Clinicopathological Characteristics and Prognosis of Retroperitoneal Castleman Disease: a Study of Combined Case Series

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Research Article

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Abstract

Background: Owing to the sporadic incidence, the clinicopathological features and prognosis of retroperitoneal Castleman disease (CD) are limited. We aimed to investigate the clinicopathological characteristics and prognosis of retroperitoneal CD.

Patients and methods: The retroperitoneal CDs were obtained from our center and case reports extracted from Pubmed and Cochrane library from 1975 to 2020. The baseline clinical and demographic data and survival data were analyzed.

Results: A total of 110 retroperitoneal CDs were enrolled in the present study. The most common symptoms were abdominal pain (34/110, 30.9%), followed by abdominal mass (22/110, 20.0%) and weight loss (10/110, 9.1%). Most tumors are 5-10 cm in diameter (61/99, 66.7%). 103/110 (93.6%) tumors are unicentric, and hyaline vascular types (93/108, 86.1%) are the most common pathological type in retroperitoneal CD. The five-year disease-free survival (DFS) and disease-specific survival (DSS) were 96.7% and 100%, respectively. Almost all tumors can be removed surgically.

Conclusions: The median diameter of retroperitoneal CD is 7.0 cm. The most common type is unicentric hyaline vascular in retroperitoneal CD. Surgical resection seems to be the most effective therapy, and the five-year DFS and DSS were 98.6% and 100%.

Introduction

Castleman disease (CD) is a rare polyclonal lymphoproliferative disease of unknown etiology. Dr. Castleman first described the condition in the form of a case report in 1954 [1]. CD usually occurs in the mediastinum, and retroperitoneum is a rare location of the disease [2]. Due to the infrequent incidence, reports on the retroperitoneal CD are limited to case reports. Here, we aim to investigate the clinicopathological characteristics and prognosis of retroperitoneal CD based on combined case series.

Patients And Methods

CD cases of the retroperitoneal were from our institution and literature. From December 2016 to November 2019, 3 cases of retroperitoneal CD were diagnosed and treated in our hospital (Fig. 1). The literature search of PUBMED was performed for all articles in English published from 1975 to 2020. Pubmed retrieved 106 case reports., and the Cochrane library retrieved 1 case report. As a result, a total of 110 patients with retroperitoneal CD were identified. In this study, written informed consent was obtained from three patients in our center.(Fig. 2)

Data including gender, age, symptoms, accompanying tumors, tumor size, surgical intervention, clinical type, histological type, adjuvant therapy, tumor progression, and survival data. For survival analysis, the inclusion criteria were listed as follows: 1. No distant metastasis; 2. No CD from other places; 3. R0 resection; 4. No other malignant tumors; 5. Patients with follow-up data.

Statistics

Data were processed using SPSS 25.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Discrete variables were expressed as N, Percentage. The Kaplan-Mewer methods were used to evaluate disease-free survival (DFS) and disease-specific survival (DSS). DFS is defined as the length of time from the date of surgery to disease recurrence. DSS is defined as the length of time from the date of surgery to the date of tumor-related death.

Results

The clinicopathological characteristics were summarized in Table 1. There were 42 males (38.2%) and 68 females (61.8%). The median age is 34.5 (3-78) years. The most common symptoms are abdominal pain (34/110, 30.9%), followed by abdominal mass (22/110, 20.0%) and weight loss (10/110, 9.1%). Eight patients received treatment for symptoms of para neoplastic pemphigus[3–7]. Two patients were found to have retroperitoneal CD due to unusual symptoms of myasthenia gravis[8, 9]. 107 patients underwent complete surgical resection, 1 patient underwent palliative resection, and 1 patient did not receive surgery[10].

