Clinical analysis of surgical treatment for retroperitoneal unicentric Castleman Disease: a single-centre experience for 10 years

Wenda Wang

Peking Union Medical College Hospital

Dexin Dong

Peking Union Medical College Hospital

Jin Wen (✉ 15120002969@163.com)

Peking Union Medical College Hospital

Hanzhong Li

Peking Union Medical College Hospital

Research

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Abstract

Objective Diagnosis of unicentric Castleman Disease (UCD) is not easy before the resection and obtainment of pathological result. We summarized 10-year experience of clinical management for retroperitoneal UCD in PUMCH.

Methods A retrospective analysis of retroperitoneal UCD between December 1st, 2009 and December 31st, 2019 in PUMCH was carried out. Epidemiological data, imaging and laboratorial examinations, and histopathological results after resection were reviewed and analyzed. The long-term follow up was performed in these retroperitoneal UCD patients.

Results 72 UCD patients with pathological diagnosis after resection were screened out. Among them 25 patients had retroperitoneal UCD. The average age of the 25 patients was 43.80 ± 12.79 , and 52.00% were male. No patients had systemic symptoms, and one patient got pre-operative treatment. The average size of masses was 5.59 ± 2.86 cm. The UCD sites included kidney, adrenal area, perinephric area, pancreas, peripancreatic area, area of descending part of duodenum, periaortic area or beside iliac artery, and others. The masses presented different degree of enhancement on CT scans and hypoecho or isoecho on ultrasound. Increased metabolism could be found on 18 F-FDG PET/CT. Some patients had positive results on somatostatin receptor imaging, but none had positive results on 131 I-MIBG. Some patients presented the elevated level of IL-6, 24h-urinary catecholamine and tumor markers. All the patients received complete resection of masses and 96.00% had hyaline-vascular type pathology except one patient (plasma cell-type). 92.00% patients received a long-term follow up with an average follow-up time of 35.48 ± 33.90 months. No patients died or experienced relapse during follow up.

Conclusions Differential diagnosis of retroperitoneal UCD may be difficult according to imaging and laboratorial examinations. Complete resection is the best treatment and could provide a final pathological diagnosis.

Introduction

Castleman Disease (CD) was firstly described by Benjamin Castleman in 1956. It is a rare, heterogeneous group of hyperimmune lymphoproliferative disorders^[1]. Unicentric Castleman Disease (UCD) is a localized disease which presents with isolated enlarged lymph nodes with no obvious systemic symptoms, and multicentric Castleman Disease (MCD) is a serious systemic condition^[2]. UCD is usually detected on radiological imaging incidentally or detected by a symptomatic lymph node mass. However, diagnosis of UCD is not easy before the resection and obtainment of pathological result. Here we summarized our 10-year experience of clinical management for retroperitoneal UCD.

Methods

Participants

We retrospectively analyzed the clinical data of patients who had the discharge diagnosis of “Castleman Disease” in Peking Union Medical College Hospital (PUMCH) from December 1st, 2009 to December 31th, 2019. Among them we further selected the patients who received surgery for “local mass”. The patients who received “mass resection” were included, and those received “mass biopsy” were excluded. The patients who had the diagnosis of “multicentric Castleman Disease” (MCD) before or after surgery were also excluded, and only patients of “unicentric Castleman Disease” (UCD) were included. At last we screened out UCD patients with retroperitoneal masses for further analysis. Our study was approved by the Ethics Committee of Peking Union Medical College Hospital.

Treatment and follow-up

All the included patients received retroperitoneal mass resection successfully. We obtained baseline data of all the patients before treatment. Pretreatment, abdominopelvic CT/MRI, ultrasonography, ¹⁸F-FDG PET/CT, ¹³¹I-MIBG imaging, and somatostatin receptor imaging were obtained in the patients. If the patients received laboratorial tests of tumor markers, 24 h-urinary catecholamine and IL-6, the results were also recorded. Outpatient or telephone follow-up for all the patients were arranged to supplement the long-term outcome information. For evaluating relapse, abdominopelvic imaging examinations were performed during follow-up.

Statistical analysis

All statistical analyses were performed using SPSS19.0 software (SPSS Inc., USA). Data were expressed as means ± standard deviation (mean ± SD) or n (%) as appropriate. We estimated relapse-free survival using the Kaplan-Meier method.

