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Hypogammaglobulinemia in Pediatric Systemic Lupus Erythematosus

Emilina Lim¹, Yu Tao², Andrew J. White¹, Anthony R. French¹, and Megan A. Cooper¹

¹Washington University School of Medicine, Departments of Pediatrics, Division of Rheumatology, St. Louis, MO 63110

²Division of Biostatistics, St. Louis, MO 63110

Abstract

Objective—Systemic lupus erythematosus (SLE) is a systemic autoimmune disease typically associated with elevated serum immunoglobulin G (IgG). Hypogammaglobulinemia in SLE patients has been attributed to immunosuppressive treatment or a transient effect associated with nephrotic syndrome. We retrospectively reviewed pediatric SLE patients from a single institution to identify patients with hypogammaglobulinemia and risk factors for hypogammaglobulinemia.

Methods—116 pediatric SLE cases from 1997–2011 were reviewed and patients with hypogammaglobulinemia (IgG <500 mg/dL) were identified. The two cohorts were evaluated for association with age, sex, presence of lupus nephritis at SLE diagnosis, disease activity at diagnosis, initial IgG level, and drug treatment.

Results—Eighty-six patients were included in our study, with a median age of 15 years and a median follow-up of 39.5 months. Seven percent (6/86) of patients had hypogammaglobulinemia with a median onset of 27 months (0–72 months) after SLE diagnosis. Significant associations were noted for white race (p-value 0.029), male sex (p-value 0.009), and the presence of lupus nephritis at SLE diagnosis (p-value of 0.004). Use of immunosuppressive treatment did not show a statistical association with hypogammaglobulinemia, although 2 of the patients with hypogammaglobulinemia did receive rituximab. Most patients with hypogammaglobulinemia received intravenous immunoglobulin (IVIG) replacement therapy due to infections and/or concern for infection.

Conclusion—Measurement of immunoglobulin levels during treatment in SLE could help identify patients with hypogammaglobulinemia that might require more aggressive follow-up to monitor for increased risk of infection and need of IVIG treatment. A prospective study is needed to validate associated risk factors identified in this study.

Key Terms

Systemic Lupus Erythematosus; Pediatrics; Hypogammaglobulinemia

Corresponding author: Dr. Megan A. Cooper, Department of Pediatrics, Washington University, 660 S. Euclid Ave, Box 8208, St. Louis, MO 63110. Phone: 314-454-6124, Fax: 314-454-4861, cooper_m@kids.wustl.edu.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Introduction

Systemic lupus erythematosus (SLE) is characterized by immune cell activation, including T and B cells, with elevated serum IgG and prominent circulating immune complexes in multiple organs, including the skin, heart, lungs, kidneys and joints.¹ SLE predominantly affects women of reproductive age, with a F:M prevalence ratio of 9:1, and approximately 15–20% of SLE patients are diagnosed prior to 16 years of age.^{1–5} Studies using standardized disease measures comparing cohorts of adult and pediatric patients with SLE suggest that children have more active disease at diagnosis and acquire more permanent organ damage compared to adults.^{2, 4}

Patients with SLE frequently have polyclonal immune activation with elevated total IgG and specific antibodies directed against nuclear antigens, including anti-dsDNA and anti-Sm antibodies.⁶ While rare, hypogammaglobulinemia has been described in SLE.^{6, 7} Patients with SLE and other autoimmune diseases typically receive immunosuppressive medications, and it is challenging to balance appropriate treatment while minimizing the risk of opportunistic and serious infections.⁸ The goal of this study is to review pediatric SLE patients from our institution to delineate the frequency of, and risk factors for, hypogammaglobulinemia with SLE. We compared clinical and laboratory findings of pediatric SLE patients with and without hypogammaglobulinemia. We did not find a significant association between hypogammaglobulinemia and medication usage or disease activity, however we did discover associations with male sex, white race, and the presence of lupus nephritis at diagnosis of SLE.

