposarcomas, and both FISH and immunohistochemistry have become extremely useful tests for confirming the diagnosis of these tumor types. Most well-differentiated/dedifferentiated liposarcomas show immunohistochemical expression of MDM2 and CDK4 (97% and 92%, respectively) [15]. The combination of CDK4, MDM2, and p16 is useful in distinguishing well-differentiated and dedifferentiated liposarcomas from other adipocytic neoplasms. All well-differentiated and 93% of dedifferentiated liposarcomas express at least 2 antigens of these markers. The most sensitive and specific marker for detecting well-differentiated/dedifferentiated liposarcomas is p16, and MDM2 is the least [16,17].

In our case, upon pathological evaluation, the macroscopic presentation of the lesion was that of a nodular solid tumor, of 68 mm in maximum size, occupying the neck of the pancreas. Microscopic examination showed that tumor cells were

Please cite this article in press as: Machado MCC, et al., Primary liposarcoma of the pancreas: A review illustrated by findings from a recent case, Pancreatology (2016), http://dx.doi.org/10.1016/j.pan.2016.07.003