Utility of Class-Switched B-Cells in Diagnosing
Common Variable Immunodeficiency

Olivia Starich1, Jared Rieck2, Wyatt Tarter, MS, Vijaya Knight, MD, PhD3,4, and Jordan K. Abbott, MD, MA3,4
1University of Colorado School of Medicine, Aurora CO; 2Colorado School of Public Health, Department of Biostatistics and Informatics, Aurora CO; 3University of Colorado School of Medicine, Department of Pediatrics, Aurora CO; 4Children’s Hospital Colorado, Aurora CO

Background

• Relative quantities of class-switched CD27+IgD− B-cells (CSBs) in peripheral blood have been proposed as useful in subclassification of Common Variable Immunodeficiency (CVID).1

• Additional studies have shown lower numbers of CSBs in CVID than in IgG deficiency, supporting the notion that CSBs may be a useful marker in making a diagnosis of CVID.2

• Neither the specific diagnostic utility of CSBs nor their application in additional cohorts have been studied to support the widespread practice among clinicians of using CSBs to form or support a CVID diagnosis.3

• This study aimed to determine whether low peripheral CSBs accurately differentiate CVID from other forms of humoral immunodeficiency.

Methods

• Chart review of all patients with comprehensive B-cell panel results from Children’s Hospital of Colorado in 2020.

• Criteria: age ≥ 5 years, absolute CD19 B-cell measurement within 60 days without daratumumab or rituximab use in the 12 months preceding the panel.

• Of the patients included (n=64): 3 met ICON criteria for CVID; 10 diagnosed by expert opinion; 24 with non-CVID immunological defect.

• Linear and Tobit regressions were performed to model the relationships between IgG or IgA and class-switched B-cell count (p<0.5).

• Multinomial logistic regression accounting for age and sex was performed to model the relationship of CVID diagnosis with class-switched B-cell count (p<0.05).

Results

Minimum IgA vs. CD27 Switched

Minimum IgG vs. CD27 Switched

Figure 1: Tobit regression shows statistically significant relationship between in-vivo IgA levels and CD27+IgD- class-switched B-cell levels (p<0.05).

Figure 2: Linear regression shows statistically significant relationship between in-vivo IgG levels and CD27+IgD- class-switched B-cell levels (p<0.05).

Table 1: Multinomial logistic regression accounting for age and sex demonstrated no significant association between absolute or percent CSB levels and whether the patient had a known or suspected CVID diagnosis.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Possible CVID Dx</th>
<th>Existing CVID Dx</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR1</td>
<td>95% CI1</td>
</tr>
<tr>
<td>Absolute CD27 Switched</td>
<td>1.00</td>
<td>0.96, 1.05</td>
</tr>
<tr>
<td>Female</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Male</td>
<td>3.14</td>
<td>0.59, 16.9</td>
</tr>
<tr>
<td>% CD27 Switched</td>
<td>1.00</td>
<td>0.95, 1.05</td>
</tr>
<tr>
<td>Female</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Male</td>
<td>3.04</td>
<td>0.57, 16.4</td>
</tr>
</tbody>
</table>

Table 2: Binary logistic regression indicated the odds of having any humoral immunodeficiency, including CVID, increased with decreasing CSB percentage (p<0.05).

Conclusions

• There is no significant association between absolute or percent CSB levels and whether the patient had a known or suspected CVID diagnosis (Table 1).

• The odds of having any humoral immunodeficiency, including CVID, increased with decreasing CSB percentage (Table 2).

• Despite a small sample, there is a statistically significant relationship between CSBs and in vivo serum IgA and IgG levels.

• This supports use of peripheral CD27+IgD-CSBs as an indicator of a general ability to class-switch to IgG or IgA production, which had previously remained unproven (Figure 1 & 2).

Ultimately these findings suggest that CSBs may serve as a general indicator of humoral immune disruption but are not adequately specific in forming a CVID diagnosis.

References

1. Warnatz K et al. Severe deficiency of switched memory B cells (CD27+IgM−IgD−) in subgroups of patients with common variable immunodeficiency: a new approach to classify a heterogeneous disease. Blood. March 1 2002;99(5).


Disclosures

There are no financial disclosures or conflicts of interest to report.