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Clinical characteristics and outcomes of Castleman disease: A multicenter study of 185 Chinese patients

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Castleman disease (CD) is a rare lymphoproliferative disorder. To assess the clinical features, outcomes, and prognostic factors of this disease, we retrospectively analyzed 185 HIV-negative CD patients from four medical centers in southern China. The median age was 37 years. One hundred and twenty-one patients (65.4%) were classified as unicentric CD (UCD) and 64 patients (34.6%) were classified as multicentric CD (MCD). The histology subtype was hyaline-vascular for 132 patients (71.4%), plasma cell for 50 patients (27%), and mixed type for 3 patients (1.6%). The 5-year overall survival (OS) of 185 CD cases was 80.3%. All UCD patients underwent surgical excision, whereas the treatment strategies of MCD patients were heterogeneous. The outcome for UCD patients was better than MCD patients, with 5-year OS rates of 93.6% and 51.2%, respectively. In further analysis of the MCD subgroup, a multivariate analysis using a Cox regression model revealed that age, splenomegaly and pretreatment serum albumin level were independent prognostic factors for OS. This multicenter study comprising the largest sample size to date suggested that MCD is a distinct entity from UCD with a significantly worse outcome. Older age (≥40 years), splenomegaly, and hypoalbuminemia were risk factors for poorer MCD prognosis.

KEYWORDS
age, Castleman disease, HIV, human herpes virus 8, splenomegaly

Abbreviations: CD, Castleman disease; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; DFS, disease-free survival; HHV-8, human herpes virus 8; IL-6, interleukin-6; MCD, multicentric Castleman disease; OS, overall survival; PNP, paraneoplastic pemphigus; POEMS, polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin abnormalities; TAFRO, thrombocytopenia, ascites (anasarca), pleural effusion, microcytic anemia, fever, myelofibrosis, renal dysfunction, and organomegaly.

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1 | INTRODUCTION

Castleman disease (CD), also known as angiofollicular or giant lymph node hyperplasia, is a rare non-neoplastic lymphoproliferative disorder that was first described in 1956.[1] According to the lesions involved, CD can be characterized as unicentric (UCD) or multicentric (MCD). Unicentric CD is typically localized, indolent, and often treated with localized therapy alone. In contrast, MCD is a systemic condition associated with heterogeneous symptoms and is usually treated with systemic therapies. Histologically, CD can be classified into 3 types: hyaline-vascular, plasma cell, and mixed cellular. The hyaline-vascular type is more common in UCD patients; in contrast, the plasma cell type is more common in MCD.[2]

Although the etiology of CD is unclear, a large body of evidence shows that IL-6 plays a pivotal role in the development of CD, especially of MCD.[3] Recent data also suggested that MCD is associated with HHV-8,[3,4] the same virus found in Kaposi's sarcoma, which encodes a structural and functional homolog of human IL-6 called viral IL-6. Human herpes virus 8 is often identified in CD patients with HIV,[5] but it is also present in some HIV-negative cases. Additionally, of all published cases of MCD, more than one-third are negative for both HHV-8 and HIV.[6] The cause of this type of idiopathic MCD is poorly understood.

As CD is a rare disease, current studies are mostly retrospective or case reports from single institutions and the clinical characteristics, optimal treatments, and prognosis of CD remain controversial. In addition, HIV status is considered to be an important prognostic factor of CD,[7,8] and recent studies have paid more attention to HIV-positive MCD.[9-12] Consequently, data on HIV-negative CD patients are limited. Here we retrospectively analyzed 185 HIV-negative CD patients from 4 large medical institutions in southern China, to better understand the characteristics, outcomes, and prognostic factors of this disease. To the authors' knowledge, this study comprises the largest sample size currently analyzed.

2 | MATERIALS AND METHODS

In this retrospective study, we collected 185 cases of CD from 4 institutions in southern China (Sun Yat-Sen University Cancer Center, The First Affiliated Hospital of Sun Yat-Sen University, Sun Yat-Sen Memorial Hospital, and Guangdong General Hospital) (all Guangzhou, China) from January 2001 to January 2015. All patients had a clinically and pathologically confirmed CD diagnosis.