Table 1
Clinicopathological characteristics of 110 cases of Castleman retroperitoneum

Characteristics	Parameters
Age (Σ = 110)	
≤60	**103(93.6%)**
>60	**7(6.4%)**
Gender(Σ = 110)	
Male	**42(38.2%)**
Female	**68(61.8%)**
Symptoms(Σ = 110)	
Abdominal pain	**34(30.9)**
Abdominal mass	**22(20%)**
Weight loss	**10(9.1%)**
PNP	**8(7.3)**
Tumor size(Σ = 99)	
<5cm	**19(19.2%)**
5-10cm	**61(61.6%)**
>10cm	**19(19.2%)**
Tumor location(Σ = 67)	
Around the kidney	**41(61.2%)**
Around the pancreas	**10(14.9%)**
Pelvic cavity	**15(22.%)**
Around the liver	**1(1.5)**
Surgical resection(Σ = 109)	
Complete resection	**107(98.2%)**
Incomplete resection	**1(0.9%)**
No surgery	**1(0.9%)**

Abbreviation: PNP, Paraneoplastic pemphigus;UMC, unicentric Castleman disease;

MC, Multicenter Castleman disease.

Data were expressed as N(%).

Characteristics	Parameters
Accompanying tumor(Σ = 85)	
Other type of tumor	**8 (9.4%)**
Histological type(Σ = 108)	
Hyaline vascular type	**93 (86.1%)**
Plasma cell type	**10 (9.3%)**
Hybrid	**5 (4.6%)**
Clinical type(Σ = 110)	
UCD	**103 (93.6%)**
MCD	**7 (6.4%)**
Follow-up(Σ = 72)	
Recrudescence	**1 (1.4%)**
Death	**1 (1.4%)**
Abbreviation: PNP, Paraneoplastic pemphigus;UMC, unicentric Castleman disease;	
MC, Multicenter Castleman disease.	
Data were expressed as N(%).	

The tumor diameters ranged from 1 to 16 cm (median, 7.0 cm). The most retroperitoneal CD most commonly located around the kidney (41/110, 37.3%), followed by the pelvis's retroperitoneum. The tumor can compress the ureter and cause symptoms such as hydronephrosis and hematuria. In pathology type, 93 patients displayed hyaline vascular type (93/108, 86.1%), 10 patients displayed plasma cell type (10/108, 9.26%), and 5 patients showed mixed type (5/108, 4.63%). 103 patients showed unicentric tumor (103/110, 93.6%), and 7 patients demonstrated multicenter tumor (7/110, 6.36%). The laboratory tests of most patients are in the normal range.

72 patients with survival data were summarized in Table 2. The follow-up time ranged from 1 to 80 months (median, 17.0 months). Only 1 patient showed recurrence, and no patients suffered from CD-related death. The patient with tumor recurrence presented with a unicentric plasma cell type[11], and was hospitalized again due to azotemia and left hydronephrosis one year after surgery. The deceased patient could not surgically remove the tumor due to severe lung disease and died of pneumonia two years later[10]. The 1-, 3-, and 5-year DFS were 100%, 98.6%, and 98.6%, respectively. The 1-, 3-, and 5-year DSS are all 100%, respectively. The DFS of Castleman disease in retroperitoneum is shown in Figure 3.

Table 2
Survival data of 72 patients with castleman retroperitoneum

Survival characteristics	Parameter
Follow-up time (m)	
Mean (m±SD)	**22.88±18.85**
Median (m, range)	**17 (1, 80)**
Survival data	
Recurrence or metastasis	**1**
CD related death	**0**
Survival rates	
1-/3-/5-year DSF	**100/ 98.6/ 98.6**
1-/3-/5-year DSS	**100/ 100/ 100**
SD: Standard deviation	
DFS: disease-free survival	
DSS: disease-specific survival	

Discussion

CD's etiology is still unclear. Aa abnormal elevation of interleukin 6, human herpesvirus type 8, or human immunodeficiency virus infection may contribute to the development of CD[12, 13]. Due to the low incidence, the studies focused on retroperitoneal CDs were mainly case reports or case series with small sample size. Our study is the most extensive analysis of retroperitoneal CD.

CD is clinically divided into either multicentric CD or unicentric CD. The clinical presentation is different corresponding to the subtypes[2]. However, we find that most retroperitoneal CDs are unicentric, and more than 85% of these cases are hyaline-vascular variants, which is consistent with the previous review on CD [14]. In our study, there is no specific symptom of retroperitoneal CD, and the most common clinical manifestations of retroperitoneal CD are abdominal pain and abdominal mass. Intestinal obstruction, myasthenia gravis, and ureteral obstruction may also be clinical manifestations of retroperitoneal CD[15, 16].

The previous study revealed that males and females were equally affected[14]. However, females accounted for more than 60% of the retroperitoneal CDs (Table 1) in our study.

