CANADIAN JOURNAL OF UROLOGY

Tech Science Press

Doi:10.32604/cju.2026.077709
ARTICLE

Clinical spectrum of retroperitoneal Castleman disease: retrospective analysis of 59 cases in a single Chinese medical center

Ting Zhu,[1,2#] Junjie Tian,[3#] Chuan Wang,[2] Zhishang Li,[2] Yanfeng Bai,[4] Shien Rao,[2] Ping Wang[1*]

[1]Department of Urology, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China
[2]Department of Urology, Jinyun People's Hospital, Lishui, China
[3]Department of Reproductive Endocrinology, Women's Hospital, Zhejiang University School of Medicine, Hangzhou, China
[4]Department of Pathology, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China

ZHU T, TIAN J, WANG C, LI Z, BAI Y, RAO S, WANG P. Clinical spectrum of retroperitoneal Castleman disease: retrospective analysis of 59 cases in a single Chinese medical center. *Can J Urol* 2026;33(4):977–987.

Backgrounds: *Castleman disease (CD) is a rare lymphoproliferative disorder. While its general clinical and pathological features are well-described, detailed data on retroperitoneal CD—a diagnostically challenging location—remain scarce. This study characterizes the clinicopathological profile, management, and long-term outcomes of retroperitoneal CD. The aim of this study is to clarify the clinical and therapeutic characteristics of retroperitoneal CD, and to provide practical evidence for its accurate diagnosis and individualized management in clinical practice.*

Methods: *A retrospective analysis of 59 patients with pathologically confirmed retroperitoneal CD (September 2010–December 2025) was conducted at a single center. Patients were classified as unicentric CD (UCD) or multicentric CD (MCD), with demographic, clinical, imaging, treatment, and follow-up data analyzed.*

Results: *The cohort included 52 UCD and 7 MCD patients. UCD patients were younger (median 38 vs. 56 years, $p = 0.021$), predominantly female (65.40%), and asymptomatic (65.40%). All MCD patients presented with systemic inflammatory symptoms. Perirenal location was the most common (36.54% of UCD). CT consistently showed well-circumscribed, hypervascular masses with intense arterial enhancement. Complete surgical resection of UCD achieved 100% disease-free survival (median follow-up 98.5 months). Multidisciplinary management (surgery, corticosteroids, or rituximab-based therapy) achieved disease control in all MCD patients.*

Conclusions: *Retroperitoneal UCD and MCD are distinct entities. UCD, a typically hyaline vascular type, is often incidentally detected and curable by complete surgical excision. MCD, usually plasma cell type with systemic symptoms, requires systemic therapy. Accurate preoperative diagnosis is critical to guide curative surgery for UCD and multidisciplinary management for MCD.*

Key Words: Castleman disease, retroperitoneum, clinical characters

Introduction

Castleman disease (CD), first described by Benjamin Castleman in 1954, is recognized as a rare and heterogeneous lymphoproliferative disorder of uncertain etiology.[1] It is postulated to arise from dysregulated immune responses and neoplastic proliferation within lymphoid tissues.[2] The disease is clinically subclassified into two distinct forms: unicentric CD (UCD), characterized by a solitary enlarged lymph

Received date 15 December 2025
Accepted for publication 16 March 2026
Published online 21 August 2026

[#]These authors contributed equally to this work.

*Corresponding Author: Ping Wang.
Email: wpyyy@zju.edu.cn

node or region of lymph nodes, and multicentric CD (MCD), a systemic illness involving multiple lymph node stations and often associated with profound inflammatory symptoms.[3,4] Histopathologically, CD encompasses a spectrum primarily defined by the hyaline vascular (HV) variant, the plasma cell (PC) variant, and mixed forms exhibiting features of both.[5]

Epidemiologically, CD is reported to predominantly affect young adults aged 15–35 years, with no significant gender predilection in most series.[6] However, its pathogenesis remains incompletely elucidated, involving complex interactions between viral infections (notably Human Herpesvirus-8 in a subset of MCD), dysregulated cytokine signaling (especially IL-6), and genetic predispositions.[7] Patients often present with a painless mass and have few systemic symptoms.[8] While the disease most commonly occurs in the thorax and neck, retroperitoneal involvement is relatively rare.[9,10] Retroperitoneal CD has been reported across a wide age range, from young females to elderly males, with the unicentric form appearing more common in younger individuals.[10] The clinical presentation of retroperitoneal CD is diverse and nonspecific, frequently leading to diagnostic delays.[11] Many patients are incidentally found to have a retroperitoneal mass during physical examinations. Symptomatic patients mostly exhibit local compressive symptoms related to the mass location, such as abdominal or back pain, lower abdominal dull pain, or urinary hesitancy.[12–14] A large mass may cause displacement of adjacent organs (e.g., the bladder).[8] Some cases may be accompanied by paraneoplastic manifestations, complicating the clinical picture further.[15] For instance, cases have been reported where patients presented with mucocutaneous lesions resembling common dermatoses, later confirmed as paraneoplastic pemphigus secondary to retroperitoneal CD.[15–17] Another retrospective analysis noted that retroperitoneal CD patients complicated by paraneoplastic pemphigus may subsequently develop bronchiolitis obliterans, which is a significant risk factor affecting prognosis.[16] The clinical presentation is remarkably heterogeneous, ranging from an incidentally discovered, asymptomatic localized mass in UCD to a debilitating systemic inflammatory syndrome in MCD, often involving fever, night sweats, weight loss, cytopenias, and multi-organ dysfunction.[18] This heterogeneity, coupled with its rarity, poses significant diagnostic and therapeutic challenges, frequently leading to delays in diagnosis or misdiagnosis as lymphoma, autoimmune disease, or infection.[19]

Despite extensive research on Castleman disease in general, a systematic and detailed description of the clinicopathological features, optimal treatment strategies, and long-term prognosis specifically for CD originating in the retroperitoneum remains lacking. This study aims to address this critical knowledge gap by comprehensively reviewing and analyzing the 14-year clinical, imaging, pathological, therapeutic, and outcome data of 59 patients with retroperitoneal CD treated at our tertiary medical center. Due to its location, a retroperitoneal mass often raises strong suspicion for cancer, such as sarcoma or lymphoma.[20] This can lead to unnecessarily extensive and risky surgeries if the true nature of Castleman disease is not considered beforehand.[21,22] Therefore, improving the recognition of CD in this specific location is a key goal for surgeons, radiologists, and pathologists.