Results

In total, 260 patients with discharge diagnosis of “Castleman Disease” were retrieved during December 1st, 2009 to December 31th, 2019 in PUMCH. Among the patients, 72 UCD patients received “isolated mass resection” with the pathological diagnosis of “Castleman Disease”. The masses of 22 patients were superficial, 13 were thoracic, 12 were intraperitoneal, and 25 were retroperitoneal. The detailed distribution was shown in Fig. 1. And the characteristics of patients with retroperitoneal UCD at baseline were shown in Table 1. One female patient who experienced an incomplete resection in another hospital received cyclophosphamide, dexamethasone, and thalidomide before the second operation.

Table 1
Characteristics of included retroperitoneal UCD patients.

Age (yr, M $\pm$ SD) (Median, range)	43.80 $\pm$ 12.79 (43, 23 ~ 75)
Gender	
Male	13 (52.00%)
Femal	12 (48.00%)
Complications	
HTN	3 (12.00%)
DM	2 (8.00%)
α -thalassemia	1 (4.00%)
Systematic manifestations	0
Pre-operative treatment	1 (4.00%)
Site	
Renal	1 (4.00%)
Adrenal area	3 (12.00%)
Perinephric (including renal hilar)	5 (20.00%)
Peripancreatic (upper or lower)	4 (16.00%)
Pancreatic	1 (4.00%)
Area of descending part of duodenum	2 (8.00%)
Periaortic/Beside iliac artery	4 (16.00%)
Others	5 (25.00%)
Size (cm, M $\pm$ SD) (Median, range)	5.59 $\pm$ 2.86 (4.8, 2.5 ~ 13.8)

All the CT scans presented various degree of enhancement, and non-enhanced necrosis area could be found in some cases (Table 2). The characteristics of other imaging examinations have been shown in Table 2. However, no specific manifestations were shown on ultrasound or ^{18}F -FDG PET/CT. Although few patients had positive somatostatin receptor imaging, no case had positive ^{131}I -labeled metaiodobenzylguanidine (^{131}I -MIBG). For serological tests, 3 patients (3/10) had an elevated level of IL-6. One patient with mild higher IL-6 (7.8 pg/ml, normal range < 5.9 pg/ml) and one patient with moderate higher IL-6 (75 pg/ml) had no systemic symptoms, and the latter had the pathology of plasma cell-type CD. The previously mentioned patient who received two operations had an obvious elevated IL-6 level (251 pg/ml) before the second surgery. All of the patients' IL-6 levels returned to normal after resection. One patient

had mildly elevated level of 24 h-urinary catecholamine (norepinephrine) with no hypertension. In addition, 3 patients had mildly elevated level of tumor markers (CA727, CA125, and CA199 with AFP, respectively).

Table 2
Radiological and laboratorial features of included retroperitoneal UCD patients.

CT scan	21
Mild enhancement	2 (9.52%)
Moderate to obvious enhancement	19 (90.48%)
With non-enhanced area	5 (23.81%)
Ultrasound	13
Hypoecho	11 (84.61%)
Isoecho	2 (15.38%)
With anechoic area	3 (23.08%)
¹⁸ F-FDG PET/CT	5
Increased metabolism	5 (100.00%)
Somatostatin receptor imaging	12
Positive	3 (25.00%)
¹³¹ I-MIBG	9
Positive	0 (0%)
IL-6	10
Elevated	3 (30.00%)
24 h-urinary catecholamine	14
Elevated	1 (7.14%)
Tumor markers	6
Elevated	3 (50.00%)

Completed resections for the retroperitoneal masses (Figs. 2 and 3) were successful in all the patients. The pathologic analysis revealed that most of cases had hyaline vascular-type pathology, but one was plasma cell-type and one was mixed type respectively. The follow-up rate was 92.30% and the average

follow-up time was 34.29 ± 33.66 months with a range of 2 ~ 115 months. No patients received post-operative treatment. No relapse or death was found (Table 3).

Table 3
Follow-up of the 25 retroperitoneal UCD patients.

