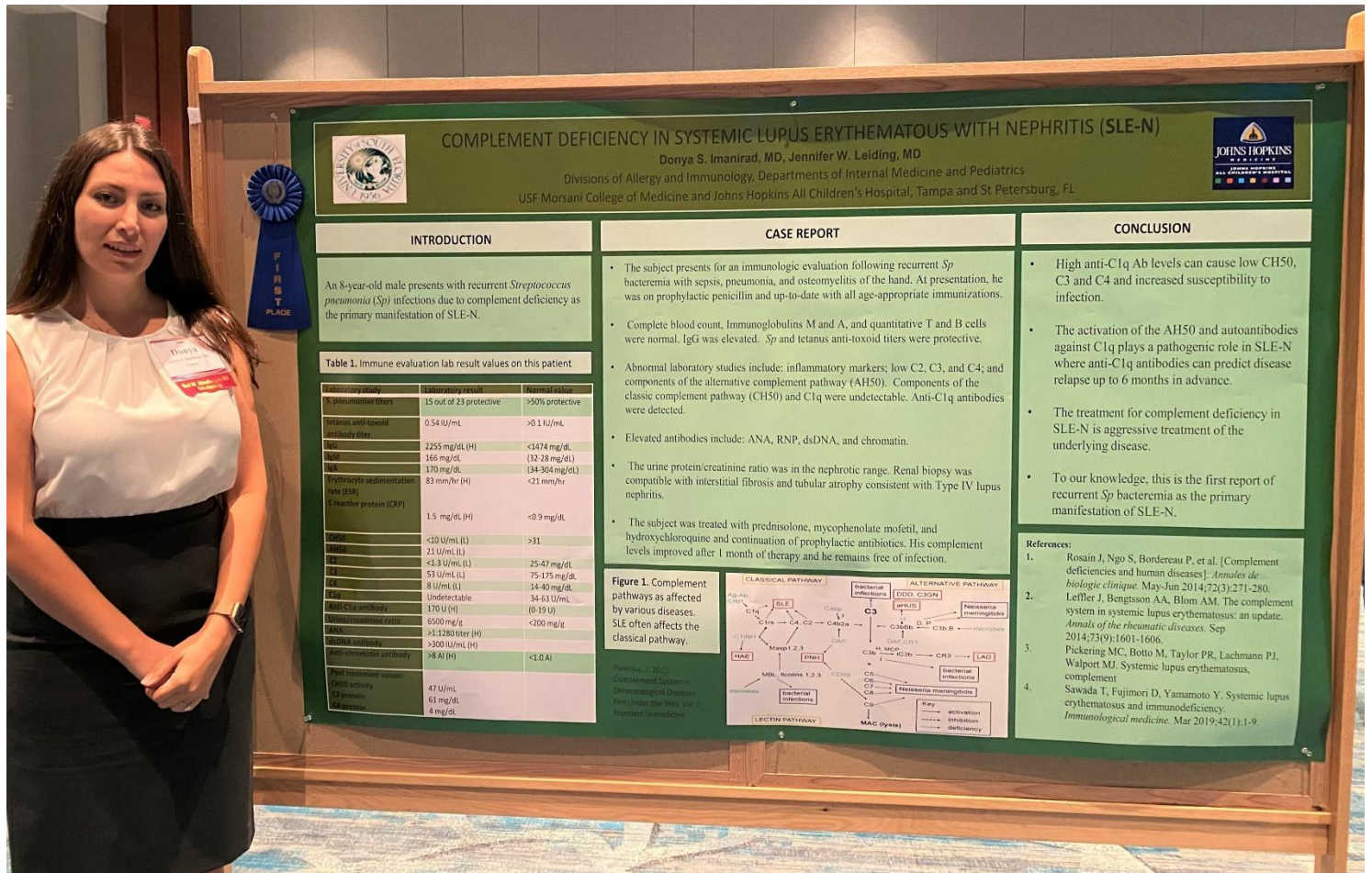


USF INTERNAL MEDICINE & PEDIATRIC DIVISIONS OF ALLERGY AND IMMUNOLOGY

"One, Two and Three - Hey Hey Hey"! Three fellows from the Internal Medicine Division of Allergy and Immunology won 1st, 2nd and 3rd place, respectively, for their posters at the 2021 Florida Allergy, Asthma & Immunology Society (FAAIS) Annual Meeting, Orlando, FL, July 16 – 18, 2021. Great achievement!