Furthermore, the long-term outcomes and ideal management for retroperitoneal CD are not well defined. For UCD, surgery is the standard, but the best surgical approach is debated.[23] For iMCD presenting with a sizable retroperitoneal mass, the potential benefit of surgery to achieve local disease control or alleviate compressive symptoms, in conjunction with first-line systemic therapy (e.g., siltuximab), is an area of ongoing evaluation and debate.[19] Our detailed, long-term study aims to provide clear answers to these practical clinical questions. By offering a clearer picture, we hope to help doctors make better decisions, avoid unneeded procedures, and improve care for patients with this unusual condition.

Methods

This was a single-center, retrospective cohort study conducted at the Department of Surgery, First Affiliated Hospital, Zhejiang University School of Medicine. From September 2010 to October 2024, consecutive patients identified from the databases were screened for eligibility. The source population comprised individuals presenting to our tertiary hospital with a suspected retroperitoneal mass. Inclusion required being aged ≥15 years with a pathologically confirmed diagnosis of Castleman disease whose epicenter was located in the retroperitoneum, as confirmed by imaging and surgery/biopsy. Patients were excluded if the diagnosis relied solely on cytology, if essential medical records or imaging data were incomplete, or if a concurrent active malignancy was

present that could confound analysis. Ultimately, 59 patients who met all inclusion criteria and none of the exclusion criteria formed the final study cohort. The diagnosis was established by postoperative pathological examination of the resected specimen in all UCD cases and by biopsy (surgical or core needle) in MCD cases, based on characteristic histomorphology and confirmed by immunohistochemical staining. The study was approved by the ethics committee of the First Affiliated Hospital, School of Medicine, Zhejiang University, China (Ethical Batch Number: IIT20251050A). Which waived the requirement for individual informed consent due to the retrospective nature of the analysis.

Medical records were meticulously reviewed by two independent researchers to extract demographic data (age at diagnosis, gender), clinical presentation (symptoms, duration, physical findings), laboratory investigations (complete blood count, serum chemistry, inflammatory markers like C-reactive protein and erythrocyte sedimentation rate where available), and details of radiological examinations.

All patients underwent contrast-enhanced abdominal CT using a 64-slice CT scanner (Siemens Somatom Definition AS, Germany). Non-contrast scans were acquired first, followed by intravenous injection of contrast medium (iohexol, 300 mgI/mL) at 3.0 mL/s. Scanning phases were timed as:

Arterial phase: 25–30 s post-contrast injection;

Venous phase: 60–70 s post-contrast injection;

Delayed phase: 3–5 min post-contrast injection.

HU values were measured by an experienced abdominal radiologist (blinded to final diagnosis) using scanner-built software. Regions of Interest (ROIs) were placed on the lesion's largest cross-section, avoiding necrotic/cystic/calcified areas. Three ROIs (each $\geq$10 mm^2) were selected, and the mean HU value was recorded for each phase.

Surgical records were analyzed for operative approach (open vs. laparoscopic/robotic), procedure performed (complete resection vs. biopsy), intraoperative findings, and complications. Pathological reports were reviewed to confirm the diagnosis, classify the histological subtype (HV, PC, or mixed), and record any atypical features. Treatment details, including type of surgery, adjuvant therapies (chemotherapy, immunotherapy, corticosteroids), and follow-up data, were collected.

Following initial treatment, patients were routinely followed up via structured telephone interviews or outpatient clinic visits until the censor date of December 2025. The follow-up duration for each patient was defined as the time from the date of initial pathological diagnosis to the date of the last recorded contact or death. For MCD patients, long-term follow-up focused on clinical status and laboratory parameters, assessed via structured telephone interviews and review of records from local physicians. Due to the retrospective nature of the study and the geographical dispersion of the MCD cohort, systematic serial cross-sectional imaging performed at this center was not uniformly available.

Statistical analysis was performed using SPSS software (version 20.0, IBM Corp., Armonk, NY, USA). Continuous variables with a normal distribution were expressed as mean $\pm$ standard deviation, while skewed data were presented as median with interquartile range (IQR). Categorical variables were expressed as frequencies and percentages. Given the fundamental clinical and prognostic differences between UCD and MCD, all analyses were performed separately for these two groups. Group comparisons for continuous variables were conducted using the independent samples *t*-test or Mann-Whitney U test, as appropriate. Categorical variables were compared using the Chi-square test or Fisher's exact test. A two-sided *p*-value of less than 0.05 was considered statistically significant.

Results

Baseline demographic and clinical characteristics

A total of 59 patients with retroperitoneal Castleman disease were included in the final analysis. The cohort comprised 52 patients (88.1%) with UCD and 7 patients (11.9%) with MCD. The baseline characteristics of the two groups are summarized in Table 1.

Among UCD patients, there was a notable female predominance (65.40% female vs. 34.60% male). The median age was 38 years IQR: 29–52. Strikingly, 34 patients (65.40%) were entirely asymptomatic, with the retroperitoneal mass discovered incidentally during imaging studies for unrelated reasons (e.g., routine health check-up, investigation of unrelated abdominal complaints). Of the 18 symptomatic UCD patients, the most common complaint was nonspecific abdominal pain (25.00%) or fatigue (3.85%). One patient presented with concurrent myasthenia gravis, a recognized paraneoplastic association. Laboratory abnormalities were uncommon in UCD.

