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Clinical characteristics, treatment strategies and oncologic outcomes of primary retroperitoneal tumours: a retrospective analysis in the Chinese population

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ABSTRACT

Introduction Primary retroperitoneal tumours (PRTs) are rare soft tissue tumours originating from the retroperitoneum. Although there has been considerable progress recently in diagnosis and treatment, the overall survival rate has not improved qualitatively. This study aimed to explore the clinical features, therapeutic strategies and prognosis of PRTs.

Methods Retrospective analysis of clinical data for 121 PRT patients admitted to Peking University Shenzhen Hospital from April 2003 to February 2017.

Results A total of 113 patients underwent surgery and 8 chose nonsurgical palliative treatment. There were 53 males and 68 females (ratio, 1:1.3; average age, 40.75 years), and the average tumour diameter was 9.69(2–40)cm. A total of 104 patients (92.04%) underwent complete resection, 5 (4.42%) underwent palliative resection and 21 (18.58%) underwent combined visceral resection. The pathological diagnosis was benign in 88 cases (72.73%) and malignant in 33 cases (27.27%). A total of 101 patients (83.47%) were followed for an average of 5.82 years. At the end of follow up, the recurrence and survival rates were 2.63% and 93.42% for benign tumours, respectively, and 24.00% and 60.00% for malignant tumours ($p<0.01$).

Conclusions Imaging plays important roles in localising and characterising tumours, guiding treatment strategies. Complete tumour resection is key to reducing postoperative recurrence and improving survival. According to the postsurgical pathological results, combinations including radiotherapy, chemotherapy or targeted therapy are beneficial for improving prognosis.

KEYWORDS
Primary retroperitoneal tumour – Laparoscopy – Surgery – Pathology

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Introduction

Primary retroperitoneal tumours (PRTs) originate from tissues in the retroperitoneal space, including fat, loose connective tissue, fascia, muscle, vascular tissue, nerve, lymphoid tissue and embryonic residual tissue but not the pancreas, kidney, adrenal glands or other substantial organs; this classification also does not include macrovascular tumours in the retroperitoneal space. PRTs are clinically rare, accounting for 0.16% to 0.20% of all malignant tumours and 0.1% of systemic tumours, with numerous pathological types, but the pathogenesis has not yet been clarified.[1,2] Patients generally exhibit nonspecific vague abdominal symptoms or just a palpable abdominal mass, which increases the difficulties in early diagnosis. And due to the bulky tumour size, involvement of multiple organs and high local recurrence (LR) rate, treatment can be challenging.[3,4]

Although there is no consensus on the optimal treatment, surgery remains the primary potentially curative method.[5] Surgical methods for retroperitoneal tumours are generally divided into radical complete resection, combined visceral resection and palliative resection. However, there is considerable controversy regarding the best range of resection, with much debate centering on combined visceral resections. To date, no guides stating the best management strategies for recurrent tumours have been developed.[6]

Therefore, this study aimed to analyse clinical data for 121 patients with PRTs and discuss the clinical features, imaging, treatment strategies and prognosis of PRTs.

Methods

Clinical data for 121 patients with PRTs diagnosed and treated at Peking University Shenzhen Hospital from April 2003 to February 2017 were analysed retrospectively.

General information

The pathological diagnoses of 121 cases were clear and met the definition of PRT. The study cohort included 53 males and 68 females (ratio 1:1.3), and the average age was 40.75 (2–87) years. Among the 121 tumours, 11 were in the middle of the abdomen, 59 on the left and 51 on the right.

Clinical manifestations

The first symptoms in 47 patients were abdominal pain and abdominal distension; 29 patients presented with an abdominal mass, 2 with chest tightness and chest pain, 1 with fever and 7 with other symptoms. A total of 35 asymptomatic cases were discovered by physical examination.

Imaging examinations

Among all patients, 81 underwent examination by B-ultrasonography, 95 by computed tomography (CT), and 24 by magnetic resonance imaging (MRI). Tumour diameter was <5cm in 17 cases, 5–10cm in 57 cases and >10cm in 47 cases, with an average diameter of 9.69cm. Before the operation, five patients underwent digital subtraction angiography (DSA), and seven patients underwent intravenous pyelography (IVP).

Surgical methods

Among 121 patients, 8 chose nonsurgical palliative treatment, and 113 underwent surgery. Among the surgery patients, 93 underwent laparotomy, including 2 patients who were converted to laparotomy due to complex tumour findings during laparoscopic surgery. Complete tumour resection was achieved in 86 cases, palliative tumour resection was performed in 5 cases, and 2 patients underwent tumour biopsy. Regarding the surgical incision, Kocher incision was adopted in 31 patients, paramedian incision in 31, midline incision in 28 and other types of surgical incisions in 3. In addition, 20 patients underwent laparoscopic surgery, including 18 cases of complete resection and 2 cases of tumour biopsy.

