The clinical picture of Castleman disease: a systematic review and meta-analysis of almost 2000 patients

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Aggressive Lymphomas: Clinical and Epidemiological

Introduction

Castleman disease (CD) encompasses a spectrum of rare disorders with characteristic histopathological features, including unicentric (UCD), idiopathic multicentric (iMCD), and cases associated with human herpesvirus 8 (HHV8+ MCD)[1]

As treatment options for each type of CD vary,[1] it is important to be able to distinguish their clinical presentation and determine the correct diagnosis

To our knowledge, there are no major review articles summarizing the clinical features of different CD subtypes

The aim of this study was to describe and compare the clinical presentation of CD subtypes reported in the literature

Methods

We performed a systematic review of publications reporting ≥5 cases of CD between 1995 and 2021

Publications were cross-checked by study location, data collection period, and investigators to identify and exclude duplicated patients

For each subtype of CD within each study, we extracted data on demographics, clinical symptoms, and laboratory parameters, as stated in the international consensus diagnostic criteria for iMCD[2]

We estimated the mean percentage of patients meeting each diagnostic criterion for each CD subtype using meta-analyses conducted with random effects logistic regression models

32 studies from 16 countries	UCD n=559	iMCD n=1023	HHV8+ MCD n=416
Male (%)	46.3	59.1	88.5
Average mean age (years)	33.6	47.4	42.8
Ethnicity (n,%)			
African/ African American/ Black	17 (3.7)	10 (1.1)	106 (42.1)
Asian	387 (84.7)	835 (91.8)	4 (1.6)
White	52 (11.4)	58 (6.4)	130 (51.6)
Others	1 (0.22)	7 (0.8)	12 (4.8)
Not reported	102	113	164

- Predominance of males in HHV8+ MCD and iMCD
- UCD patients tended to be younger than iMCD and HHV8+ MCD patients
- Most UCD and iMCD patients were Asian. Few Asian HHV8+ MCD patients

Pediatric UCD patients had more signs of systemic inflammation compared with adult UCD patients

Five publications with 88 pediatric UCD cases

Elevated C-reactive protein was reported in 45.1% of pediatric UCD patients (95% CI 20.9–71.8, n=50 vs. 19.7% of adults [95% CI 11.2–30.9])

Constitutional symptoms were reported in 44.4% of patients (95% CI 21.5–69.2, n=18)—significantly higher than the rate in adult patients with UCD (4.5%, 95% CI 1.6–12.3; p=0.0005)

Results

Average percentage (95% CI) of lab findings and symptoms in patients with UCD, iMCD, or HHV8+ MCD, identified using a random effects meta-analysis

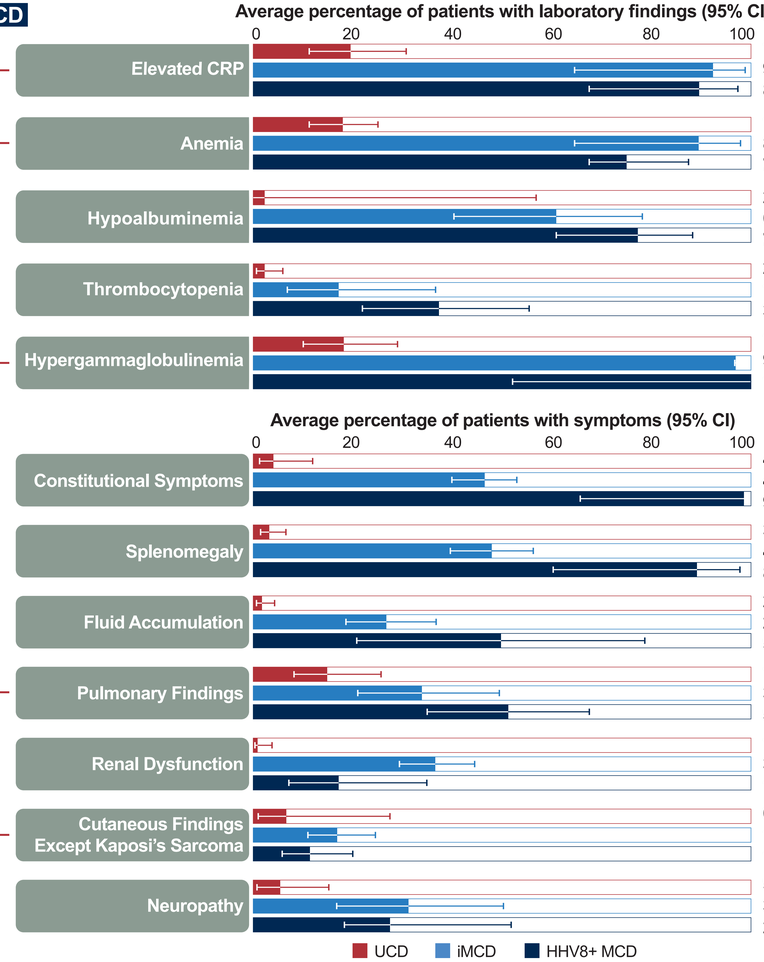
UCD vs. **iMCD** and **HHV8+ MCD**

Patients with UCD had **significantly lower rates of lab abnormalities** vs. those with iMCD and HHV8+ MCD

Elevated CRP, anemia, and hypergammaglobulinemia occurred in almost 20% of patients with UCD

Pulmonary findings were observed in 15.3% of UCD cases

Except for **cutaneous findings**, patients with UCD had **significantly lower rates of symptoms** vs. those with either iMCD or HHV8+ MCD



iMCD vs. **HHV8+ MCD**

Many symptoms and lab abnormalities occurred at similar rates in patients with iMCD and HHV8+ MCD

No significant differences in lab findings between patients with iMCD and HHV8+ MCD

Patients with iMCD had **significantly lower rates of constitutional symptoms and splenomegaly** vs. those with HHV8+ MCD

Renal dysfunction appeared more commonly in patients with iMCD than those with HHV8+ MCD (not significantly different)

n indicates number of patients with available data; * p<0.05; † Hypergammaglobulinemia was only reported in one HHV8+ MCD study. CI=confidence interval; CRP=C-reactive protein; HHV8+ MCD=multicentric Castleman disease associated with human herpesvirus 8; iMCD=idiopathic multicentric Castleman disease; ns=not significant; UCD=unicentric Castleman disease

Conclusions

We **found several distinct differences between iMCD and HHV8+ MCD**, which may reflect heterogeneity in underlying pathophysiology and/or different comorbidity burdens of these CD subtypes

We confirmed that **systemic symptoms may be present in up to 20% of patients with UCD**. Whether these cases represent a distinct entity and if intermediate CD cases require systemic therapy beyond surgery remains to be elucidated

References

1. Oksenhendler E, Boutboul D, Fajgenbaum D, *et al*. Br J Haematol 2018; 180: 206–16

2. Fajgenbaum DC, Uldrick TS, Bagg A, *et al*. Blood 2017; 129: 1646–57

Acknowledgments, Disclosures and Contact

Acknowledgements: Poster funded by Recordati and medical writing assistance was provided by TVF Communications

Disclosures: K. Kanhai is an employee of Recordati. C. Hoffmann has received research funding and honoraria from Janssen-Cilag, EUSA Pharma, Gilead Sciences, MSD and ViiV Healthcare

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