METHODS

We retrospectively reviewed records of patients with a diagnosis of SLE (ICD-9 code 710.0) seen in our Pediatric Rheumatology clinic at Washington University from 1997–2011. All patients fulfilled at least 4 of the 1997 American College of Rheumatology (ACR) classification criteria for SLE.⁹ To evaluate for hypogammaglobulinemia, inclusion criteria included having an evaluable IgG level within 3 months of diagnosis and two or more IgG levels during follow-up. Patients with insufficient data for SLEDAI scoring at diagnosis or presence of known immunodeficiency states were excluded. Clinical and laboratory characteristics including a disease activity score (SLEDAI) were determined at the time of SLE diagnosis for all patients. We determined whether SLE patients ever had hypogammaglobulinemia, defined as an IgG level of <500 mg/dL (2 standard deviations below mean for age 4 years to adulthood).^{10, 11} For patients with hypogammaglobulinemia, their clinical course and SLEDAI scores were also determined at the time of detection of low IgG. Charts of patients with hypogammaglobulinemia were also further reviewed for symptoms related to infection, immunoglobulin levels, and vaccine response. Comparisons of categorical variables were made using Chi-square or Fisher's exact tests as appropriate. Comparisons of continuous and ordinal variables were made using the Wilcoxon-Mann-Whitney test due to the non-normal distribution of these variables. Tests were two-tailed and $p < 0.05$ was considered significant. All statistical analyses were performed using SAS 9.2 (SAS Institute Inc., Cary NC USA). This research was conducted in accordance with the

guidelines for research studies from the Human Resources Research Protection Office at Washington University.

Results

Patient characteristics

116 SLE patients were treated in our Pediatric Rheumatology clinic from 1997–2011. A total of 86 patients fulfilled our inclusion and exclusion criteria with a median age of 15 years and a mean follow-up of 39.5 months. Half of the patients were African Americans (43/86), most were females (78/86, 91%), and 42% (36/86) had lupus nephritis at diagnosis of SLE (Tables 1 and 2). There were 6 pediatric patients with SLE who had hypogammaglobulinemia (Table 1). There was no difference in the age or SLEDAI scores of the two cohorts at presentation. The mean IgG level for all patients at diagnosis was 1,812 mg/dL (range of 170–5860 mg/dL), consistent with prior observations that most SLE patients have hypergammaglobulinemia.^{12, 13}

Factors associated with hypogammaglobulinemia

To determine whether medications affected patient's IgG level, we compared medication usage in the two groups (Table 1). All patients received prednisone at some point during their clinical course. There was no statistically significant difference in the use of cyclophosphamide, rituximab, or mycophenolate mofetil (MMF) between the two groups (Table 1). Two patients with hypogammaglobulinemia received B cell depleting therapy with rituximab prior to development of hypogammaglobulinemia (indicated on Table 3). 12.5% of patients without hypogammaglobulinemia also received rituximab, which while lower, was not statistically different (Table 1). There was a significant association with hypogammaglobulinemia and male sex ($p=0.009$), lupus nephritis at diagnosis of SLE ($p=0.004$), and white race ($p=0.029$) (Tables 1 and 2). Indeed, all patients with hypogammaglobulinemia had nephritis at SLE diagnosis. Interestingly, while males comprised a minority of patients with SLE (9.3%, 8 of 86), 50% (3/6) of SLE patients with hypogammaglobulinemia were white males, and 37.5% (3/8) of all male patients had hypogammaglobulinemia.