In stark contrast, all 7 MCD patients were symptomatic at presentation. It is noteworthy that MCD patients tended to be older, with a median age of 56 years, compared to 38 years in the

TABLE 1. **Characteristics of included retroperitoneal UCD & MCD patients**

Characteristics	UCD (n = 52)	MCD (n = 7)	*p*-Value
Age (Median, range)	38 (15–65)	56 (28–70)	0.021
Gender			0.107
Female	34 (65.40%)	4 (57.14%)	
Male	18 (34.60%)	3 (42.86%)	
Side			0.065
Right	32 (61.54%)	3 (42.86%)	
Left	20 (38.46%)	4 (57.14%)	
Size (cm) (Median, range)	4.56 (2–14.5)	5.10 (2–9)	0.412
Location			0.023
Adrenal area	3 (5.77%)	0 (0.00%)	
Perinephric	19 (36.54%)	3 (42.86%)	
Peripancreatic	2 (3.85%)	0 (0.00%)	
Duodenum	2 (3.85%)	0 (0.00%)	
Periaortic	12 (23.08%)	1 (14.29%)	
Iliac artery	6 (11.54%)	2 (28.57%)	
Pelvic cavity	8 (15.38%)	2 (28.57%)	
Clinical characteristics			0.643
Anemia	2 (3.85%)	3 (42.86%)	
Leukopenia	0 (0.00%)	3 (42.86%)	
Hypoproteinemia	0 (0.00%)	2 (28.57%)	
Fever	1 (1.92%)	0 (0.00%)	
Abdominal discomfort	13 (25.00%)	3 (42.86%)	
Fatigue	2 (3.85%)	1 (14.29%)	
Laboratory investigations			0.535
CRP (mg/L) (Average, range)	6.48 (0.03–53)	48.25 (1.8–176.4)	
ESR (mm/h) (Average, range)	7.69 (1–23)	16.8 (1–44)	
Treatment			0.479
Surgery	52 (100%)	2 (28.57%)	
Conservative therapy	0 (0.00%)	5 (72.43%)	
Outcomes			0.438
Complete remission	52 (100%)	1 (14.29%)	
Stable lymphadenopathy	0 (0.00%)	6 (85.71%)	
Relapse or progression	0 (0.00%)	0 (0.00%)	

Note. UCD: Unicentric castleman disease; MCD: Multicentric castleman disease; CRP: C-reactive Protein; ESR: Erythrocyte Sedimentation Rate.

UCD group. Systemic B-symptoms were prevalent: fatigue/malaise (14.29%), and abdominal discomfor (42.86%). Laboratory findings consistently reflected systemic inflammation and cytokine-driven effects, with a high prevalence of anemia (42.86%) and hypoalbuminemia (2.57%). Inflammatory markers (CRP/ESR) were elevated in all tested MCD patients. Given the small number of MCD cases (n = 7), these findings are presented as descriptive observations, and statistical comparisons are not emphasized.

Anatomic distribution and imaging features

All lesions were primary to the retroperitoneal space. The detailed anatomical distribution is illustrated in Figure 1 and summarized below for each group.

UCD: The most common site was the perirenal region (19 cases, 36.5%), followed by the periaortic/paracaval region. A distinct right-sided predominance was observed: 32 lesions were on the right, 20 lesions on the left.

MCD: Due to multicentricity, defining a single "primary site" is less meaningful, but among the

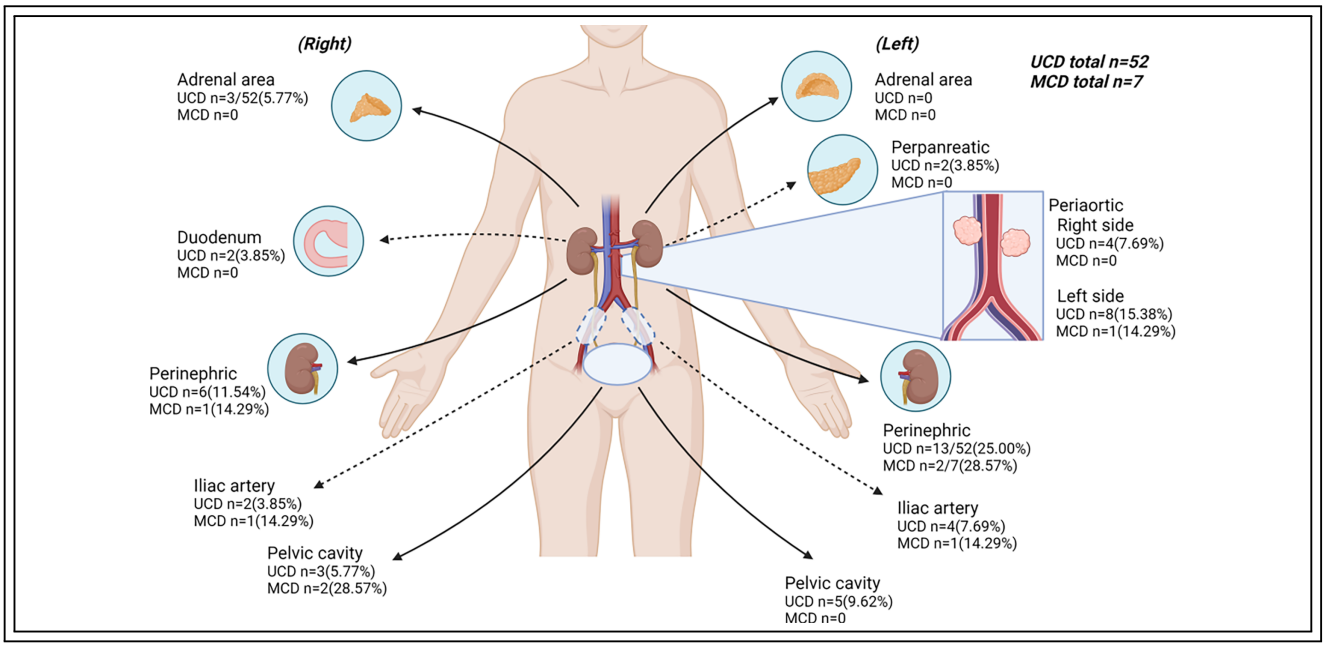

FIGURE 1. Anatomical distribution of retroperitoneal Castleman disease (CD) subtypes. A schematic showing the anatomical location of lesions in 52 patients with unicentric CD (UCD) and 7 patients with multicentric CD (MCD). The perirenal region was the most common site for both subtypes. UCD exhibited a distinct right-sided predominance, while MCD lesions were more evenly distributed between left and right sides

dominant or initially detected retroperitoneal lesions, the perirenal region was the most common. Notably, one patient had extensive involvement spanning the iliac vessel and pelvic regions. In terms of lateral distribution, there was no obvious side predominance, with lesions more evenly distributed: 3 lesions on the right and 4 lesions on the left.