COMPLEMENT DEFICIENCY IN SYSTEMIC LUPUS ERYTHEMATOUS WITH NEPHRITIS (SLE-N)
 Donya S. Imanirad, MD, Jennifer W. Leiding, MD
 Divisions of Allergy and Immunology, Departments of Internal Medicine and Pediatrics
 USF Morsani College of Medicine and Johns Hopkins All Children's Hospital, Tampa and St. Petersburg, FL

INTRODUCTION		
An 8-year-old male presents with recurrent <i>Streptococcus pneumoniae</i> (Sp) infections due to complement deficiency as the primary manifestation of SLE-N.		
Table 1. Immune evaluation lab result values on this patient		
Laboratory	Laboratory result	Normal value
S. pneumoniae titer	15 out of 23 protective	>50% protective
Immune antihypox antibody titer	0.54 IU/mL	>0.1 IU/mL
Asp	2255 mg/dL (H)	<1474 mg/dL
WBC	166 mg/dL	(32-28 mg/dL)
Hem	170 mg/dL	(34-304 mg/dL)
Erythrocyte sedimentation rate (ESR)	83 mm/hr (H)	<21 mm/hr
C reactive protein (CRP)	1.5 mg/dL (H)	<0.9 mg/dL
ANCA	<10 U/mL (L)	>31
RF	21 U/mL (L)	>10
ESR	<1.3 U/mL (L)	25-47 mg/dL
UAE	53 U/mL (L)	75-175 mg/dL
UACR	8 U/mg (L)	14-40 mg/dL
BUN	Undetectable	34-63 U/mL
Anti-C1q antibody	170 U (H)	(0-19 U)
Anti-pneumococcal titer	6500 mg/g	>1280 titer (H)
Anti-DNA antibody	>300 IU/mL (H)	<200 mg/g
Anti-chromatin antibody	>8 AI (H)	<1.0 AI
Anti-creatinine antibody	47 U/mL	
ESR activity	61 mg/dL	
ESR protein	4 mg/dL	

CASE REPORT	
• The subject presents for an immunologic evaluation following recurrent Sp bacteremia with sepsis, pneumonia, and osteomyelitis of the hand. At presentation, he was on prophylactic penicillin and up-to-date with all age-appropriate immunizations.	• Complete blood count, Immunoglobulins M and A, and quantitative T and B cells were normal. IgG was elevated. Sp and tetanus anti-toxoid titers were protective.
• Abnormal laboratory studies include: inflammatory markers; low C2, C3, and C4; and components of the alternative complement pathway (AH50). Components of the classic complement pathway (CH50) and C1q were undetectable. Anti-C1q antibodies were detected.	• Elevated antibodies include: ANA, RNP, dsDNA, and chromatin.
• The urine protein/creatinine ratio was in the nephrotic range. Renal biopsy was compatible with interstitial fibrosis and tubular atrophy consistent with Type IV lupus nephritis.	• The subject was treated with prednisone, mycophenolate mofetil, and hydroxychloroquine and continuation of prophylactic antibiotics. His complement levels improved after 1 month of therapy and he remains free of infection.