Lupus nephritis and hypogammaglobulinemia

We then evaluated the course of patients with hypogammaglobulinemia, with particular attention to lupus nephritis. All six patients with hypogammaglobulinemia had kidney involvement at presentation (Table 4). The onset of decreased IgG ranged from 0–72 months after diagnosis of SLE and lupus nephritis, with a median onset of 27 months. Two patients had IgG levels less than 500 mg/dL within three months of SLE diagnosis, suggesting that their hypogammaglobulinemia preceded or coincided with the onset of SLE. Hypogammaglobulinemia patients had different types of lupus nephritis (Table 4), including type II, II/III, IV, and V (based on WHO 1982 Lupus Nephritis Classification). At the time of diagnosis of hypogammaglobulinemia, most patients had dsDNA antibodies, indicative of active disease¹⁴. Serum complements (C3 and/or C4) were low in 4/6 patients at the time of low IgG. All of the patients had elevated urine protein:creatinine ratio (>0.2) at the time hypogammaglobulinemia was first observed, suggestive of urinary protein loss as a potential

mechanism of hypogammaglobulinemia. However, only 3/6 patients had nephrotic-range proteinuria (ratio >3.5), and only 2/6 patients had concomitant low serum albumin, indicating that urinary protein losses alone could not account for hypogammaglobulinemia in all patients.

Treatment and course of patients with hypogammaglobulinemia

Most patients (4/6) with hypogammaglobulinemia received IVIG replacement therapy, 400 mg/kg every 4 weeks (Table 5). The decision to treat with IVIG was based on immunoglobulin levels, infection history, and/or response to vaccination, in addition to infection risk due to immunosuppressive therapy for their SLE (Table 5). Antibody responses to vaccination, including *Tetanus*, *Haemophilus influenza* type B (Hib), and/or *S. pneumoniae*, were measured in 5 patients prior to initiation of IVIG (Table 5). The patients who did not receive IVIG (Pt. 1 & 5) did not have infections and had improvement of IgG levels to >500 mg/dL after 2–5 months of immunosuppressive treatment for their SLE. Patient #2 had recurrent sinusitis and poor response to boosting with a non-conjugated *S. pneumonia* vaccine. He was started on IVIG therapy, and has continued to receive subcutaneous immunoglobulin replacement 16 months after detection of hypogammaglobulinemia. Patient #3 had recurrent infections with low IgM and IgA levels and non-protective titers to *S. pneumoniae* and Hib. She received two courses of rituximab which may have contributed to her hypogammaglobulinemia. She has continued on IgG replacement for >30 months. Patient #4 also had a history of rituximab treatment and started IVIG due to persistence of clinical pneumonia that did not improve with IV antibiotics. Patient #6 was started on IVIG due to very low IgG (65 mg/dL) and concern for an increased risk of infection. Patients #4 and #6 had normalization of their IgG and were able to stop IVIG after 2 months (Pt. 4) and 4 months (Pt. 6).

Discussion

Herein, we describe risk factors for development of hypogammaglobulinemia in our cohort of pediatric SLE patients. While infrequent, we observed hypogammaglobulinemia in 6.9% (6/86) of pediatric patients. Strikingly, 50% of patients with hypogammaglobulinemia were white males, even though males only constituted 9.3% (8/86) of all patients. In addition to male sex and white race, the presence of nephritis at SLE diagnosis also correlated with hypogammaglobulinemia. However, there was no statistically significant correlation between medication usage, including rituximab, and hypogammaglobulinemia, suggesting that prospective investigation of this in a larger study is warranted.

Various forms of antibody deficiencies, both congenital and acquired, have been described in patients with SLE, including: 1) selective IgA deficiency, 2) common variable immunodeficiency (CVID), 3) drug induced hypogammaglobulinemia, 4) selective IgM deficiency, and 5) hypogammaglobulinemia secondary to nephrotic syndrome.^{6, 15} Selective IgA deficiency is also the most common antibody deficiency reported in SLE, and is also the most common primary immunodeficiency disorder in the general population, with an incidence of approximately one in 600 in western countries.¹⁶ Previous studies have suggested a possible link between selective IgA deficiency and autoimmunity.¹⁷