All 59 patients underwent preoperative contrast-enhanced CT. The imaging features were remarkably consistent, particularly for UCD. The masses were typically well-circumscribed, oval or round, and of soft tissue density. Partial lobulation was seen in approximately 40% of cases. On non-contrast scans, the mean attenuation was 56.3 ± 4.2 HU. Post-contrast imaging revealed a characteristic hypervascular pattern: avid and homogeneous arterial phase hyperenhancement with mean attenuation values reaching 112–145 HU, followed by persistent enhancement and delayed washout in the venous and delayed phases (mean 85–95 HU). Notably, non-enhancing central or stellate hypodense areas were often observed, suggesting fibrous or hyalinized components (Figure 2A,B). This pattern of "avid arterial enhancement followed by persistent enhancement/delayed washout" is highly suggestive of CD and aids in its differentiation from hypovascular tumors such as lymphoma or some sarcomas.

Treatment modalities and surgical outcomes

Unicentric CD: All 52 patients underwent complete surgical resection with curative intent. The surgical approach was open laparotomy in 38 patients (73.07%) and minimally invasive surgery (laparoscopic or robotic-assisted) in 14 patients (26.92%), adopted more frequently in recent years. The choice of surgical approach was primarily determined by the admitting surgical department's specialization and prevailing clinical practice: The mean operative duration was 220.8 ± 71.5 min for open surgeries (n = 38) and 184.6 ± 113.1 min for minimally invasive surgeries (n = 14). The corresponding mean estimated blood loss was 750.0 ± 357.1 mL and 625.0 ± 441.3 mL, respectively. For tumors located in the perirenal and peri-adrenal regions, surgeons preferred a retroperitoneal approach. In contrast, for tumors situated near the duodenum or within the pelvis, a transabdominal approach was more commonly selected. Additionally, the mean length of postoperative hospital stay was 8.5 days (range: 3–12 days). Intraoperatively, tumors were described as solid, well-encapsulated, and highly vascularized, often with prominent feeder vessels. The median maximum tumor diameter was 4.56 cm (range: 2.0–14.5 cm). No major intraoperative complications (e.g., significant hemorrhage, visceral injury) were recorded. Three patients (two

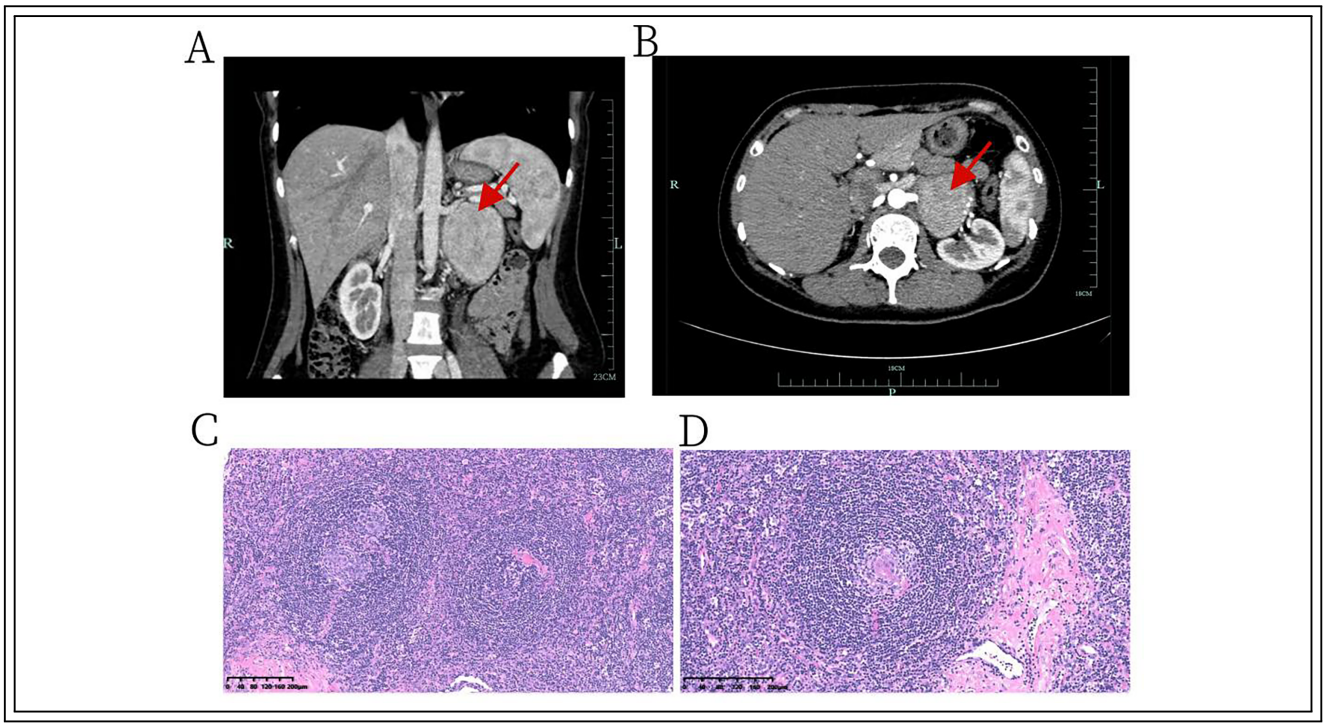

FIGURE 2. Typical imaging and pathological features of castleman disease. (A) Delayed phase contrast-enhanced Computed Tomography (CT): Mass with persistent enhancement and delayed washout, accompanied by a non-enhancing central stellate hypodense area (arrow). (B) Arterial phase contrast-enhanced CT: Well-circumscribed mass with avid and homogeneous hyperenhancement, synchronous with aortic enhancement. (C) Low-power histopathology (hematoxylin-eosin staining): Hyaline vascular variant showing the classic "onion-skin" appearance of lymphocytes surrounding atrophic germinal centers. (D) High-power histopathology (hematoxylin-eosin staining): "Lollipop lesion" with a hyalinized blood vessel penetrating the germinal center, plus interfollicular vascular proliferation

with mixed-type and one with PC-type UCD) underwent postoperative bone marrow biopsy to rule out occult systemic disease or plasma cell dyscrasias, all of which were negative. No patient received adjuvant radiotherapy or systemic therapy following complete resection.

