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

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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

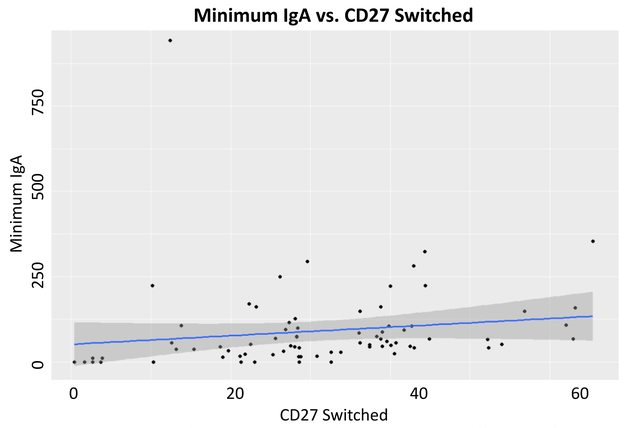

Figure 1: *Tobit regression shows statistically significant relationship between in-vivo IgA levels and CD27+IgD- class-switched B-cell levels ($p<0.05$).*

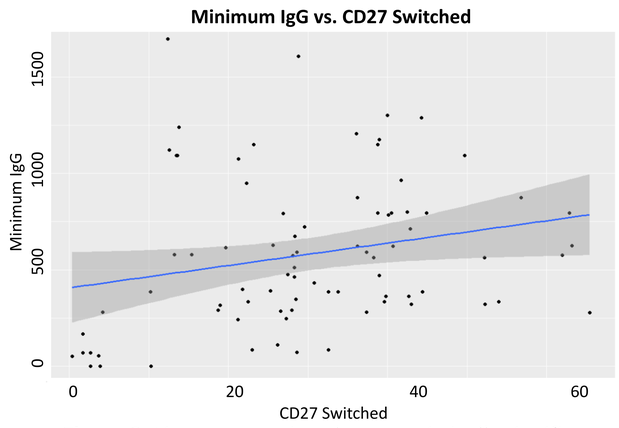

Figure 2: *Linear regression shows statistically significant relationship between in-vivo IgG levels and CD27+IgD- class-switched B-cell levels ($p<0.05$).*

Characteristic	Possible CVID Dx			Existing CVID Dx		
	OR[1]	95% CI[1]	p-value	OR[1]	95% CI[1]	p-value
Absolute CD27 Switched	1.00	0.96, 1.05	0.8	0.95	0.84, 1.06	0.4
Female	—	—		—	—	
Male	3.14	0.59, 16.9	0.2	1.08	0.14, 8.45	>0.9
% CD27 Switched	1.00	0.95, 1.05	>0.9	0.97	0.91, 1.04	0.4
Female	—	—		—	—	
Male	3.04	0.57, 16.4	0.2	0.96	0.13, 7.30	>0.9

[1] OR = Odds Ratio, CI = Confidence Interval

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.*

	Immunodeficiency – Absolute CD27			Immunodeficiency – % CD27		
Predictors	Odds Ratios	CI	p	Odds Ratios	CI	p
(Intercept)	1.11	0.50 – 2.49	0.801	2.15	0.68 – 7.43	0.202
CD27 Switched	0.97	0.94 – 1.00	**0.073**	0.96	0.93 – 0.99	**0.026**
Sex [Male]	2.28	0.92 – 5.78	0.077	2.10	0.84 – 5.37	0.116
Observations	81			81		
R^2 Tjur	0.088			0.109		

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

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Disclosures

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

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