A total of 21 patients underwent combined visceral resection, including 5 with nephrectomy, 1 with adrenalectomy, 1 with partial gastric resection, 1 with splenectomy, 1 with small intestine resection, 2 with ureterectomy, 1 with ileal resection, 2 with ascending colectomy, 7 with appendectomy, 1 with cholecystectomy, 1 with left lower pneumonectomy and 2 with adnexectomy.

Statistical analysis

Measurement data were expressed as the mean after analysis by the independent samples *t*-test. Enumeration data were compared using the Fisher's exact test or Pearson's chi-square test. All tests were two-sided and $p<0.05$ was considered statistically significant. SPSS v.23 and Microsoft Office 2010 were used for statistical analysis and data presentation.

Results

Pathological types

Among 121 cases, 88 were benign (72.7%), and 33 were malignant (27.3%). Among the 53 males, 34 had benign disease and 19 had malignant disease. Among the 68 females, the disease was benign in 54 and malignant in 14. The specific pathological distribution is shown in Table 1.

Index statistics of different surgical methods

Of the 113 surgical cases, 104 underwent complete resection, including 80 benign tumours and 24 malignant tumours. Palliative resection was performed in 5 cases and 4 cases underwent surgical biopsy.

A total of 93 patients underwent laparotomy, including 68 with benign tumours and 25 with malignant tumours; 91 patients underwent open tumour resection and 2 underwent open biopsy. The average tumour diameter was 10.19(2–40)cm, the average volume of blood loss was 742.03ml and the average operation time was 3.01h. Blood transfusion was required in 42 patients, with an average transfusion of 4.86U red blood cell suspension. The average postoperative hospital stay was 10.57 days. Three cases of fat liquefaction of the incision occurred after laparotomy and necessitated two-stage sutures. Two cases of postoperative haemorrhage occurred, and reoperation was performed to stop bleeding.

Among the 20 patients who underwent laparoscopic surgery, 19 had benign tumours and 1 had a malignant tumour. Moreover, 18 underwent laparoscopic complete resection, and 2 underwent laparoscopic biopsy. The average tumour diameter was 8.89(3–35)cm, the average volume of blood loss was 68.89ml and the average operation time was 2.44h. One patient required a blood transfusion of 2U red blood cell suspension. The average postoperative hospital stay was 7.06 days. The data were related to the surgical method. The volume of blood loss, number of blood transfusions and length of the postoperative hospital stay were significantly higher and longer in the laparotomy group than in the laparoscopic surgery group ($p<0.05$). Thus, laparoscopic surgery had obvious advantages over laparotomy.

Follow up

Complete follow-up data were available for 101 patients, including 76 with benign tumours and 25 with malignant tumours. The average follow-up time was 5.82 (0.1–13) years. All follow-ups were conducted by telephone, primarily to determine whether the patient was alive and whether they had experienced LR or distant metastasis. A total of 15 of 101 patients died, including 5 with benign tumours and 10 with malignant tumours. The survival rate of patients with malignant tumours (60.00%) was significantly lower than that of patients with benign tumours (93.42%) ($p<0.01$).

Table 1 The pathological types of 121 cases of primary retroperitoneal tumour (case count)

Histologic origin	Benign	Malignant
Mesenchymal tissue	Lipoma (2)	Liposarcoma (8)
	Fibroma (2)	Leiomyosarcoma (4)
	Leiomyoma (2)	Rhabdomyosarcoma (1)
	Angioma (1)	Malignant stromal tumours (3)
	Lymphangioma (7)	Malignant fibrous histiocytoma (2)
	Mesothelioma (1)	Aggressive fibromatosis (2)
	Angiomyolipoma (4)	
Lymphoid tissue	Pseudolymphoma (2)	Malignant lymphoma (6)
	Lymphoma (3)	
	Castleman's disease (5)	
Nervous tissue	Schwannoma (16)	Malignant schwannoma (1)
	Neurofibroma (2)	Neuroectodermal tumour (1)
	Ganglioneuroma (12)	
	Pheochromocytoma (2)	
	Paraganglioma (7)	
Embryo remnant, urogenital tissue	Benign cystic teratoma (4)	
Other or unknown origin	Cyst (7)	Low-grade malignant granuloma (1)
	Ectopic bronchogenic cyst (1)	Follicular dendritic cell sarcoma (1)
	Pseudocyst (1)	Myxoid tumour (1)
	Myxoid cystadenoma (3)	Malignant small round cell tumour (1)
	Angioma (1)	Poorly differentiated carcinoma (1)
	Retroperitoneal neoplasm (1)	
	Inflammatory mass (1)	
	Pseudomyxoma (1)	