Multicentric CD: Two patients (28.57%) underwent surgical resection of a large, symptomatic dominant retroperitoneal mass (one perirenal, one pelvic). One of these received subsequent systemic chemotherapy with the CHOP regimen (cyclophosphamide 750 mg/m², doxorubicin 50 mg/m², vincristine 1.4 mg/m², prednisone 100 mg/day for 5 days per cycle) for 6 cycles, administered every 3 weeks; the other declined further treatment post-surgery. Five patients (71.53%) did not undergo therapeutic resection. Diagnostic confirmation was obtained via image-guided core needle biopsy (3 patients) or laparoscopic excisional biopsy (2 patients). Subsequent systemic treatments included: a rituximab-lenalidomide-dexamethasone regimen (rituximab 375 mg/m² on day 1, lenalidomide 25 mg/day on days 1–21, dexamethasone 40 mg/day on days 1–4, 9–12, 17–20) for 4 cycles (every 28 days per cycle) in 1 patient; prednisone monotherapy (initial dose 60 mg/day, tapered by 10 mg every 2 weeks to a maintenance dose of 10 mg/day, with total treatment duration ranging from 6 to 12 months) in 3 patients. One patient refused all forms of systemic therapy and was managed with active surveillance.

Disease control was evaluated primarily through the resolution of systemic B-symptoms (fever, fatigue, weight loss) and the normalization of inflammatory markers (CRP, ESR). Clinical stability was defined as the sustained absence of symptomatic progression alongside stable or improving laboratory parameters over the follow-up period. Among the six treated patients, this clinical-laboratory definition of disease

control was achieved in all cases following intervention. The single untreated patient remained clinically stable during surveillance.

Pathological features

Histopathological examination was diagnostic. In the hyaline vascular type (Figure 2C,D), the classic "onion-skin" appearance was seen, with concentrically arranged layers of small lymphocytes surrounding atrophic, regressed germinal centers. The germinal centers were often penetrated by a single hyalinized blood vessel ("lollipop lesion"). There was marked interfollicular vascular proliferation with hyalinization. The plasma cell variant showed preserved or hyperplastic germinal centers with massive, sheet-like infiltration of mature plasma cells in the interfollicular zones. The mixed type had features of both.

Long-term follow-up

The median follow-up duration was 98.5 months (range: 27–188 months) for UCD and 65 months (range: 27–97 months) for MCD.

UCD Outcomes: All 52 patients who underwent complete surgical resection were alive at the last follow-up. Crucially, no patient developed local recurrence or distant metastasis during surveillance imaging. The disease-free survival rate was 100%.

MCD Outcomes: The clinical course was variable. Among the six patients who received some form of therapy (surgery, immunosuppression, or targeted therapy), all achieved at least partial clinical improvement (symptom relief, normalization of laboratory parameters). One patient on prednisone monotherapy experienced relapse upon tapering and required re-initiation of therapy. The patient who refused any treatment remained clinically stable, though with persistent mild symptoms and laboratory abnormalities, over a 27-month surveillance period. There were no disease-related deaths in the MCD group during the follow-up period.

All MCD patients were followed up via structured telephone interviews until December 2025, without laboratory/imaging tests. Treatment response was assessed by self-reported symptoms: treated patients were followed every 3–4 weeks during treatment and 3-monthly post-treatment (response = symptom relief/stabilization); the surveillance-only patient was followed 3-monthly (control = no symptom worsening). All treated patients achieved partial improvement, and the surveillance patient remained stable.

Discussion

This retrospective study of 59 patients represents one of the largest single-center series focusing exclusively on Castleman disease localized to the challenging retroperitoneal compartment. Our findings corroborate, refine, and expand upon the existing literature regarding this rare entity.

UCD patients were notably younger (median 38 years) and showed a prominent female predominance (65.40%)—a gender bias more pronounced than in general CD cohorts. This discrepancy may stem from either referral selection bias inherent to our surgical center or represent a genuine trait of retroperitoneal UCD, warranting validation in multi-institutional studies. The high rate of incidental discovery (65.40%) underscores UCD's indolent, localized nature: many patients were referred to surgeons with a preoperative diagnosis of a "suspicious mass," emphasizing the need for clinical teams to include benign entities like UCD in the differential diagnosis of retroperitoneal space-occupying lesions.

In stark contrast, MCD patients presented a decade later (median 56 years) with universal systemic inflammatory symptoms (e.g., fatigue, fever, weight loss) and marked laboratory derangements (anemia, hypoalbuminemia, elevated CRP/ESR), aligning with its pathogenesis as a cytokine-driven disorder.[19,24]

Notably, one UCD patient presented with concurrent myasthenia gravis—a recognized paraneoplastic association—highlighting the importance of considering CD in retroperitoneal mass patients with autoimmune comorbidities.[25] Surgical resection of the CD lesion can ameliorate such paraneoplastic syndromes, likely mediated by cross-reactive antibodies or shared autoimmune mechanisms.[26]

The retroperitoneal distribution observed—with perirenal and para-aortic regions being most common for UCD—is anatomically logical, corresponding to major lymph node basins. The striking right-sided predominance (61.54%) in UCD is an interesting and less commonly reported finding. Its explanation remains speculative but could relate to asymmetrical lymphatic drainage patterns or mere chance in our cohort; validation in larger studies is needed. This finding, if confirmed, could have implications for surgical planning and approach selection for minimally invasive procedures.