Surgical resection is the preferred therapy for retroperitoneal CD. Even cytoreductive surgery should be considered in the condition that the tumor cannot be completely resected. Our study demonstrated, almost all retroperitoneal CD patients can be entirely removed by surgical resection. For unresectable patients, systematic therapy such as radiotherapy, or chemotherapy, and/or steroids can be considered[2, 17], This study found that for paraneoplastic pemphigus symptoms caused by retroperitoneal unicentric CD, surgical removal of the tumor can significantly alleviate the symptoms[18]. Studies have found that patients with wholly resected unicentric CD demonstrate a good prognosis, with a 10-year overall survival rate of over 95%[19]. In our study, almost no patients had tumor recurrence after R0 resection. Besides, we found that retroperitoneal CD's prognosis has nothing to do with the clinical or group type. The 5-year DFS and DSS were 96.7% and 100%, respectively.

Our research has some limitations. First, this study is a retrospective study, and the data details are limited. Secondly, the sample size is small, which will lead to statistical bias. Third, the clinical case characteristics of retroperitoneal CD were not compared with CDs in other sites. However, our study still provides the largest sample size of retroperitoneal CD on the baseline and clinical characteristics, treatment, and prognosis.

Conclusion

The median diameter of retroperitoneal Castleman disease is 7.0 cm. The most common type of retroperitoneal CD is the unicentric hyaline vascular type. Surgical resection is the most effective treatment. Almost all the retroperitoneal CDs can be surgically resected, and the five-year DFS and DSS were 96.7% and 100%.

Abbreviations

CD: Castleman disease; UCD: Unicentric Castleman disease; MCD: Multi-center Castleman disease; DSS: Disease-specific survival; DFS: Disease-free survival; IL-6: Interleukin-6; HHV-8: human herpesvirus 8; HIV: human immunodeficiency virus.

Declarations

Acknowledgements

None

Authors' contributions

All authors conceptualized and designed the study. Kun Liu and Liang Liu were responsible for collection and analyzed the data. Kun Liu and Xueyi Liang performed data analysis, drafted, and revised the manuscript. Zhiqiang Liu and Heshui Wu helped to draft and revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

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

Ethics approval and consent to participate

Not applicable

Consent for publication

Written, informed consent was obtained from the patients for published images of this article. A copy of the written consent is available for review by the Editor of this journal.

Competing interests

The authors declare that they have no competing interests.

