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Clinical characteristics and prognosis of primary leiomyosarcoma of the pancreas: a systematic review

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Abstract

Background: Primary pancreatic leiomyosarcoma (PLMS) is rare. The clinical characteristics and prognosis is still not completely understood. The aim of the present study is to identify the clinical characteristics and long-term outcomes of PLMS from the existing reported cases in different scientific literature.

Methods: PLMS cases reported in Chinese and English journals were collected and reviewed. Clinical features and long-term outcomes of these cases were summarized and analyzed statistically.

Results: A total of 69 cases reported from both Chinese and English journals were included in the present study. An equal incidence in gender was observed. The mean age was 53.9 ± 14.7 years. The most common symptoms were abdominal mass, abdominal pain, and weight loss. The mean size of the tumor was 11.4 ± 7.1 cm. The incidence of PLMS between the head and body-tail of the pancreas had a similar pattern. Twenty-five percent of patients had distant metastasis and 19% of patients had adjacent organs/vessels invasion at the time of diagnosis. But lymph node metastasis was documented in only one (1.5%) patient. The median survival time was 48 months. The overall 1-, 3-, 5-, and 10-year survival rates were 66.6%, 51.2%, 43.9%, and 29.3%, respectively. Results from the multivariate analysis showed that non-radical resection ($P = 0.000$; hazard ratio (HR) 5.128; 95% confidence interval (CI) 2.041-12.987) was the independent adverse prognostic factor. Adjacent organs/vessels invasion (yes) may be considered as an another potential independent adverse prognostic factor ($P = 0.071$; HR 2.708; 95% CI 0.981-7.474).

Conclusions: PLMS is rare without specific clinical features. PLMS is an aggressive tumor and has a poor prognosis. Radical resection can prolong survival time of the patients.

Keywords: Pancreatic tumor, Leiomyosarcoma, Sarcoma, Resection, Prognosis

Background

Primary leiomyosarcoma is an extremely rare mesenchymal tumor of the pancreas, which accounts for 0.1% of malignant pancreatic tumors [1]. Primary pancreatic leiomyosarcoma (PLMS) was first described by Ross in 1951 [2], and to date 64 cases have been reported [3]. However, most of them have been documented as single cases, with clinical characteristics and prognosis which cannot be completely understood. To understand the characteristics and long-term outcomes of PLMS, the present study reviews earlier

reported cases in Chinese and English journals across the globe.

Methods

The systematic literature search was performed via China Knowledge Resource Integrated (CNKI) database to identify the cases reported in Chinese journals, with the last search on 1 March 2013. A similar search was made in MEDLINE, EMBASE, and the Cochrane databases for cases reported in English journals. The primary key words used were 'pancreas and leiomyosarcoma', 'pancreatic and leiomyosarcoma', 'pancreas and mesenchymal tumor', 'pancreatic and mesenchymal tumor', 'pancreas and sarcoma', and 'pancreatic and sarcoma'. Only the cases originated from the pancreas were

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included in the study. Clinical features and long-term outcomes of these cases were summarized and analyzed.

SPSS v.13.0 (SPSS, Inc., Chicago, IL, USA) was used for all analyses. The Pearson χ^2 test and Fisher's exact test were used to compare categorical variables. The Kaplan-Meier method was used to calculate overall survival (OS) using the log-rank test. Cox regression analysis was performed for multivariate survival analysis. A two-sided P value <0.05 was considered statistically significant.

Results

Demographic and clinical data

Twenty cases were reported in Chinese journals (Additional file 1), and 49 cases were reported in English journals [1,2,4-35] (Additional file 2). A total of 69 cases were included in the present study. The gender of 68 patients in these 69 cases was documented, which was 35 men and 33 women. An equal incidence in gender was observed (male-female ratio of 1.06) in the data. The mean age was 53.9 ± 14.7 years (median, 53 years; range, 14-87 years).

Symptoms were described in 63 cases and of which 58 patients had symptoms. The most common symptoms were abdominal mass (29 cases), abdominal pain (25 cases), and weight loss (19 cases). Other symptoms like jaundice (8 cases), anemia (6 cases), gastrointestinal bleeding (5 cases), and vomiting (5 cases) were also reported.

The tumor location was documented in 63 cases. The tumors were located in the head of the pancreas in 30 cases, and in the body-tail in 32 cases. One case had tumor in the whole pancreas. The mean size was 11.4 ± 7.1 cm (median, 10 cm; range, 1-30 cm). The gross morphology was recorded in 49 cases. Twenty-six tumors were solid mass, eight tumors were cystic mass, and fifteen were mixed mass.