The consistency of imaging features, particularly the hypervascular "avid arterial enhancement followed by persistent enhancement/delayed washout" pattern on CT, is a critical takeaway.[27,28] This signature, while not 100% specific, should immediately

place CD high on the differential for a well-circumscribed retroperitoneal mass. It distinguishes CD from the typically homogeneous but less vascular enhancement of lymphoma and the often heterogeneous, necrotic appearance of sarcomas.[10,13]

A correct pre-operative suspicion can lead to a more targeted biopsy and avoid unnecessary extensive surgery for a benign condition. In our cohort, while this classic enhancement pattern was observed in 92.3% (48/52) of UCD cases, a specific preoperative imaging diagnosis of CD was suspected in only 25.4% (15/59) of all patients. This gap highlights the ongoing diagnostic challenge.[27,29] This is particularly relevant for perirenal masses, where preoperative uncertainty often leans towards suspicion of renal cell carcinoma or sarcoma.[27,30] Indeed, case reports from other centers describe patients with UCD who were misdiagnosed with "renal malignancy" and consequently underwent nephrectomy, with the correct diagnosis only revealed postoperatively on histopathology.[20,21,31] Elevating CD in the differential diagnosis based on this pattern has direct clinical implications: in 5 of the 7 MCD cases, preoperative suspicion successfully guided a core needle biopsy-first strategy, establishing the diagnosis and averting non-curative surgery. For UCD, recognition of this pattern can inform more conservative surgical planning and prompt consideration of preoperative embolization for large, hypervascular masses. Thus, a correct preoperative suspicion optimizes management by steering the approach towards minimally invasive diagnosis for systemic disease (MCD) or tissue-preserving resection for localized disease (UCD).

Our results strongly support complete surgical excision as the definitive and curative treatment for retroperitoneal UCD, yielding a 100% disease-free survival in our series with long-term follow-up. This aligns with global consensus.[12,32] The successful use of minimally invasive techniques in over a quarter of our recent cases highlights its feasibility and advantages for well-localized tumors, offering reduced morbidity and faster recovery. The choice between open and minimally invasive surgery should be based on tumor size, location, and surgeon expertise, with the primary goal being complete resection. The key surgical principle is en-bloc resection with an intact capsule to ensure complete removal and prevent local recurrence.[33] The role of lymph node dissection is limited to sampling for staging and should not be extensive, as CD is not a metastasizing carcinoma.[34]

For MCD, surgery plays a limited but important role, primarily for obtaining adequate tissue for diagnosis (via biopsy) or for debulking a dominant, symptomatic mass. The cornerstone of MCD management is systemic therapy.[35] Our experience reflects the evolution in treatment: from non-specific chemotherapy (CHOP) and corticosteroids to targeted agents. The treatment strategy must be tailored to the patient's symptoms, the severity of the disease, and the presence of specific virus infections like HHV-8.[36] The use of rituximab (anti-CD20) aligns with its established efficacy in HHV-8-negative MCD by targeting B-cell compartments involved in cytokine production.[37] The use of rituximab (anti-CD20) aligns with its established efficacy in HHV-8-negative iMCD (idiopathic MCD) by targeting B-cell compartments involved in pathogenic cytokine production, particularly interleukin-6 (IL-6).[38] The observed response in our patient treated with a rituximab-based regimen supports this approach. Furthermore, siltuximab is the established first-line therapy for idiopathic multicentric Castleman disease (MCD).[37] This recommendation is based on its well-documented efficacy, survival benefit, and long-term safety profile, and is now enshrined in international consensus treatment guidelines.[39] Our study, though not employing siltuximab, underscores the necessity of a hematology-oncology guided, systemic treatment plan for MCD. Patients with MCD should be managed by a specialized team familiar with these newer biologic drugs. The stable disease in our untreated patient under short surveillance is noteworthy but does not contradict the generally progressive nature of MCD; longer follow-up is essential. Some MCD cases may have a slower course, but active monitoring is crucial as the condition can worsen quickly.

Limitations

The strengths of our study include a relatively large, homogeneous cohort from a single institution, detailed clinicopathological correlation, and long-term follow-up data. However, limitations must be acknowledged. The retrospective design inherits its potential selection and information biases. The small number of MCD cases limits robust statistical comparisons and definitive conclusions about this subtype. Our findings on MCD should be seen as descriptive observations rather than firm evidence. As a surgical department series, there is an inherent referral bias towards resectable UCD, potentially underrepresenting complex or medically managed cases. A major limitation of our study is the lack of systematic radiographic follow-up for the

MCD subgroup. While clinical and laboratory data support the effectiveness of the multidisciplinary management approach, the absence of uniform serial imaging precludes a precise radiographic assessment of treatment response and detailed characterization of relapse kinetics. This reflects a common challenge in retrospective studies of rare diseases involving regional referral centers. Future prospective studies should mandate protocol-based imaging surveillance to objectively quantify tumor response and further validate treatment strategies. Importantly, HHV-8 status and serum IL-6 levels were not routinely tested, limiting accurate subtyping and pathophysiological insight into MCD. Future studies should include these tests to better understand the disease biology in each patient.

Future prospective, multi-institutional registries for retroperitoneal CD are warranted. These should incorporate standardized biomarker panels IL-6, VEGF, CRP, viral serologies, and genetic profiling from tissue samples. Such efforts will not only validate our anatomical and clinical observations but also help identify predictive biomarkers for treatment response in MCD and explore the molecular etiology of UCD. Furthermore, comparative studies on the long-term quality of life and cost-effectiveness of minimally invasive versus open resection for UCD would be valuable. Finally, international collaboration is key to gathering enough MCD cases to run meaningful clinical trials and improve care for this rare and complex disease.

Conclusion

In conclusion, Castleman disease of the retroperitoneum exhibits distinct subtype-specific clinical, radiological, therapeutic and prognostic characteristics: UCD is a localized benign lesion with typical and specific CT enhancement features, and complete surgical resection yields an excellent long-term prognosis with no recurrence; MCD is a systemic inflammatory lymphoproliferative disease with non-specific imaging manifestations, requiring multidisciplinary management with systemic therapy as the core and surgery as an auxiliary treatment, and rational systemic therapy can effectively control disease progression and improve clinical outcomes. The characteristic hypervascular CT enhancement pattern of retroperitoneal UCD is an important basis for preoperative non-invasive diagnosis and differential diagnosis, and subtype-based individualized diagnosis and treatment is the key to improving the clinical outcomes of retroperitoneal CD. This study enriches the clinical and radiological data of retroperitoneal CD, and provides a valuable practical reference for the clinical diagnosis, treatment and follow-up of this rare disease.