Interestingly, the frequency of IgA deficiency in SLE patients has been reported as higher than the general population, and was seen in approximately 2–5% of adult and 5% of pediatric SLE patients.^{15, 18, 19} Patients with SLE and IgA deficiency do not appear to have more severe disease than SLE patients with normal IgA levels.^{18, 19} In the current study, half of patients who developed hypogammaglobulinemia had concomitantly decreased IgA levels. In two of these patients (Pt. 1 & 6), their low/absent IgA persisted despite resolution of their hypogammaglobulinemia. The third patient (Pt. 3) continues to have hypogammaglobulinemia and undetectable IgA. IgA levels in patients presented here without hypogammaglobulinemia are not known, however the presence of IgA deficiency in 50% (3/6) of hypogammaglobulinemia patients here, compared to historical estimates of 5% in pediatric SLE patients, suggests that it may be worth evaluating prospectively whether IgA deficiency in SLE is also a risk factor for hypogammaglobulinemia.

Secondary factors have previously been attributed to a decrease in IgG levels in SLE patients including nephrotic-range proteinuria and immunosuppressive treatment.^{6, 7} Cronin et. al reported 18 adult SLE patients who developed low IgG with a median onset of 4 years following their original SLE diagnosis.²⁰ Hypogammaglobulinemia was transient in 10 patients, while 4 developed recurrent infections. While all patients continued to have significant lupus activity, they did not find a correlation with presence of low IgG levels and the amount of protein excreted in the urine.²⁰ All of the patients with hypogammaglobulinemia presented here had lupus nephritis at presentation (Class II–V), and there was a significant correlation between lupus nephritis at diagnosis and development of hypogammaglobulinemia. However, only two patients had nephrotic-range proteinuria with decreased albumin, suggesting that similar to the findings by Cronin et al, urinary losses might not account for hypogammaglobulinemia in all patients.

Immunosuppressive treatment, such as B cell depleting therapy with rituximab has been reported to cause prolonged (>6 months) hypogammaglobulinemia in children with autoimmune hemolytic anemia.²¹ Cyclophosphamide (CYC) use in adults with ANCA-associated vasculitis caused a decrease in IgG values (median value of 12.8 g/L to 9.17 g/L), at 14.5 and 30 months.²² Further IgG decline (7.11 g/L) was observed in patients who received rituximab after having previously received CYC.²² Two of the 6 patients with hypogammaglobulinemia presented here received rituximab, and both initially had elevated IgG (4,080 and 1,600 mg/dl), suggesting that rituximab may have played a role in their hypogammaglobulinemia. One of these patients has required >30 months of IVIG replacement (Pt. 3), while the second had transient hypogammaglobulinemia, which would be more consistent with rituximab, and only required a short (2 months) course of IVIG.

The diagnosis and treatment of an autoimmune disease with an underlying immune deficiency can be challenging, and there is overlap in these disease processes. For example, SLE and CVID both involve dysregulation of T and B cells, and patients with CVID frequently have autoimmune manifestations.^{6, 7} However, while hypergammaglobulinemia is a frequent finding in SLE, CVID is characterized by failure of antibody response.^{12, 13, 23} Factors that have been attributed as common etiologies in both diseases include disturbed T and B cell homeostasis and selection, altered antigen receptor signaling, increased BAFF levels, and possibly altered TLR signaling.²⁴ Among our six patients with

hypogammaglobulinemia, only one (Pt. 3) met criteria for CVID with persistently low IgG, IgA and IgM, recurrent infections, and poor vaccine response. However, she had no evidence of immune deficiency at presentation (IgG 4,080 g/dL). She developed hypogammaglobulinemia 72 months after her SLE diagnosis and treatment. Her CVID-phenotype is perhaps caused by prolonged immunosuppressive treatment for SLE, including rituximab and cyclophosphamide. While other patients did not meet criteria for CVID, most (4/6) did require IVIG replacement therapy at some point in their treatment due to either infection or low IgG. However, only 2 patients required IVIG long-term (>12 months) due to infection, persistently low IgG, and poor response to vaccination.

