Increased comorbidities and hospitalizations associated with idiopathic multicentric Castleman disease

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Introduction

- Castleman disease (CD) describes a group of disorders that share characteristic lymph node histopathology with heterogeneous symptoms
- Unicentric Castleman disease (UCD) involves a solitary region of enlarged lymph nodes (LNs), localized mild symptoms, and is typically curable with surgical excision
- Multicentric Castleman disease (MCD), however, involves multiple regions of enlarged LNs, systemic inflammation, cytopenias, and in some cases life-threatening multiorgan dysfunction
- HHV8-negative/idiopathic multicentric Castleman disease (iMCD), is difficult to diagnose and presents with multiple phenotypes, including the most severe, TAFRO (**T**hrombocytopenia, **A**nasarca, **F**ever, **R**eticulin Fibrosis, **O**rganomegaly) phenotype
- Although siltuximab is the only FDA/EMA-approved therapy for iMCD, many patients do not ever receive siltuximab and a subset do not respond
- We sought to elucidate the burden of iMCD following diagnosis by interrogating real world comorbidity and hospitalization data

Methods

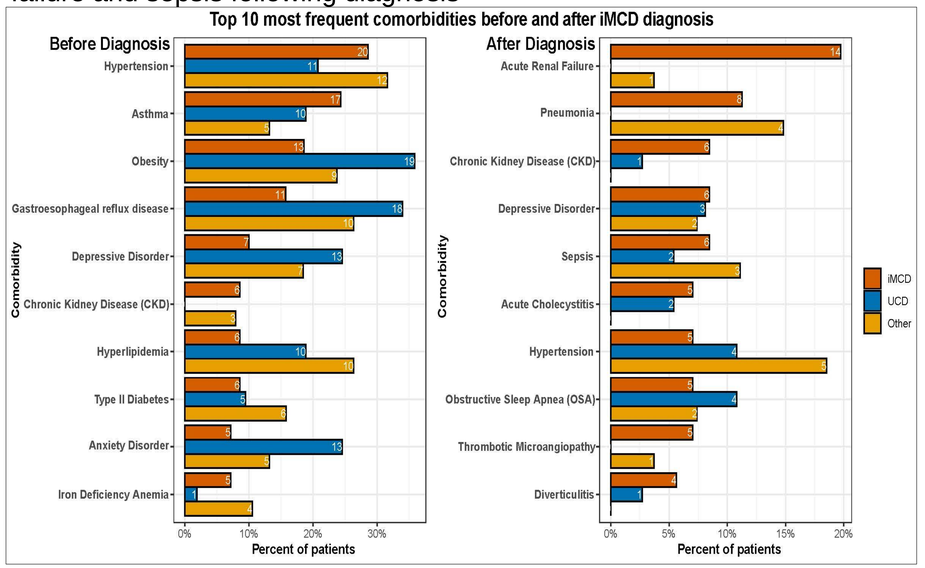
- 193 patients from the ACCELERATE Natural History registry (NCT02817997) with pathology reports suggestive of CD were identified
- All 193 patients were reviewed case-by-case by a panel of expert CD physicians to confirm or reject a CD diagnosis
- After review, 85 patients were categorized as iMCD-with 49 (58%) being iMCD-TAFRO
- Statistical analyses were performed between groups on both comorbidity and hospitalization data

Results

Table 1. Cohort Breakdown

Group	Definition	N	Demographics	
iMCD	Panel-reviewed and confirmed as iMCD	85	Age, Mean (SD) :	36 (16)
			Female:	48%
			Male :	51%
			TAFRO :	49 (58%)
UCD	Panel-reviewed and confirmed as UCD	65	Age, Mean (SD) :	35 (20)
			Female:	74%
			Male:	26%
Other	Demonstrated iMCD-like features, but expert panel review determined another unspecified disease to be more likely	43	Age, Mean (SD) :	41 (9)
			Female :	61%
			Male :	38%
			Other :	2%

Figure 1. iMCD patients demonstrate common comorbidities prior to diagnosis but develop life-threatening comorbidities such as acute renal failure and sepsis following diagnosis



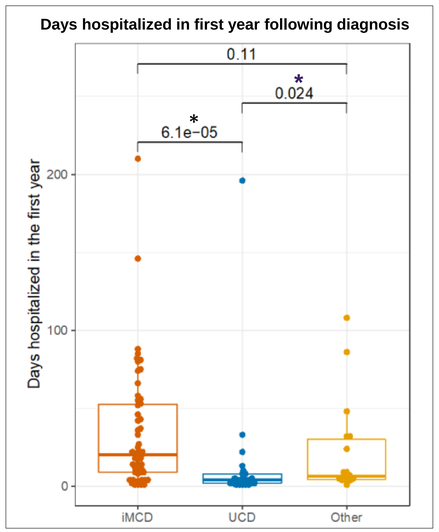


Figure 2. iMCD patients spent a significantly greater amount of time hospitalized in the first year following diagnosis compared to UCD (mean 34.3 days vs. 14.0 days), but not to 'Other' patients with an iMCD-like reactive process (mean 22.0 days)

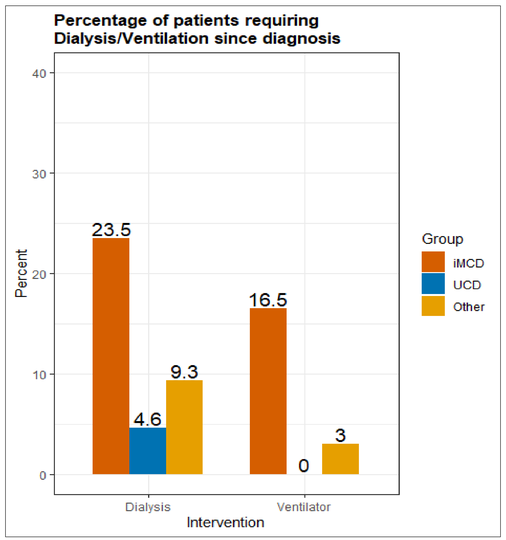


Figure 3. iMCD patients require more supportive interventions such as dialysis and mechanical ventilation compared to both UCD patients and 'Other' patients with an iMCD-like reactive process

Summary and Discussion

- iMCD patients face a significant disease burden, even years after a diagnosis is rendered and treatment is initiated
- Hospitalization and costly interventions, such as dialysis and extended mechanical ventilation, are required in iMCD
- iMCD patients demonstrate relatively common comorbidities prior to diagnosis, but develop life threatening conditions such as acute renal failure and sepsis
- The high proportion of TAFRO patients may skew our data due to its severity
- This data highlights the importance of continuing research into iMCD in order to better control the burden of disease and improve outcomes and prognosis for this severely ill group of patients

Future Directions

- We will further examine the long-term burden of iMCD by examining real world flare vs. remission data
- We will describe healthcare utilization in iMCD patients by analyzing concomitant medications, frequencies of radiological scans, and frequencies of procedures commonly required in iMCD such as transfusions and thoracentesis

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