Acknowledgement

None.

Funding Statement

This study was supported by grants from the Zhejiang Province's Ling-Yan Science and Technology Project (2024C03165).

Author Contributions

The authors confirm contribution to the paper as follows: Conceptualization, Ting Zhu and Junjie Tian; methodology, Ting Zhu; validation, Ting Zhu and Junjie Tian; formal analysis, Chuan Wang and Zhishang Li; investigation, Ting Zhu and Shien Rao; resources, Ting Zhu and Junjie Tian; data curation, Ting Zhu and Junjie Tian; writing—original draft preparation, Ting Zhu; writing—review and editing, Ting Zhu and Junjie Tian; visualization, Yanfeng Bai; supervision, Ping Wang; project administration, Ting Zhu and Junjie Tian; funding acquisition, Ping Wang. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

Not applicable.

Ethics Approval

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). The current study was approved by the ethics committee

of the First Affiliated Hospital, School of Medicine, Zhejiang University, China (Ethical Batch Number: IIT20251050A). Which waived the requirement for individual informed consent due to the retrospective nature of the analysis.

Conflict of Interests

The authors declare no conflict of interest.

Abbreviations

CD	Castleman disease
UCD	Unicentric castleman disease
MCD	Multicentric castleman disease
HV	Hyaline vascular
PC	Plasma cell
IL-6	Interleukin-6
IQR	Interquartile range
CRP	C-reactive Protein
ESR	Erythrocyte Sedimentation Rate
CT	Computed Tomography
HU	Hounsfield Unit
ROI	Regions of Interest
CHOP	C—Cyclophosphamide; H—Doxorubicin; O—Oncovin; P—Prednisone
HHV-8	Human Herpesvirus 8
CD20	Cluster of Differentiation 20
VEGF	Vascular Endothelial Growth Factor

References

1. Pertusa Mataix R, Loaiza Cabello D, García Morillo JS. Castleman's disease, pathophysiology, advances in diagnosis and treatment. *Med Clin* 2024;162(6):283–290. doi:10.1016/j.medcle.2023.10.016.
2. Esteban-Sampedro J, Martín-Portugués M, Campo PD, Fernández-Güitián R, Ruiz-Becerra JE, Moreno-Torres V. Castleman's disease: one disease, multiple etiologies. *AIDS Rev* 2024;26(4):158–172. doi:10.24875/AIDSRev.M25000079.
3. Kolokotroni V, Perlepe G, Cheva A, Foroulis C, Gourgoulianis KI. A 44-year-old man with a solitary, slowly enlarging mediastinal lesion. *Chest* 2025;168(4):e107–e110. doi:10.1016/j.chest.2025.04.037.
4. Patel JP, Patel DP, Amin TH et al. Castleman disease: a rare lymphoproliferative disorder with diverse clinical presentation, diagnosis, and treatment approach. *Cureus* 2024;16(9):e69149. doi:10.7759/cureus.69149.
5. Wang W, Liu Z, Zhao X. Overview of research status in castleman disease. *Clin Lymphoma Myeloma Leuk* 2024;24(10):e359–e365. doi:10.1016/j.clml.2024.05.024.
6. Abo-Alhassan F, Faras F, Bastaki J, Al-Sihan MK. Castleman disease of the parotid gland: a report of a case. *Case Rep Otolaryngol* 2015;2015(8):265187. doi:10.1155/2015/265187.
7. Carbone A, Borok M, Damania B et al. Castleman disease. *Nat Rev Dis Primers* 2021;7(1):84. doi:10.1038/s41572-021-00317-7.
8. Patil MB, Sindgikar VU, Kulkarni S, Biradar D, Siddesh A. Castleman's disease presenting as an unusual pelvic retroperitoneal mass. *Cureus* 2024;16(10):e72196. doi:10.7759/cureus.72196.
9. Zhao Q, Zhang X, Yang X, Huang S. Castleman's disease in the pelvic retroperitoneum: a case report. *Exp Ther Med* 2022;24(5):660. doi:10.3892/etm.2022.11596.
10. Khadga A, Adhikari MB, Maharjan B et al. Unicentric retroperitoneal Castleman's disease in young Nepalese women. *J Surg Case Rep* 2025;2025(2):rjaf086. doi:10.1093/jscr/rjaf086.
11. Jaishanker S, D'Cruze L, Muralidharan S, Gunabooshanam B, Singh KB. A huge retroperitoneal Castleman's disease-rare entity. *J Cancer Res Ther* 2023;19(Suppl 2):S980–S982. doi:10.4103/jcrt.jcrt_61_22.
12. Miratashi Yazdi SA, Nazar E. Retroperitoneal Unicentric Castleman's disease, a case report. *Ann Med Surg* 2022;79:104109. doi:10.1016/j.amsu.2022.104109.
13. Pham KC, Le TM. Retroperitoneal unicentric hyaline vascular variant of Castleman's disease: a case report. *J Surg Case Rep* 2025;2025(7):rjaf543. doi:10.1093/jscr/rjaf543.
14. Feldman S, Mitta A, Lyles L, Enjamuri D, Vega KJ. Unicentric hyaline-vascular castleman disease presenting as a peridуodenal mass: a rare retroperitoneal manifestation. *Cureus* 2025;17(8):e90156. doi:10.7759/cureus.90156.
15. Paladugu SV, Tandup C, Mitra S, Sahu SK. Retroperitoneal unicentric Castleman disease presenting with paraneoplastic pemphigus. *BMJ Case Rep* 2024;17(12):e263134. doi:10.1136/bcr-2024-263134.
16. Tang JQ, Chen HK, Wang X et al. Retrospective analysis of 45 cases of localized retroperitoneal Castleman disease from a single center. *Hepatobiliary Surg Nutr* 2020;9(3):304–311. doi:10.21037/hbsn.2019.05.05.
17. Dieudonné Y, Silvestrini MA, Dossier A et al. Paraneoplastic pemphigus uncovers distinct clinical and biological phenotypes of western unicentric Castleman disease. *Br J Haematol* 2023;202(2):267–278. doi:10.1111/bjh.18847.
18. Hoffmann C, Hentrich M, Tiemann M et al. Recent advances in castleman disease. *Oncol Res Treat* 2022;45(11):693–704. doi:10.1159/000526640.
19. Chen LYC, Zhang L, Fajgenbaum DC. Expert perspective: diagnosis and treatment of castleman disease. *Arthritis Rheumatol* 2025;78(1):12–25. doi:10.1002/art.43269.
20. Vishwajeet V, Kakkar N, Singhal P, Mandal AK. Synchronous retroperitoneal Castleman's disease with clear cell renal cell carcinoma. *BMJ Case Rep* 2019;12(9):e230919. doi:10.1136/bcr-2019-230919.
21. Fu D, Yang B, Yang M et al. Misdiagnosis of renal pelvic unicentric Castleman disease: a case report. *Front Surg* 2023;10:1225890. doi:10.3389/fsurg.2023.1225890.
22. Schulte KM, Sinha P, Talat N, Diaz-Cano S. Retroperitoneal unicentric Castleman's disease with multiple lymph node involvement. *BMJ Case Rep* 2011;2011:bcr0320113938. doi:10.1136/bcr.03.2011.3938.
23. Bucher P, Chassot G, Zufferey G, Ris F, Huber O, Morel P. Surgical management of abdominal and retroperitoneal Castleman's disease. *World J Surg Oncol* 2005;3(1):33. doi:10.1186/1477-7819-3-33.
24. Zhao H, Zhang MY, Shen KN et al. A phase 2 prospective study of bortezomib, cyclophosphamide, and dexamethasone in patients with newly diagnosed iMCD. *Blood* 2023;141(21):2654–2657. doi:10.1182/blood.2023020009.