A database was established from the medical records and included: gender, age, presenting symptoms, involved sites, physical examinations, blood test results, radiological findings, pathological diagnosis, and treatments. All patients were followed up by outpatient reviews or by telephone conversations; the last follow-up date was 1 January 2016. Overall survival was defined as time from pathological diagnosis until death, lost to follow-up, or last follow-up. Disease-free survival was defined as time from surgery until tumor recurrence or the last follow-up.

All patients underwent computerized tomography scans or an ultrasound of the involved regions/organs or superficial lymph nodes; some patients received a systemic PET/computed tomography examination. Unicentric CD was defined as a solitary site of lymphadenopathy, and MCD was defined by the involvement of 2 or more lymph nodes or regions.[13-15] A total of 185 patients underwent HIV serology testing and all the results were negative. Ninety cases were screened for HHV-8 by latency-associated nuclear antigen immunocytochemistry on pathological tissue sections.

2.1 | Statistical analysis

Statistical analyses were carried out using SPSS 22.0 (IBM, Armonk, NY, USA). Pearson's χ^2-test was used to identify differences in clinicopathologic features between UCD and MCD patients. The Kaplan-Meier method was used for survival analysis, and the log–rank test was used to analyze the survival rate between the 2 groups. Variables achieving a significance level of $P < .05$ were entered into the Cox proportional hazards regression model for multivariate analyses. Independent prognostic factors were determined by having a significant effect in the Cox model ($P < .05$).

2.2 | Ethics approval and consent to participate

The study was led by the Sun Yat-Sen University Cancer Center and approved by the Ethics Committee of the Cancer Center, Sun Yat-Sen University (approval reference no. 2017-FXY-071 internal medicine). Written informed consent was provided by the patients. All experiments were carried out in accordance with relevant guidelines and regulations. The raw data of this study was deposited in the Research Data Deposit public platform (www.researchdata.org.cn), with the approval RDD number as RDDA2017000387, which could be obtained under reasonable request from the corresponding authors.

3 | RESULTS

3.1 | Clinical features

The clinical characteristics of 185 HIV-negative CD patients are shown in Table 1. The ratio of male to female patients was 1.03:1.00. The median age was 37 years (range, 7-74 years). One hundred and twenty-one patients (65.4%) were classified as UCD and 64 patients (34.6%) were classified as MCD. The histology subtype was hyaline-vascular for 132 patients (71.4%), plasma cell for 50 patients (27%), and mixed type for 3 patients (1.6%). Ninety patients were screened for HHV-8 by latency-associated nuclear antigen staining, and 16 patients (17.8%) were positive. B symptoms (fever, night sweats, and weight loss) were present in 33 patients (17.8%). Paraneoplastic pemphigus was found in 7 patients (3.8%) and POEMS syndrome was found in 5 patients (2.7%).

We compared the clinical characteristics between UCD and MCD patients and the results are shown in Table 2. The median age of the

TABLE 1 Clinical characteristics of 185 patients with Castleman Disease

Item	Cases	Proportion (%)
Gender		
Male	94	50.8
Female	91	49.2
Male : Female	1.03:1.00	
Age, years		
<40	105	56.8
≥40	80	43.2
Median age	37	
Clinical subtype		
UCD	121	65.4
MCD	64	34.6
Histological subtype		
HV	132	71.4
PC	50	27.0
Mix	3	1.6
HHV-8 status		
Positive	16	8.6
Negtive	74	40.0
Unknown	95	51.4
B symptoms	33	17.8
Splenomegaly	26	14.1
Ascites and/or pleural effusion	15	8.1
Paraneoplastic pemphigus	7	3.8
POEMS syndrome	5	2.7

HHV-8, human herpes virus 8; HV, hyaline-vascular; MCD, multicentric Castleman disease; PC, plasma cell; Mix, mixed cellular; POEMS, polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin abnormalities; UCD, unicentric Castleman disease.

UCD group was younger than the MCD group (33 years vs 42 years; $P < .001$). Histologically, most UCD patients were of the hyaline-vascular type, whereas most MCD patients were of the plasma cell type ($P < .001$). B symptoms, splenomegaly, ascites and/or pleural effusion occurred more frequently in MCD patients. All 5 patients with POEMS syndrome were in the MCD group, but the frequencies of PNP were not significantly different between the UCD and MCD groups. Among the tested patients, latency-associated nuclear antigen staining identified HHV-8 infection more frequently in MCD than in UCD. Of tested MCD patients, 39.3% were HHV-8-positive; the percentage of UCD patients was only 8.1% ($P < .001$).