To our knowledge, this is the first study that explores the prevalence of and risk factors for hypogammaglobulinemia in pediatric SLE. Our findings suggest that while a minority of patients develops hypogammaglobulinemia, there may be identifiable risk factors, including male sex, white race, and lupus nephritis at onset, and some patients may require IVIG replacement. Intriguingly, a high percentage of pediatric SLE patients with hypogammaglobulinemia were white males, a population not typically associated with SLE. It is interesting to speculate an underlying immune defect which makes them susceptible to immune dysregulation, as they do not have traditional risk factors for SLE. We also found that half of the patients with hypogammaglobulinemia had persistent IgA deficiency, and it will be interesting to determine if this is an independent risk factor. Lupus nephritis at diagnosis was associated with an increased risk of hypogammaglobulinemia, possibly related to urinary protein loss or a marker of more severe disease. Finally, we did not find a statistical significance in the role of immunosuppressive treatment, although the absolute number of patients with hypogammaglobulinemia was small and this will require further investigation. Our study suggests the need for prospective studies evaluating risk factors identified here. In summary, our findings document hypogammaglobulinemia requiring intervention in a small, but significant percentage (~7%) of pediatric SLE patients. Serial monitoring of immunoglobulin levels at diagnosis and during therapy may be helpful in early identification of patients with hypogammaglobulinemia who are at risk for potentially serious infections.

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References

1. Tsokos GC. Systemic lupus erythematosus. *N Engl J Med*. 2011; 365:2110–2121. [PubMed: 22129255]
2. Brunner HI, Gladman DD, Ibanez D, Urowitz MD, Silverman ED. Difference in disease features between childhood-onset and adult-onset systemic lupus erythematosus. *Arthritis Rheum*. 2008; 58:556–562. [PubMed: 18240232]
3. Brunner HI, Huggins J, Klein-Gitelman MS. Pediatric SLE--towards a comprehensive management plan. *Nature reviews Rheumatology*. 2011; 7:225–233.