Management after relapse or metastasis

Recurrence and metastasis are the most common problems after surgery for PRT. Eight patients with recurrence or metastasis were followed up (two with benign recurrence and six with malignant recurrence), and two of these patients died. The recurrence rate was 2.63% among patients with benign tumours and 24% among those with malignant tumours, for an overall recurrence rate of 7.92%. Two patients experienced LR of ganglioneuroma, one at 1 month and the other at 9 months after surgery and then underwent reoperation for complete resection. One patient experienced recurrence of malignant lymphoma at 6 months after chemotherapy and was treated with chemoradiotherapy again. One patient developed a recurrence of aggressive fibromatosis 2.5 years after the first operation; this patient underwent a second operation entailing a larger resection, and recurrence occurred again 18 months later. In total, tumour resection was performed three times in this patient. One case of liposarcoma recurrence occurred 3 years after surgery and was treated by extensive resection. One case of malignant fibrous histiocytoma recurred; chemotherapy was administered after the first operation, and recurrence was detected 4 months later and treated with another operation for complete resection. In addition, there were two deaths; one patient died of lung metastasis and LR without reoperation 1 year after surgery for primary neuroectodermal tumours, and the other patient died of acute renal failure due to uremia after the recurrence of peritoneal leiomyosarcoma.

Prognostic survival analysis

Factors relevant to benign and malignant retroperitoneal tumours (sex, complete resection, combined visceral resection, tumour size, recurrence, surgical method, radiotherapy and chemotherapy) were analysed by single-factor analysis. The results suggested no significant differences among the factors of benign retroperitoneal tumours except complete resection. Further multifactor analysis revealed that complete tumour resection was an independent prognostic factor

Table 2 Single-factor survival analysis of retroperitoneal tumours

		Benign		Malignant	
Variable	**Classification**	**Cases**	***p* value**	**Cases**	***p* value**
Sex	Male	30	1.000	15	0.442
	Female	46		10	
Complete resection	Complete resection	68	0.038	17	0.638
	Palliative resection	4		1	
	Biopsy	4		7	
Combined visceral resection	Yes	13	0.200	6	0.345
	No	63		19	
Tumour size	<5 cm	9	1.000	3	1.000
	5–10 cm	41		8	
	>10 cm	26		14	
Recurrence	Yes	2	1.000	6	1.000
	No	74		19	
Surgical method	Laparotomy	55	1.000	17	1.000
	Laparoscopic surgery	17		1	
Adjuvant radiotherapy	Yes	/	/	10	0.442
	No	/		15	
Adjuvant chemotherapy	Yes	/	/	15	1.000
	No	/		10	

for patients with benign PRT (p=0.03<0.05). However, there were no significant differences among the factors of malignant retroperitoneal tumours (Table 2).

Discussion

PRTs are a group of soft tissue tumours originating from the retroperitoneum, accounting for approximately 15% to 20% of soft tissue tumours.[7] PRT can occur at any age, but most patients are diagnosed at 50–70 years of age. In the US, there are approximately 1,000 new cases of retroperitoneal tumours each year, and the incidence is approximately 0.27/100,000.[8] However, there are no complete reports on the incidence of retroperitoneal tumours in China.

PRTs have widely disparate histology and complex pathology, and the majority are malignant (approximately 60%–85%).[9] In this case series, 33 cases (27.27%) were malignant tumours, which is inconsistent with the literature; this may be related to study deviation caused by the single-centre design and the small number of cases. Ganglioneuroma, schwannoma, cyst and teratoma are common benign tumours, and liposarcoma and leiomyosarcoma are common malignant tumours.[10,11] These are consistent with findings in our study. According to the study by the Trans-Atlantic RPS Working Group (TARPSWG), various histologic subtypes had statistically significant differences in recurrence patterns, survival outcomes and infiltration ability.[7] Confirming the histologic subtype of the tumour helps predict the risk of LR and distant metastasis and guide the treatment strategy.

Early diagnosis of PRT becomes difficult due to complex anatomy.[1] Serological investigations, imaging and biopsy contribute to the diagnosis of PRT. B-Ultrasound is usually preferred for the initial assessment of suspicious abdominal masses, as it is noninvasive, widely available and has no contraindications. CT and MRI are complementary to each other, both allow a comprehensive evaluation of tumours, indicate the benign or malignant nature of the tumour and reveal tumour location, size, number and shape.[12–14] Meanwhile, intratumoural haemorrhage, necrosis, cystic changes, calcification, tissue around the tumour, and enhancement features, etc, can be discovered. In addition, biopsy is essential for clinicians to confirm the histologic subtype. Thus, the tumour can be localised and qualitatively diagnosed to guide the formulation of optimal surgical plan.[10,15]

At present, surgery is the cornerstone of treatment.[16] The surgical methods for PRT consist mainly of traditional open surgery and laparoscopic surgery. In our study, there were 93 cases of laparotomy and 20 cases of laparoscopic surgery. The potential reasons for the significantly higher number of laparotomy than laparoscopic surgery are as follows.