3.2 | Treatment and survival of CD patients

All 121 UCD patients underwent primary lesion resections alone. For the 64 MCD patients, the treatment modalities are shown in Table 3. Seventeen asymptomatic patients without complications received a "watch and wait" strategy. They were followed up regularly every 3-6 months. Five patients underwent surgery and 6 patients who could

TABLE 2 Comparison of clinical characteristics between patients with unicentric (UCD) and multicentric (MCD) Castleman disease

Item	UCD (n = 121)	MCD (n = 64)	*P*-value
Gender, n (%)			
Male	58 (47.9)	36 (56.2)	.282
Female	63 (52.1)	28 (43.8)	
Age, years			
<40	80 (66.1)	25 (39.1)	<.001
≥40	41 (33.9)	39 (60.9)	
Median age	33	42	
Histological subtype, n (%)			
HV	111 (91.7)	18 (28.1)	<.001
PC	10 (8.3)	43 (67.2)	
Mix	0 (0.0)	3 (4.7)	
HHV-8 status			
Positive, n (%)	5 (4.1)	11 (17.2)	<.001
Negative, n (%)	57 (47.1)	17 (26.6)	
Unknown, n (%)	59 (48.8)	36 (56.3)	
B symptoms, n (%)	6 (5.0)	27 (42.2)	<.001
Paraneoplastic pemphigus, n (%)	5 (4.1)	2 (3.1)	.733
POEMS syndrome, n (%)	0 (0.0)	5 (7.8)	<.001
Splenomegaly, n (%)	4 (3.3)	23 (35.9)	<.001
Ascites and/or pleural effusion, n (%)	3 (2.5)	12 (18.8)	<.001

HHV-8, human herpes virus 8; HV, hyaline-vascular; Mix, mixed cellular; PC, plasma cell; POEMS, polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin abnormalities.

TABLE 3 First-line treatment of 64 patients with multicentric Castleman disease

Treatment	Cases (n)	Proportion (%)
Watch and wait	17	26.6
Surgery	5	7.8
Best supportive care	6	9.4
Prednisone	6	9.4
Prednisone + immunoglobulin	1	1.6
Prednisone + thalidomide	1	1.6
CTX	1	1.6
CTX + prednisone + thalidomide	2	3.1
CTX + MTX + prednisone	1	1.6
COP	10	15.6
CHOP/CHOP-like	9	14.1
CHOPE	1	1.6
Rituximab–CHOP	2	3.1
Tocilizumab	2	3.1

CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOPE, cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide; COP, cyclophosphamide, doxorubicin, and prednisone; CTX, cyclophosphamide; MCD, multicentric Castleman disease; MTX, methotrexate.

not tolerate other treatments received supportive care. Eight patients were treated with steroids, with or without immunoglobulin or thalidomide. A total of 26 patients underwent systemic chemotherapy, of which 20 cases received cyclophosphamide, doxorubicin, and prednisone, CHOP, or CHOP-like chemotherapy, and 2 received rituximab-CHOP. Two patients were treated with tocilizumab, a humanized mAb against the IL-6 receptor.

The median follow-up for all CD patients was 50 months (range, 2-161 months). By the date of the last follow-up, 30 deaths occurred (38.6%), of which 27 patients died of tumor progression and 3 died due to the treatment; 6 patients were UCD and 24 patients were MCD. The 5-year OS was 80.3% (Figure 1). For UCD patients, the 5-year OS and DFS were 93.6% and 91.2%, respectively (Figures 2 and 3). For MCD patients, the 5-year OS was 51.2% (Figure 2). The log–rank test for OS showed a statistically significant difference between UCD and MCD patients ($P < .001$).