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Figures

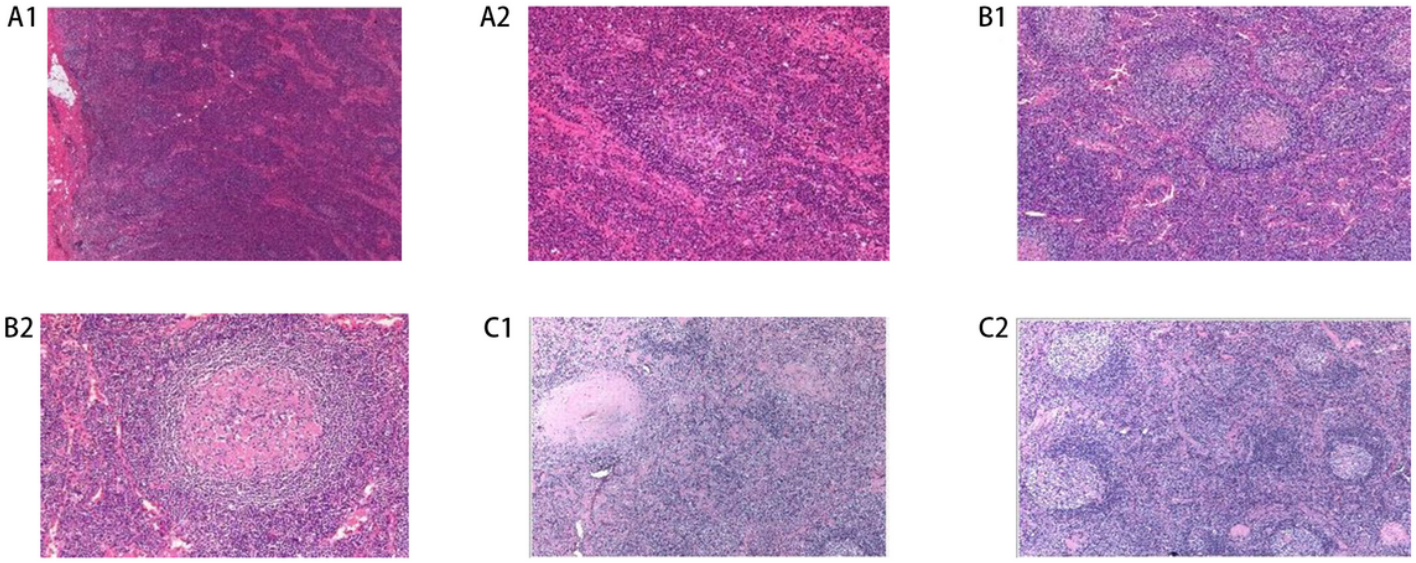

Figure 1

Pathological information of three patients. A1 and A2 Retroperitoneal plasma cell type Castleman disease; B1 and B2 Plasma cell type Castleman disease in the head of the pancreas; C1 and C2: Retroperitoneal hyaline vascular type Castleman disease.

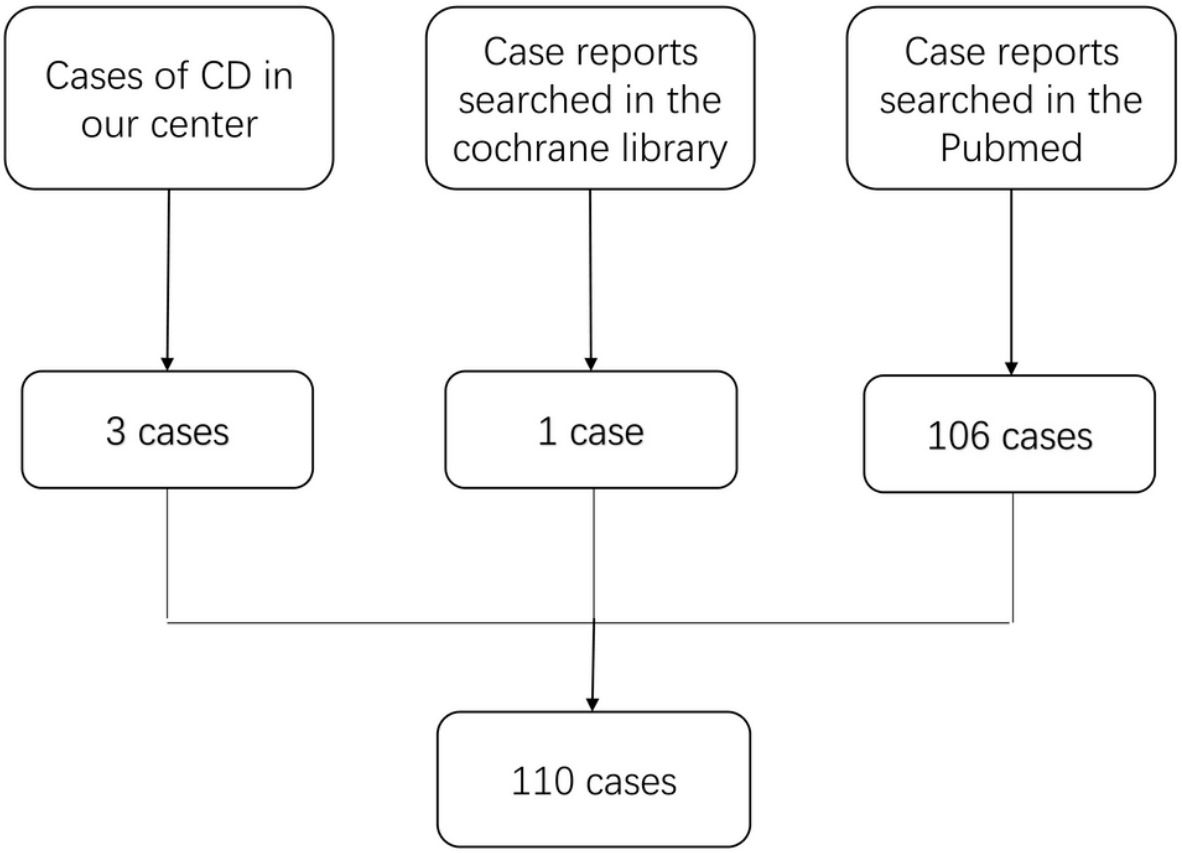

Figure 2

Flow chart retroperitoneal Castleman disease patients.