Pathology	
Hyaline vascular-type	24 (96.00%)
Plasma cell-type	1 (4.00%)
Follow-up	
Follow-up rate	23/25 (92.00%)
Follow-up time (months) (Median, range)	35.48 ± 33.90 (22, 2 ~ 115)
Post-operative treatment	0
Relapse	0
Death	0

Discussion

According to results of histopathology, CD could be subclassified into three types, hyaline-vascular, plasma-cell, and mixed types, and also could be subclassified into UCD and MCD on the basis of clinical features^[3]. MCD may present as thrombocytopenia, anasarca, fever, reticulin fibrosis and organomegaly^[2]. However, UCD patients usually have no symptoms mentioned above. Some patients may present the symptoms of enlarged lymph node's compression. In this study, all of the retroperitoneal UCD patients have no systemic symptoms. UCD can occur at any age with the median age of 30–34 years old^[4]. The median age in our study was 43. Most UCD cases (74 ~ 91%) had a pathology of hyaline vascular-type histology but a small part of cases (9 ~ 26%) had the pathology of plasma cell-type histology^[4]. Only one patient's pathology (4%) was plasma cell-type in our study.

A systematic review which includes 278 patients with UCD reports that the common sites include chest (29%), neck (23%), abdomen (21%), retroperitoneum (17%) and others (10%)^[5]. However, in our study, the most lesions were found to be retroperitoneal (34.72%) which was followed by superficial (30.55%), thoracic (18.06%) and abdominal (16.67%). In previous studies, unusual sites such as lung, orbits, nasopharynx, spleen and small bowel have been reported^[4]. In our study, UCD lesions were also found in some rare sites including lung, kidney, small bowel, parotid gland and pharynx.

For UCD patients, imaging examinations are usually used for the evaluation of diagnosis. UCD may present as a solitary mass with heterogeneous enhancement on CT scan because of hypervascularity of lesions^[5]. Intralesional calcification may be found in UCD and this may help for differentiating CD from

lymphoma^[6]. For MRI, UCD lesions are usually isointense or hyperintense relative to skeletal muscle on T1WI and hyperintense on T2WI^[7]. On ultrasonography, most UCD appear as hypoechoic masses, and peripheral and penetrating feeding vessels can be seen^[7]. On the other hand, ¹⁸F-FDG uptake is usually moderately increased in UCD on PET/CT^[5, 8]. However, all of the imaging manifestations mentioned above are not specific for distinguishing UCD from malignant tumors or neuroendocrine tumors. For retroperitoneal mass, pheochromocytoma/paraganglioma should be considered because some pheochromocytomas/paragangliomas are silent. However, these silent tumors may cause serious hypertension in surgery. Somatostatin receptor imaging and ¹³¹I-MIBG are usually used for pheochromocytoma/paraganglioma diagnosis. In our study, 12 patients received somatostatin receptor imaging and 3 patients had a positive result. But none of 9 patients who got ¹³¹I-MIBG presented a positive result. One of 14 patients who received 24 h-urinary catecholamine test had a mildly elevation of norepinephrine. Thereby, it's difficult to distinguish UCD from pheochromocytoma/paraganglioma according to imaging and laboratorial examinations, and pre-operative drug preparation may be unavoidable. ¹³¹I-MIBG may have reference value for differential diagnosis. When UCD occurs in kidney, pancreas, or periampullary area, malignant tumors should be considered. According to our results, imaging and serological tests are also not useful for the differentiation.

The preferred resolution for UCD is complete surgical resection^[5], and the latter could provide the final and gold-standard diagnosis for UCD. 10-year overall survival rates of UCD patients with a complete resection may be more than 95%^[5]. In patients with unresectable lesions, radiotherapy may offer a good long-term response rate as overall survival of 82% at 20 months^[9]. HV-type pathology may lead to a better prognosis than PC-type^[10]. No patients had relapse or death during long term follow-up in our study. The female patient who received two surgeries for retroperitoneal UCD resection also had a stable situation at about 6 months after the second surgery.

Conclusions

UCD presents as an isolated retroperitoneal mass, and differential diagnosis may be difficult according to imaging and laboratorial examinations. Complete resection is the best treatment for retroperitoneal UCD and could provide a final pathological diagnosis.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Peking Union Medical College Hospital (Beijing, China).

Consent for publication

Consent for publication was obtained from all the authors.

Competing interests

The authors declare that they have no competing interests.

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None.

Authors' contributions

JW and HL conceived and designed the study. WW and DD performed the data collection. WW conducted data analysis and produced the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

Figure 1

The flow chart of patient filtration and the site distribution of UCD.

Figure 2

The CT scan (A to D) and gross specimen (E and F) of a periaortic UCD patient. The pre-operative CT scan showed that the mass had moderate and uneven enhancement.

Figure 3

The pre- and post-operative CT scans of the patient who received a second surgery for retroperitoneal UCD (A to C, pre-operative; D to F, post-operative).