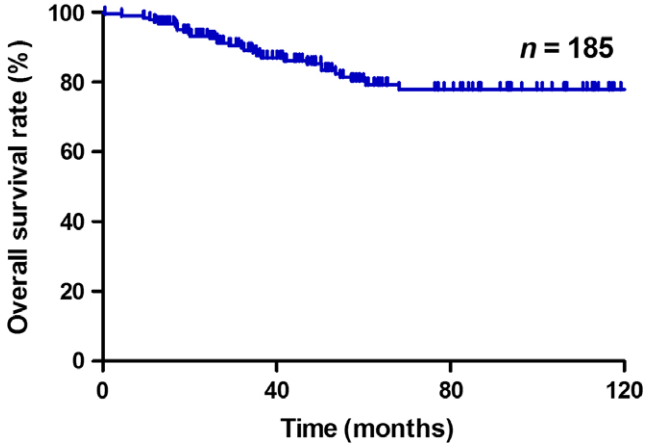

FIGURE 1 Overall survival of 185 Chinese patients with Castleman disease

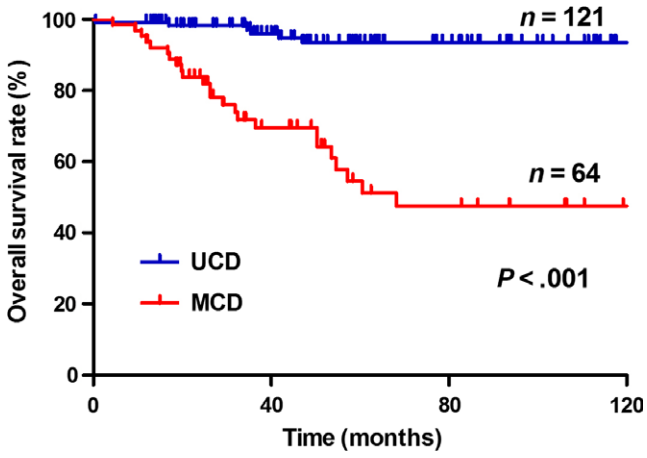

FIGURE 2 Overall survival of Chinese patients with unicentric (UCD) and multicentric (MCD) Castleman disease. The 5-year overall survival rate was 93.6% among patients with UCD (n = 121) vs 51.2% in those with MCD (n = 64) ($P < .001$)

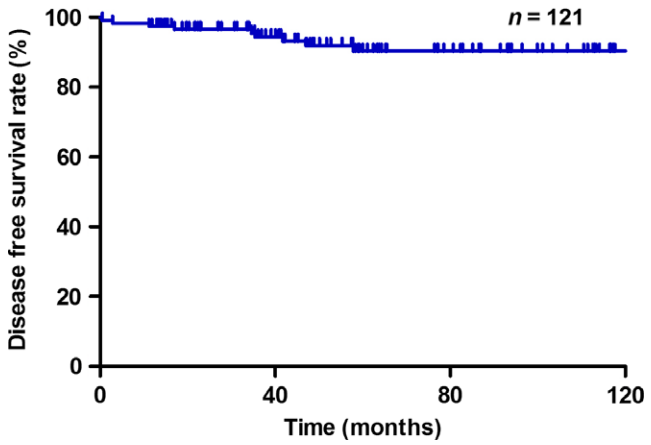

FIGURE 3 Disease-free survival of 121 Chinese patients with univariate Castleman disease. The 5-year disease-free survival rate was 91.2%

3.3 | Analysis of prognostic factors in patients with MCD

Considering the excellent prognosis of UCD patients receiving primary lesion resections, we only analyzed prognostic factors for the 64 MCD patients. The Kaplan-Meier method and log–rank test was used to complete univariate analyses. The results showed that older age (≥40 years), plasma cell or mixed histological type, B symptoms, splenomegaly, ascites and/or pleural effusion, hypoalbuminemia, and hyperglobulinemia were associated with worse OS. The HHV-8 status was only available for 28 MCD patients, and there was no statistical significance for OS between HHV-8-positive and HHV-8-negative groups. Patients with anemia or elevated C-reactive protein also appeared to have poorer prognosis, but the trend did not reach statistical significance ($P = .065$ and $P = .066$, respectively). These results are shown in Table 4.

Multivariate analysis using a Cox proportional hazards regression model showed that age, splenomegaly, and serum albumin level were independent factors for OS in MCD patients (Table 5, Figure 4).

4 | DISCUSSION

Because of its rarity, our understanding of CD is mainly from retrospective studies and case reports. Only a few studies have focused on the prognostic factors of CD, especially in HIV-negative patients. To better understand this disease, we presented a large series of CD patients from southern China in this multicenter study. Notably, our study comprises the largest sample size analyzed to date.