25. Dong Y, Wang M, Nong L et al. Clinical and laboratory characterization of 114 cases of Castleman disease patients from a single centre: paraneoplastic pemphigus is an unfavourable prognostic factor. *Br J Haematol* 2015;169(6):834–842. doi:10.1111/bjh.13378.
26. Lv GT, Zhao YH, Zhao JL, Zheng ZY, Liu ZJ. Unicentric Castleman disease with paraneoplastic pemphigus in a young woman: a case report. *Front Med* 2025;12:1749601. doi:10.3389/fmed.2025.1749601.
27. Jin C, Deng M, Zhang J, Lu J, Hao Y. Multimodal imaging diagnosis of pancreatic Castleman disease with abdominal and retroperitoneal lymphadenopathy: a case report and literature review. *Front Oncol* 2024;14:1502878. doi:10.3389/fonc.2024.1502878.
28. Chan SJ, Soderquist CR, Berger DM, Kuo EJ. Castleman disease presenting as DOTATATE-positive retroperitoneal mass. *BMJ Case Rep* 2025;18(2):e261970. doi:10.1136/bcr-2024-261970.
29. Cao Y, Shi E, Ye J et al. Different imaging features of retroperitoneal unicentric castleman's disease: a case report. *Case Rep Oncol* 2020;13(1):468–473. doi:10.1159/000507111.
30. Yazdi NA, MomeniAmjadi A, Kermanipour RG, Alizadeh S, Salahshour F, Tahamtan M. Castleman disease mimicking accessory spleen on imaging: a case report. *Radiol Case Rep* 2025;20(1):651–656. doi:10.1016/j.radcr.2024.09.143.
31. Hoshi A, Nitta M, Tokunaga M et al. Castleman's disease in the pararenal retroperitoneal space, which is indistinguishable from renal cell carcinoma: a case report. *Hinyokika Kiyo* 2007;53(1):43–48. doi:10.3126/jpn.v3i6.9004.
32. Kitakaze M, Miyoshi N, Fujino S et al. Surgical resection for pelvic retroperitoneal Castleman's disease: a case report and review literature. *Biomed Rep* 2021;14(3):29. doi:10.3892/br.2021.1405.
33. Sawaya Z, Semaan DB, Nicolas G, Dib A, Tayar C. Unicentric castleman's disease: laparoscopic approach of a paraduodenal retroperitoneal mass. *Am J Case Rep* 2020;21:e918444. doi:10.12659/ajcr.918444.
34. Jhan JH, Li CC, Wu WJ, Lee HY. Isolated retroperitoneal Castleman's disease: a case report and literature review. *Clin Case Rep* 2018;6(8):1543–1548. doi:10.1002/ccr3.1654.
35. Lang E, van Rhee F. Idiopathic multicentric Castleman disease: an update in diagnosis and treatment advances. *Blood Rev* 2024;64(1):101161. doi:10.1016/j.blre.2023.101161.
36. van Rhee F, Voorhees P, Dispenzieri A et al. International, evidence-based consensus treatment guidelines for idiopathic multicentric Castleman disease. *Blood* 2018;132(20):2115–2124. doi:10.1182/blood-2018-07-862334.
37. Pierson SK, Lim MS, Srkalovic G et al. Treatment consistent with idiopathic multicentric Castleman disease guidelines is associated with improved outcomes. *Blood Adv* 2023;7(21):6652–6664. doi:10.1182/bloodadvances.2023010745.
38. Ismayilov R, Cinar OE, Ozdede M et al. Coexistence of HHV-8-associated plasmacytic multicentric castleman disease, kaposi's sarcoma, and multiple myeloma in a HIV-negative patient. *Eur J Case Rep Intern Med* 2024;11(10):004876. doi:10.12890/2024_004876.
39. Fajgenbaum DC, Wu D, Goodman A et al. Insufficient evidence exists to use histopathologic subtype to guide treatment of idiopathic multicentric Castleman disease. *Am J Hematol* 2020;95(12):1553–1561. doi:10.1002/ajh.25992.