The status of metastasis and regional invasion at the time of diagnosis were identified in 68 patients. Seventeen (25%) patients had distant metastasis and 13 (19%) patients had adjacent organs/vessels invasion. Lymph node metastasis was documented in only one (1.5%) patient. Men had a higher incidence of metastasis and regional invasion than women (19/35 vs. 11/33; $P = 0.082$). The surgical treatment method was illustrated in 62 cases, of which 40 cases achieved radical resection, and 22 cases underwent palliative resection or biopsy.

Survival analysis

Forty-nine cases with long-term outcomes data were included in the survival analysis. The median survival time was 48 months. The overall 1-, 3-, 5-, and 10-year survival rates were 66.6%, 51.2%, 43.9%, and 29.3%, respectively. Univariate analysis showed that age ≥ 55 years, distant metastasis (yes), adjacent organs/vessels invasion (yes), and radical resection (no) were the potential adverse

prognostic factors (Table 1). Multivariate analysis of the cases showed that non-radical resection ($P = 0.000$; hazard ratio (HR) 5.128; 95% confidence interval (CI) 2.041-12.987) was the independent adverse prognostic factor. Adjacent organs/vessels invasion (yes) might be also considered as another independent adverse prognostic factor ($P = 0.071$; HR 2.708; 95% CI 0.981-7.474) (Table 2).

Discussion

PLMS is rare. Earlier studies by Baylor et al. showed only five leiomyosarcomas among 5,057 pancreatic malignant tumors screened [1]. PLMS is considered to originate either from the smooth muscle region of the pancreatic ducts or the wall of small intra-pancreatic vessels [4]. Leiomyosarcomas originating from the stomach, duodenum, and retroperitoneal organs often invade

Table 1 Univariate analysis of potential prognostic factors

Variables	Survival time (median \pm SE, year)	1-year survival rate, %	3-year survival rate, %	P value
Gender				0.398
Male	33 \pm 15.8	58.4	41.7	
Female	98 \pm 55.5	73.2	57.6	
Age (years)				0.049
< 55	None	72.7	68.1	
≥ 55	22 \pm 7.9	59.1	27.9	
Locations				0.477
Head	48 \pm 26.5	70.8	58.8	
Body-tail	33 \pm 16.4	71.2	41.9	
Size (cm)				0.092
< 10	33 \pm 17.6	74.3	67.5	
≥ 10	None	67.9	43.6	
Gross morphology				0.142
Solid	None	75.6	56.7	
Cystic	12 \pm 3.3	40	20	
Mixed	None	80	80	
Distant metastasis				0.007
Yes	12 \pm 6.3	50.0	0	
No	98 \pm 46.1	76.6	63.6	
Adjacent organs/vessels invasion				0.011
Yes	6 \pm 1.4	25.0	25.0	
No	48 \pm 29.4	82.8	56.6	
Radical resection				0.000
Yes	98 \pm 45.2	80.5	72.2	
No	8 \pm 3.5	40.3	0	

Due to censored data $\geq 50\%$, the median survival time cannot be calculated. A two-sided P value <0.05 was considered statistically significant. SE, standard error.

Table 2 Multivariate analysis of potential prognostic factors

Variables	P value	Hazard ratio	95% Confidence interval	
			Lower	Upper
Adjacent organs/vessels invasion (yes)	0.071	2.708	0.981	7.474
Radical resection (no)	0.000	5.128	2.041	12.987

A two-sided *P* value <0.05 was considered statistically significant.

the pancreas, mimicking PLMS [36]. A definite diagnosis of PLMS is needed to rule out tumors originating from these adjacent organs.

A generally equal incidence of PLMS in gender was observed. There were 35 men and 33 women with a ratio of 1.06. The age of the patients ranged from 14 to 87 years (median, 53 years). The most common symptoms observed in the patients were abdominal mass, abdominal pain, and weight loss, but no specific symptoms were recorded from any of the patients diagnosed with PLMS. Small tumors usually had no symptoms and were found incidentally [36]. The mean size of tumors was 11.4 ± 7.1 cm (range, 1-30 cm). Twenty-three of 49 tumors were mixed or cystic mass. Large tumors with cystic degeneration presented a highly aggressive malignancy, such as adjacent organ invasion and distant metastasis [6]. The tumors were located in the head of the pancreas in 30 cases and in the body-tail in 32 cases. There was a similar incidence between the head and body-tail.