According to previous studies, HIV infection is an important factor in the pathogenesis of CD and strongly influences the prognosis.[7,8,10] Previous studies with relatively large cohorts have presented high-quality data regarding HIV-positive CD patients,[9-12] but few reports have focused on HIV-negative patients.[15-17] The prevalence of HIV in China is very low.[18] All the CD patients included in our study were proven to be HIV-negative. The present

TABLE 4 Univariate analysis of 64 patients with multicentric Castleman disease

Item	Cases, n	5-year OS, %	*P*-value
Gender			
Male	36	47.2	.257
Female	28	66.3	
Age, years			
<40	25	72.7	.022
≥40	39	43.0	
Histological subtype			
HV	18	88.9	.007
PC or Mix	46	41.8	
HHV-8 status			
Positive	14	62.0	.332
Negative	22	50.4	
B symptoms			
Yes	37	69.6	.011
No	27	35.7	
Splenomegaly			
No	41	74.4	.005
Yes	23	26.5	
Ascites and/or pleural effusion			
No	52	63.4	.016
Yes	12	28.6	
WBC, 10^9/L			
≥4.0	59	57.0	.673
<4.0	5	40.0	
Lym, 10^9/L			
≥1.0	57	58.5	.118
<1.0	7	28.6	
Hgb, g/L			
≥100	43	64.9	.065
<100	21	38.0	
Plt, 10^9/L			
≥100	61	56.7	.072
<100	3	0.0	
LDH			
Normal	42	62.5	.498
Elevated	4	50.0	
Glob, g/L			
≤35	33	65.9	.039
>35	31	44.4	
Alb, g/L			
≥35	35	73.2	.002
<35	29	31.3	
Serum creatinine			
Normal	56	49.2	.137
Elevated	8	31.3	
CRP			
Normal	18	75.0	.066
Elevated	13	41.0	

Alb, albumin; CRP, C-reactive protein; Glob, globulin; Hgb, hemoglobin; HHV-8, human herpes virus 8; HV, hyaline-vascular; LDH, lactate dehydrogenase; Lym, lymphocyte count; Mix, mixed cellular; PC, plasma cell; Plt, platelet count; WBC, white blood cell count.

TABLE 5 Multivariate analysis on the effect on survival of patients with multicentric Castleman disease

Risk factor	RR	95% CI	*P*-value
Age, years			
≥40 vs <40	2.663	1.019-6.959	.046
Albumin level, g/L			
<35 vs ≥35	3.959	1.590-9.854	.003
Splenomegaly			
Yes vs no	3.249	1.391-7.590	.006

CI, confidence interval; RR, relative risk.

study investigated prognostic factors for CD other than HIV status and the results will therefore contribute greatly to the information available on HIV-negative CD.

With quite different clinical features and prognosis, UCD and MCD are considered 2 distinct diseases. The heterogeneity between UCD and MCD is confirmed in our study. Consistent with previous studies,[16,17,19] our study found that UCD cases were more common than MCD. For the UCD group, patients were younger (median age, 33 years) and most cases were asymptomatic. The most common histological type of UCD was the hyaline-vascular variant, accounting for 91.7% of UCD cases, similar to previous studies.[16,17,19] Compared with the UCD group, our MCD patients were older (median age, 42 years) and appeared to be more symptomatic. Plasma cell variant cases were also more common in the MCD group. Other complications such as splenomegaly, ascites, pleural effusion, and POEMS syndrome also occurred more frequently in MCD patients.

For UCD, complete resection of the involved lesion is considered the gold standard treatment[20] and is curative in almost all cases reported so far, with a 5-year OS rate approaching 100%.[21-23] For patients whose tumor mass is unresectable because of size or location, radiotherapy can be utilized to reduce tumor size.[24,25] In our study, all 121 UCD patients received primary lesion resection alone as the initial treatment and the outcome was excellent, with the 5-year DFS rate and OS rate being 91.2% and 93.6%, respectively. Unlike UCD, the optimal treatment for MCD has not been well established and the outcome is less favorable. In our study, MCD patients had significantly worse survival rates compared with UCD patients, with the 5-year OS rate being 51.2% ($P < .001$). These results were consistent with previous reports.[13,15,16]

A variety of agents have been used to treat MCD, including corticosteroids, cytotoxic chemotherapy, thalidomide, i.v.