First, because of the large tumour size, involvement of multiple organs and great vessels and limited operative space in the retroperitoneum, laparotomy was considered safer and more effective.[17] Second, surgeons at our centre might lack experience of laparoscopic surgery in the early stages of performing retroperitoneal tumour surgery. However, compared with laparotomy, laparoscopic surgery has many advantages, such as smaller wounds, less blood loss, shorter hospital stays, more rapid recovery and better cosmetic outcomes.[18,19] Recently, da Vinci robotic surgery has rapidly become widespread due to the advantages of three-dimensional (3D) imaging, wristed instrumentation and a shorter learning cycle compared with laparoscopic techniques.[20] Nevertheless, for retroperitoneal tumours, the specific choice of surgical method depends on the clinical experience of the surgeons and the specific characteristics of the case.

The surgical approach can also be divided into radical complete resection, combined visceral resection and palliative resection based on the extent of resection. Complete tumour resection is key for achieving cure and directly affects the survival time and risk of recurrence;[21] combined visceral resection has become a necessary surgical approach. Large centres at home and abroad have reported that the combined visceral resection rate of retroperitoneal tumours was generally 25%–40%.[22]

Similarly, the corresponding rate in our study was 19.27%, and combined nephrectomy was the most common (5/21 patients, 23.8%). However, the academic community has different opinions on the optimal extent of combined visceral resection. The controversy focusses mainly on the necessity of resecting adjacent and macroscopically unrelated organs. Traditionally, only directly infiltrated organs were resected to ensure negative margins, but two European centres put forward a more aggressive way concerning complete compartmental resection: adjacent organs, regardless of involvement, should be resected to minimise positive margins under the microscope and decrease the LR rate. No randomised trials have proven the survival benefits yet.[7] In our opinion, to ensure negative margins, it is necessary to resect directly involved adjacent organs. The decision to expand the extent of resection depends on a comprehensive evaluation of patient condition, tumour anatomy and histologic subtype.

Shibata *et al* compared patients with partially resected tumours with those with unresected tumours (only exploration or biopsy) and reported median survival time of 26 months and 4 months, respectively. This indicated the survival time was significantly different.[23] In this study, the survival rates of the follow-up biopsy and partial tumour resection groups were 45.45% and 80%, respectively. Therefore, patients with retroperitoneal tumours who may be good candidates for surgical resection cannot be easily abandoned.

Adjuvant chemotherapy and radiotherapy are beneficial for shrinking tumours and damaging residual tumour cells, and are thus recommended for the treatment of locally advanced and metastatic disease.[24,25] Targeted therapy and immunotherapy are emerging therapeutic methods. Imatinib is currently recognised as an effective drug for the treatment of retroperitoneal stromal sarcomas, and its advent has brought PRT treatment into the era of molecular targeting.[26,27] In this study, two pathological specimens tested positive for CD117. After 3–6 months of preoperative imatinib administration, the tumours shrank significantly. Thereafter, the patients underwent surgery, and no recurrence was observed during follow up.

Study limitations

Our study had some limitations and drawbacks. First, there were no significant differences among the prognostic factors of malignant tumours. It was possible that there was truly no significant correlation between these factors and outcomes. It was also possible that group study and patients lost to follow up led to the small number of cases. Thus, individual patient's conditions might have a considerable influence on the statistical analysis, leading to the lack of positive results. Second, data collection did not focus on chemotherapy or radiotherapy. In addition, due to the long timespan and considerable difficulty in history collection and follow up, the chemotherapy and radiotherapy data in this study were insufficient; thus, it was impossible to conduct effective data analysis.

Conclusion

Imaging plays important roles in localising and characterising tumours, guiding treatment strategies. Comprehensive treatment is the best therapeutic strategy for retroperitoneal tumours. With the help of new technologies such as laparoscopy and macrovascular reconstruction, more complete tumour resections can be achieved. Meanwhile, new chemotherapy drugs and molecular targeted drugs are being actively developed to reduce recurrence and improve the survival rate of patients.

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Author contributions

Conceptualisation, JX and RC; methodology, JX; software, LO; validation, LO and ZW; formal analysis, JX; investigation, YW and LC; resources, ZW; data curation, RC; writing—original draft preparation, JX and RC;

writing—review and editing, JX; visualisation, JX; supervision, BS; funding acquisition, BS. All authors have read and agreed the published version of the manuscript.

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