TITLE: Class-Switched B-Cells Lack Specificity for Diagnosing Common Variable Immunodeficiency

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ABSTRACT:

Measuring the relative quantity of peripheral blood class-switched CD27+IgD- B-cells (CSBs) has previously been proposed as useful in the subclassification of CVID diagnoses. Perhaps incautiously, this practice has been adopted widely among clinical immunologists and has even been included as supportive diagnostic criteria for CVID. Existing research has also shown lower numbers of CSBs in CVID than in IgG deficiency; however, the diagnostic utility of CSBs was not evaluated and additional cohorts have not been studied. This study aimed to determine if low peripheral blood CSB numbers accurately differentiate CVID from other forms of humoral immunodeficiency.

We performed a retrospective chart review of all patients at Children's Hospital of Colorado with 8-marker comprehensive B-cell panel results from the time of the panel's implementation in 2020. Inclusion criteria included: age ≥5 years and absolute CD19 B-cell measurement within 60 days of B-cell panel results. Subjects were assigned a diagnosis of CVID based on ICON criteria and by expert opinion when the workup was incomplete, such as in cases with borderline serum immunoglobulin levels or where polysaccharide antibody responses were not available. Patients that did not meet CVID criteria but were considered to have a humoral immunodeficiency based on immunoglobulin levels were separately categorized. Of the patients included (n=64), 3 met all ICON criteria, 10 had a diagnosis by expert opinion, and 24 had a non-CVID immunological defect. 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; however, binary logistic regression indicated the odds of having any humoral immunodeficiency, including CVID, increased with decreasing CSB percentage (p=0.026). Additionally, a linear regression between percent CSBs and in vivo serum IgG levels found a statistically significant relationship (p=0.046), which has not been demonstrated previously. This observation is consistent with peripheral blood CD27+IgD- CSBs reflecting a person's general ability to class-switch to IgG production. Ultimately these findings suggest that CSBs may have utility as a general indicator of humoral immune disruption but are not an adequately specific metric in forming a CVID diagnosis.

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