4. Tucker LB, Uribe AG, Fernandez M, et al. Adolescent onset of lupus results in more aggressive disease and worse outcomes: results of a nested matched case-control study within LUMINA, a multiethnic US cohort (LUMINA LVII). *Lupus*. 2008; 17:314–322. [PubMed: 18413413]
5. Wallace, DJ.; Hahn, BH. Dubois' Lupus Erythematosus and Related Syndromes. Wallace, DJ.; Hahn, BH., editors. Philadelphia: Elsevier; 2013.
6. Yong PF, Aslam L, Karim MY, Khamashta MA. Management of hypogammaglobulinaemia occurring in patients with systemic lupus erythematosus. *Rheumatology*. 2008; 47:1400–1405. [PubMed: 18625660]
7. Fernandez-Castro M, Mellor-Pita S, Citores MJ, et al. Common variable immunodeficiency in systemic lupus erythematosus. *Seminars in arthritis and rheumatism*. 2007; 36:238–245. [PubMed: 17276173]
8. Cunningham-Rundles C. How I treat common variable immune deficiency. *Blood*. 2010; 116:7–15. [PubMed: 20332369]
9. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum*. 1997; 40:1725. [PubMed: 9324032]
10. Agarwal S, Cunningham-Rundles C. Assessment and clinical interpretation of reduced IgG values. *Ann Allergy Asthma Immunol*. 2007; 99:281–283. [PubMed: 17910333]
11. Jolliff CR, Cost KM, Stivins PC, et al. Reference intervals for serum IgG, IgA, IgM, C3, and C4 as determined by rate nephelometry. *Clin Chem*. 1982; 28:126–128. [PubMed: 7055895]
12. Dörner T, Giesecke C, Lipsky PE. Mechanisms of B cell autoimmunity in SLE. *Arthritis Res Ther*. 2011; 13:243. [PubMed: 22078750]
13. Ehrenstein MR, Isenberg DA. Hypergammaglobulinaemia and autoimmune rheumatic diseases. *Ann Rheum Dis*. 1992; 51:1185–1187. [PubMed: 1466592]
14. Matrat A, Veyseyre-Balter C, Trolliet P, et al. Simultaneous detection of anti-C1q and anti-double stranded DNA autoantibodies in lupus nephritis: predictive value for renal flares. *Lupus*. 2011; 20:28–34. [PubMed: 20943718]
15. Jesus AA, Liphau BL, Silva CA, et al. Complement and antibody primary immunodeficiency in juvenile systemic lupus erythematosus patients. *Lupus*. 2011; 20:1275–1284. [PubMed: 21813590]
16. Suyama K, Kawasaki Y, Abe Y, et al. Development of common variable immunodeficiency in IgA- and IgG2-deficient patients with systemic lupus erythematosus. *Pediatric nephrology*. 2012; 27:489–492. [PubMed: 22207346]
17. Wang N, Shen N, Vyse TJ, et al. Selective IgA deficiency in autoimmune diseases. *Molecular medicine*. 2011; 17:1383–1396. [PubMed: 21826374]
18. Cassidy JT, Kitson RK, Selby CL. Selective IgA deficiency in children and adults with systemic lupus erythematosus. *Lupus*. 2007; 16:647–650. [PubMed: 17711902]
19. Rankin EC, Isenberg DA. IgA deficiency and SLE: prevalence in a clinic population and a review of the literature. *Lupus*. 1997; 6:390–394. [PubMed: 9175025]
20. Cronin ME, Balow JE, Tsokos GC. Immunoglobulin deficiency in patients with systemic lupus erythematosus. *Clinical and experimental rheumatology*. 1989; 7:359–364. [PubMed: 2531646]
21. Quartier P, Brethon B, Philippet P, Landman-Parker J, Le Deist F, Fischer A. Treatment of childhood autoimmune haemolytic anaemia with rituximab. *Lancet*. 2001; 358:1511–1513. [PubMed: 11705566]
22. Venhoff N, Effelsberg NM, Salzer U, et al. Impact of rituximab on immunoglobulin concentrations and B cell numbers after cyclophosphamide treatment in patients with ANCA-associated vasculitides. *PloS one*. 2012; 7:e37626. [PubMed: 22629432]
23. Agarwal S, Cunningham-Rundles C. Autoimmunity in common variable immunodeficiency. *Curr Allergy Asthma Rep*. 2009; 9:347–352. [PubMed: 19671377]
24. Warnatz K, Voll RE. Pathogenesis of autoimmunity in common variable immunodeficiency. *Frontiers in immunology*. 2012; 3:210. [PubMed: 22826712]

Table 1
Factors associated with hypogammaglobulinemia in pSLE

Patient characteristics including age, lupus nephritis, SLEDAI score, and IgG at time of pSLE diagnosis.

		SLE with low IgG (n=6)	SLE without low IgG (n=80)	p-value
Age (years)		13.66 ± 2.73	14.41 ± 2.76	0.52
Sex	M	3 (50%)	5 (6.3%)	0.009**
	F	3 (50%)	75 (93.8%)	
Median follow-up (months)		71	39	0.26
Lupus nephritis at diagnosis		6 (100%)	30 (37.5%)	0.004**
SLEDAI score at diagnosis	<10	1 (17%)	23 (29%)	1.00
	10	5 (83%)	57 (71%)	
IgG at diagnosis (mg/dL)	<1500	4 (66%)	21 (26%)	0.05
	1500	2 (34%)	59 (74%)	
Prednisone use		6 (100%)	80 (100%)	1.00
Cyclophosphamide use		5 (83%)	33 (41%)	0.08
Rituximab use		2 (33%)	10 (12.5%)	0.19
Mycophenolate mofetil use		5 (83%)	39 (49%)	0.19

* p-value < 0.05;

** p-value < 0.01.

Table 2
Racial distribution of patients with and without hypogammaglobulinemia

Race	SLE with hypogam (n=6)	SLE without hypogam (n=80)	p= value
African-American	1 (17%)	42 (52%)	NS
White	5 (83%)	28 (35%)	0.02 *
Biracial	0	2	NS
Hispanic	0	3	NS
Middle Eastern	0	1	NS
Asian	0	1	NS
Unknown	0	2	NS
Other	0	1	NS

NS, non-significant;

*
p-value < 0.05.

