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 (Thrombocytopenia, Anasarc, Fever, Reticulin Fibrosis, Organomegaly) 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

Table 1. Cohort Breakdown

<table>
<thead>
<tr>
<th>Group</th>
<th>Definition</th>
<th>N</th>
<th>Demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>iMCD</td>
<td>Panel-reviewed and confirmed as iMCD</td>
<td>85</td>
<td>Age, Mean (SD): 36 (16)</td>
</tr>
<tr>
<td>UCD</td>
<td>Panel-reviewed and confirmed as UCD</td>
<td>65</td>
<td>Age, Mean (SD): 35 (20)</td>
</tr>
<tr>
<td>Other</td>
<td>Demonstrated iMCD-like features, but expert panel review determined another unspecified disease to be more likely</td>
<td>43</td>
<td>Age, Mean (SD): 41 (9)</td>
</tr>
</tbody>
</table>

Results

- iMCD patients demonstrate common comorbidities prior to diagnosis but develop life-threatening comorbidities such as acute renal failure and sepsis following diagnosis
- ▪ We will describe healthcare utilization in patients who receive siltuximab and those who do not.

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 1](image1.png)

Figure 2. Days hospitalized in first year following diagnosis

![Figure 2](image2.png)

Figure 3. Percentage of patients requiring Dialysis/Intervention since diagnosis

![Figure 3](image3.png)

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
- We will conduct a large-scale, multi-center, randomized controlled trial to evaluate the efficacy and safety of siltuximab in iMCD patients

Contact

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Table 2. Comorbidities and hospitalizations among iMCD patients

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Kidney Disease</td>
<td>45</td>
<td>54%</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>30</td>
<td>36%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>20</td>
<td>24%</td>
</tr>
<tr>
<td>Acute Renal Failure</td>
<td>15</td>
<td>18%</td>
</tr>
</tbody>
</table>

Figure 4. Percentage of patients requiring Dialysis/Intervention since diagnosis

![Figure 4](image4.png)