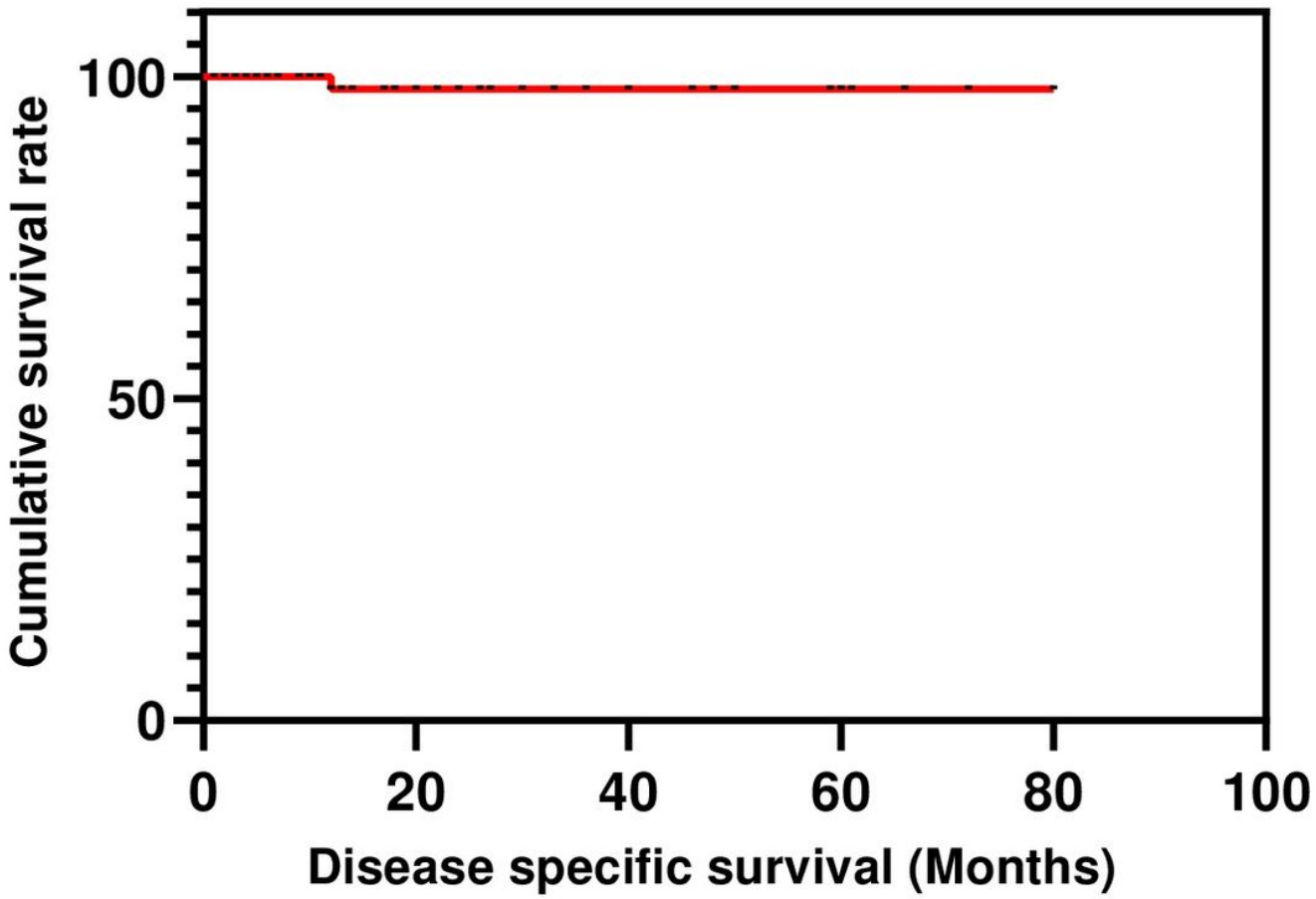

Figure 3

Disease specific survival curve of retroperitoneal Castleman disease.