Table 3
Immunosuppressive treatment(s) received by patients prior to or concurrent with diagnosis of hypogammaglobulinemia

Pt. #	Diagnosis to low IgG (months)	Prednisone	Cyclophosphamide	MMF	Rituximalab
1	0	N	N	N	N
2	2 mo	Y	N	Y	N
3	72 mo	Y	Y	Y	Y
4	18 mo	Y	Y	Y	Y
5	60 mo	Y	Y	Y	N
6	36 mo	Y	Y	Y	N

N= no; Y=yes.

Table 4
Lupus nephritis in patients with hypogammaglobulinemia

Age at diagnosis of SLE, sex, and race (W, white; AA, African American); lupus nephritis (LN) classification and albumin (Alb) at initial diagnosis. The time from diagnosis of SLE until hypogammaglobulinemia (hypogam) is shown in months, followed by ds-DNA antibody (+, positive; neg, negative), complement, C3 and C4 (L, low; N, normal; n.d. not determined) values, serum albumin, and urine protein:creatinine ratio (UP:UC) at the onset of hypogammaglobulinemia.

Pt. #	Age/ Sex	Race	At SLE Diagnosis			At time of hypogam				
			LN	Alb (g/dL)	Time to hypogam	dsDNA	C3/ C4	Alb (g/dL)	UP:UC Ratio	
1	12Y/M	W	class IV	2.2	0	+	L/L	2.2	9.9	
2	18Y/M	W	class IV	3.9	2 mo	+	N/L	4.6	0.5	
3	10Y/F	AA	class V	2.8	72 mo	neg	N/N	3.5	1.9	
4	13Y/F	W	class II	3.2	18 mo	+	N/n.d	3.5	8.3	
5	14Y/F	W	class III	3.4	60 mo	+	L/N	3.6	2.2	
6	15Y/M	W	class III/V	2.9	36 mo	+	L/L	2.0	6.4	

Albumin reference value: 3.2–5.0 g/dL

Table 5
Immunologic studies and treatment of patients with hypogammaglobulinemia

Total IgG levels at the time of SLE diagnosis (or within 3 months of diagnosis), lowest IgG, and IgM/IgA at the time of low IgG, infection history, antibody responses to vaccination, and IVIG treatment among patients with hypogammaglobulinemia. For S. pneumonia, numbers indicate # serotypes with protective titers/total tested.

Pt. #	Dx IgG (mg/dL)	Low IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	Infections	Vaccine responses	IVIG Rx	Length of IVIG
1	170	170	57	<7	None	Tet (L); Hib (N), Strep 1/7	No	n/a
2	366	322	68	102.4	Sinusitis	Tet (N); Hib (N); Strep 4/23 ^d	Yes	>16 mo
3	4,080	264	<1	<7	Chronic OM Sinusitis, cellulitis	Tet (N); Hib (NP); Strep 0/23	Yes	>30 mo
4	1,600	187	74	66	Pneumonia	Tet (N)	Yes	2 mo
5	1,220	301	35	179	None	Tet (N); Hib (NP); Strep 1/7	No	n/a
6	1,440	65	96	<7	None	n.d.	Yes	4 mo

Abbreviations: Dx, diagnosis; Rx, treatment; Tet, tetanus; Hib, Haemophilus influenzae type B; Strep, Streptococcus pneumoniae; N, normal; L, low but protective; and NP, non-protective; O.M., otitis media; n.d., not determined; n/a, not applicable. IgG reference range 700–1450 mg/dL; IgM 30–210 mg/dL; and IgA 70–370 mg/dL.

^d Patient did not respond to Pneumovax booster.