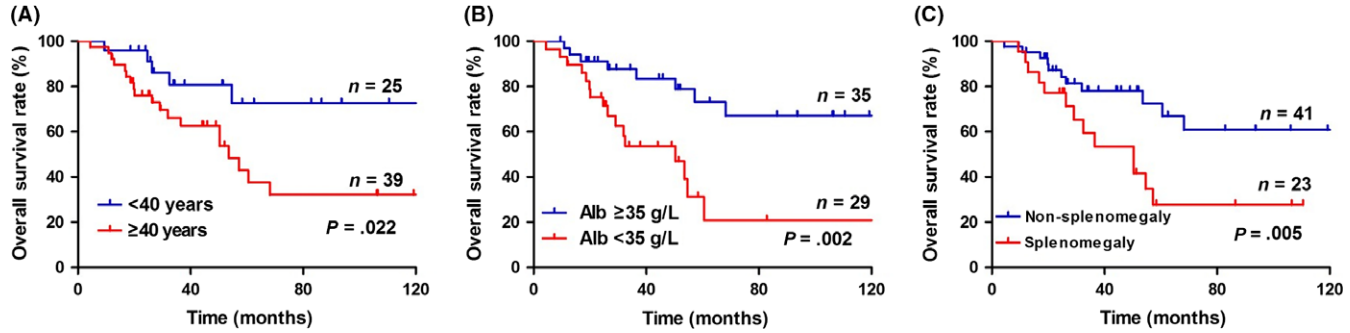

FIGURE 4 Prognostic factors for overall survival in patients with multicentric Castleman disease. A, Overall survival (OS) according to age. B, OS according to serum albumin levels (Alb). C, OS according to splenomegaly

immunoglobulin, rituximab, and anti-IL-6 antibody (siltuximab and tocilizumab). Most of the traditional treatment strategies were borrowed from lymphoma and multiple myeloma treatment regimens. Corticosteroids may have activity as monotherapy in controlling symptoms, but patients often relapse upon steroid taper and are generally short-lived.[24,26] Cytotoxic chemotherapy based on those used in lymphoma therapy may induce responses, but many patients will progress or experience infectious toxicities.[25-27] Rituximab, a monoclonal anti-CD20 antibody, is proven to be highly effective in HIV-positive MCD.[12,28,29] Although its activity in HIV-negative MCD is only supported by a small case series,[30-32] rituximab or rituximab-based therapy is still recommended as first-line therapy for HIV-negative MCD in the 2016 National Comprehensive Cancer Network (NCCN) guidelines for non-Hodgkin's lymphomas.[33] First reported by Yoshizaki et al,[34] anti-IL-6 drugs have been developed as a promising new therapy for MCD over the past decade. Tocilizumab, a humanized mAb to the IL-6 receptor, was approved for treatment of CD in Japan in 2005 based on the results of a phase II, open-label, single-arm study.[35] Siltuximab, a humanized anti-IL6 mAb, was approved for idiopathic MCD in the USA, Canada, and Europe, based on data from a double-blind, placebo-controlled, phase II trial showing significantly higher durable tumor response and symptomatic response compared with placebo ($P = .0012$).[36] In our study, more than half of MCD patients received corticosteroids or cytotoxic chemotherapy as first-line therapy. However, the treatments given to these patients were quite heterogeneous and few patients received new agents such as anti-IL-6 antibody and rituximab. Therefore, we were unable to identify the optimal treatment strategy for MCD in this study.

Due to the lack of optimal treatment for MCD, it is important to identify prognostic factors to help determine treatment strategies. However, no generally accepted prognostic factors of MCD have been found because of the low incident of CD and limited sample size of each study. In the present study, univariate and multivariate analysis identified older age, splenomegaly, and hypoalbuminemia as independent prognostic factors of MCD patients.

Older age has been widely reported to be a negative risk factor for various lymphoproliferative diseases, including Hodgkin's and non-Hodgkin's lymphomas. Consistent with our findings, Dong et al[14] showed that CD patients aged more than 40 years had a poorer prognosis. A meta-analysis by Talat et al[17] also identified age as prognostic factor of HIV-negative CD patients by univariate analysis. Mantovani et al[37] found that serum levels of IL-6 were significantly higher in elderly cancer patients. Considering IL-6 is related to the pathogenesis of CD, the poorer prognosis of older MCD patients may be due to increased IL-6 levels, which should be confirmed by further investigations.