Due to its presence as an obvious mass, the tumor can be found easily by imaging studies. Trans-abdominal ultrasonography (TAUS), computed tomography (CT), positron emission tomography and computed tomography (PET/CT), magnetic resonance imaging (MRI), angiography, and endoscopic ultrasonography (EUS) were all effective in diagnosing the PLMS, but there are no specific imaging features [7]. PLMS appears as a heterogeneous, hypervascular mass on CT scan. As the tumor volume increases, hemorrhagic, necrotic, and cystic changes can be observed [5,8]. Tumors with cystic lesions can be confused with pseudocysts of the pancreas [6,9]. PLMS appears as a high incidence of distant metastasis and regional invasion with rare lymphatic involvement, which could be the key point to differential diagnosis. It is difficult to do preoperative qualitative diagnosis by non-invasive diagnostic method. CT or US guided fine-needle aspiration biopsy (FNAB) is an alternative diagnostic method for PLMS. Three of four cases showed a definite diagnosis through US-guided FNAB reported in literature [3].

The accurate diagnosis of PLMS depends mainly on the histological examinations and immunohistochemical staining. Histologically, PLMS showed well-formed fascicles of

spindle cells with blunt-ended nuclei intersecting at vertical angles, varying degrees of pleomorphism, and a substantial number of mitosis [10,11]. However, it is difficult to histologically differentiate PLMS from inflammatory myofibroblastic tumors and non-myogenic spindle cell sarcomas, namely fibrosarcomas, malignant fibrous histiocytomas, and malignant peripheral nerve sheath tumors [10]. Therefore, an immunohistochemical staining is crucial for an accurate diagnosis. Immunohistochemical examinations have an important value in evaluating spindle cell tumors which were supposed to be of smooth muscle origin. These tumors are positive for muscle markers (such as α -smooth muscle actin, MSA, and desmin), with negative expression of epithelial (such as cytokeratin, EMA, and CEA) and neural (such as S100 protein) markers [10].

PLMS is an aggressive tumor. In the present systematic review, 25% of patients had distant metastasis and 19% of patients had adjacent organs/vessels invasion at the time of diagnosis. Lymph node metastasis was not common which was documented only in one patient (1.5%). This feature helps us to differentiate PLMS from other pancreatic malignant tumors and more surgeons prefer to perform a local radical resection rather than extensive node dissection based on this feature. Gender may be related to the degree of malignancy. Men seemingly had a higher incidence of metastasis and regional invasion than women ($P = 0.082$).

Survival analysis showed that median survival time of PLMS was 48 months. The overall 1-, 3-, 5-, and 10-year survival rates were 66.6%, 51.2%, 43.9%, and 29.3%, respectively. From univariate analysis, we showed that age ≥ 55 years, distant metastasis (yes), adjacent organs/vessels invasion (yes), and radical resection (no) were the potential adverse prognostic factors of PLMS. Multivariate analysis indicated that non-radical resection was the independent adverse prognostic factor. Radical resection was associated with prolonged overall survival time. Adjacent organs/vessels invasion (yes) might be another independent adverse prognostic factor, but statistical difference was not observed ($P = 0.071$). Although the dimension of tumors is an important indicator with regard to resectability, large tumor size was not an effective predictor of adverse prognosis in the current study. Mitotic counts >10 mitoses per 10 high-powered fields (HPFs) was reported as another adverse predictor [10]. Since data of this retrospective study extracted from the literature were not in detail, a comprehensive prognosis analysis could not be performed.

Conclusion

PLMS is a very rare malignant tumor of the pancreas. Clinical features and imaging examinations are no specific. The accurate diagnosis of PLMS depends on histological examinations and immunohistochemical staining.

PLMS is an aggressive tumor with poor prognosis. Radical resection can prolong survival time of the patient.

Additional files

Additional file 1: Reported cases of PLMS in Chinese literature.

Additional file 2: Reported cases of PLMS in English literature.

Abbreviations

CEA: Carcinoembryonic antigen; CI: Confidence interval; CNKI: China Knowledge Resource Integrated database; CT: Computed tomography; EMA: Epithelial membrane protein; EUS: Endoscopic ultrasonography; FNAB: Fine-needle aspiration biopsy; HPFs: High-powered fields; HR: Hazard ratio; MSA: Muscle-specific actin; MRI: Magnetic resonance imaging; OS: Overall survival; PET/CT: Positron emission tomography and computed tomography; PLMS: Primary pancreatic leiomyosarcoma; TAUS: Trans-abdominal ultrasonography.

Competing interests

All the authors declare no competing interests.

Authors' contributions

Xu drafted the manuscript. Zhang and Zhao designed the study and helped in drafting the manuscript. Xu, Wang, and You collected the data and performed the statistical analysis. All authors have read and approved the final manuscript.

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