In previous studies, splenomegaly was reported to be a common symptom of MCD patients, with a frequency ranging from 30% to 72%.[13,16,38,39] In our study, the frequency of splenomegaly was 36% and both univariate and multivariate analyses indicated that splenomegaly had a significant negative impact on MCD prognosis. Shin et al[16] suggested that the DFS of MCD patients with splenomegaly was significantly worse than those without splenomegaly. Similarly, splenomegaly was also identified by previous studies as a predictable risk factor for some types of lymphoma.[40,41] We hypothesize that some MCD patients with splenomegaly have true splenic involvement, which may suggest a more aggressive disease and cause the poorer prognosis. However, this hypothesis could not be further confirmed in our study because none of our patients with splenomegaly underwent a spleen biopsy.

Serum albumin level has been widely reported to be a prognostic factor of solid malignancies[42-44] and several hematological malignancies.[45-48] In the present study, hypoalbuminemia was found in 48.4% MCD patients and was associated with poorer OS. We suggest that serum albumin level is not only a reflection of the general condition of MCD patients, but is also a powerful factor for predicting patient prognosis. Therefore, it should be closely monitored in clinical practice.

Recently, 2 other large-scale studies identified renal function and PNP as independent prognostic factors of MCD.[14,15] However, these findings were not consistent with ours.

Previous data suggested that HHV-8 is present in 100% of HIV-infected MCD patients and in 40%-50% of HIV-negative cases.[49] Consistent with another report from Korea,[16] our study showed that the prevalence of HHV-8 infection in patients from southern China with MCD is 39.3%, much higher than that in UCD patients (8.1%). This result helps to confirm the important role of HHV-8 in the pathogenesis of MCD, which has been well established by previous studies.[3,4] Recent data also suggested that HHV-8 status may be associated with the prognosis of MCD,[16,39] but the clinical evidence was limited. In this study, we failed to identify HHV-8 as a

prognostic factor for MCD due to limited sample size. Of note, although the prevalence is low, positive HHV-8 status can also be found in UCD cases. However, the role of HHV-8 in these UCD cases is unknown. Therefore, the potential association between HHV-8 and CD requires further verification.

A new disease concept characterized by thrombocytopenia, anasarca including pleural effusion and ascites, fever, renal dysfunction, and organomegaly, known as TAFRO syndrome, was first described by Takai et al[50,51] The histological features of lymph nodes in TAFRO syndrome can be consistent with MCD, but some clinical characteristics are different between these 2 disease concepts. In the 2015 diagnostic criteria for TAFRO syndrome proposed by Masaki et al,[52] although lymph node biopsy is strongly recommended, CD-like histological features are not a necessarily part of the diagnosis. According to the criteria, 1 of 64 MCD patients in our series can be diagnosed as TAFRO syndrome, who presented with fever, thrombocytopenia, pleural effusion, and splenomegaly before a biopsy of an axillary lymph node confirming CD. This patient received 8 cycles of tocilizumab and was alive at the last follow-up date, with OS of 26 months. The mechanism and etiology of TAFRO syndrome is unclear, and whether TAFRO syndrome is a disease entity distinct from MCD, a subset of MCD, or an overlapping syndrome with MCD remains controversial.[53,54] Differences between TAFRO syndrome and MCD need to be discussed more. It can help in exploring the etiology of TAFRO syndrome and finding new therapeutic targets in the future.

This study has some limitations. First, as a retrospective study, there may be a bias for patient selection and data collection. Second, because of the heterogeneous treatments of MCD patients in our study, we could not further compare the effect of different treatment strategies. In addition, only a small number of MCD patients in our study received anti-IL-6 therapy or rituximab as first-line therapy, mostly for economic reasons. The role of these new agents in MCD treatment requires further investigation in the Chinese population.

In conclusion, with the largest sample size to date, this multicenter study identified the clinical characteristics and prognosis of HIV-negative CD patients. The results indicated that UCD patients have favorable outcome with primary lesion resections and that age, splenomegaly, and pretreated serum albumin level were independent prognostic factors for MCD patients. Further studies are needed to confirm these prognostic factors and investigate the optimal treatment for MCD.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

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