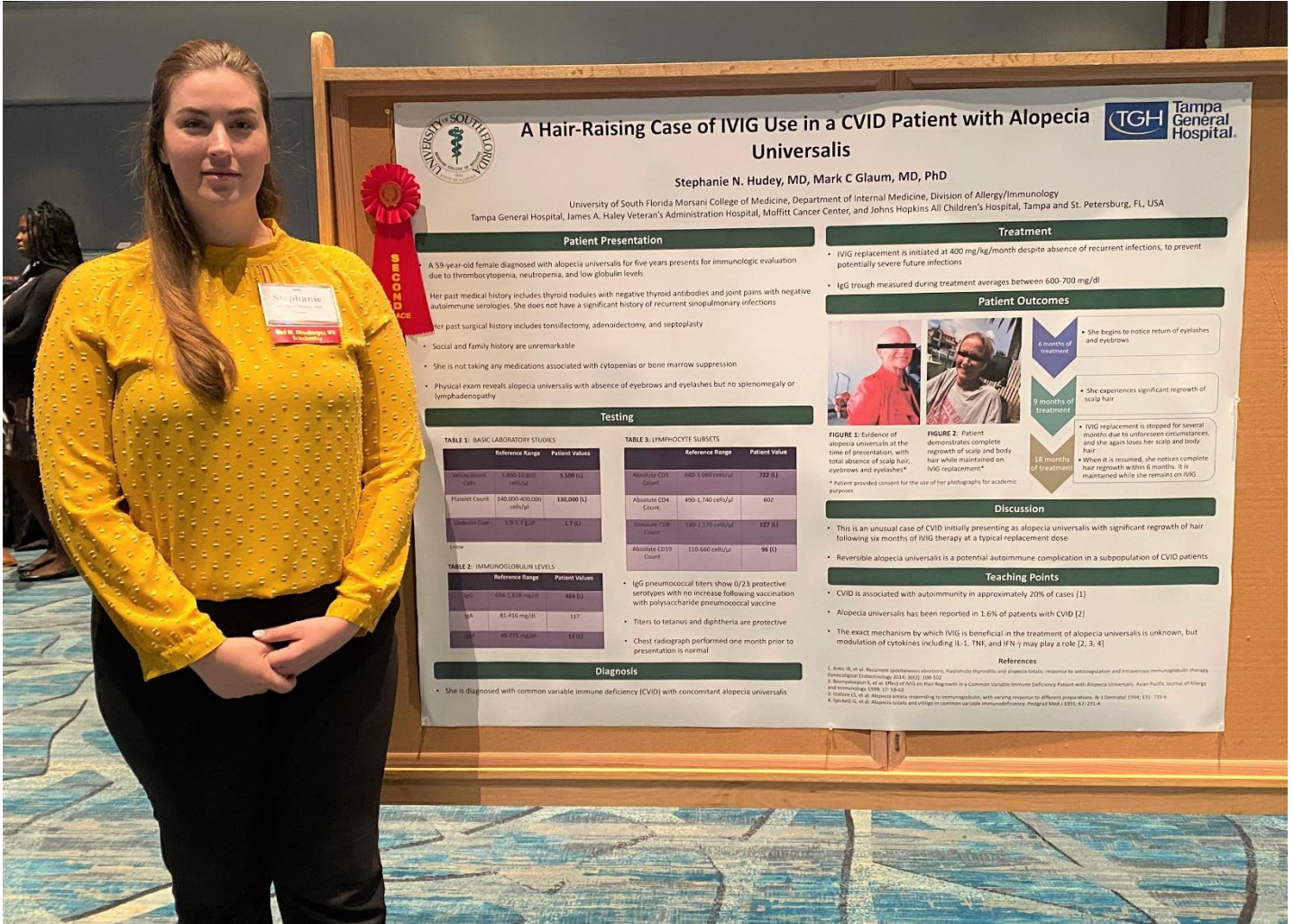
CONCLUSION	
• High anti-C1q Ab levels can cause low CH50, C3 and C4 and increased susceptibility to infection.	• The activation of the AH50 and autoantibodies against C1q plays a pathogenic role in SLE-N where anti-C1q antibodies can predict disease relapse up to 6 months in advance.
• The treatment for complement deficiency in SLE-N is aggressive treatment of the underlying disease.	• To our knowledge, this is the first report of recurrent Sp bacteremia as the primary manifestation of SLE-N.

Figure 1. Complement pathways as affected by various diseases. SLE often affects the classical pathway.


References:

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- Leffler J, Bengtsson AA, Blom AM. The complement system in systemic lupus erythematosus: an update. *Annals of the rheumatic diseases*. Sep 2014;73(9):1601-1606.
- Pickering MC, Botto M, Taylor PR, Lachmann PJ, Walport MJ. Systemic lupus erythematosus, complement.
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Donya Imanirad, MD, 2nd year fellow, Division of Allergy and Immunology, Department of Internal Medicine, wins 1st prize for her poster entitled "Complement Deficiency in Systemic Lupus Erythematosus with Nephritis (SLE-N)" at the 2021 Annual Florida Asthma & Immunology Society (FAAIS) Meeting, Orlando, FL, July 16 – 18, 2021.




Stephanie Hudey, MD, 2nd year fellow (graduated), Division of Allergy and Immunology, Department of Internal Medicine, wins 2nd prize for her poster entitled "A Hair-Raising Case of IVIG Use in a CVID Patient with Alopecia Universalis" at the 2021 Annual Florida Asthma & Immunology Society (FAAIS) Meeting, Orlando, FL, July 16 – 18, 2021.



A Hair-Raising Case of IVIG Use in a CVID Patient with Alopecia Universalis

Stephanie N. Hudey, MD, Mark C. Glaum, MD, PhD

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Tampa General Hospital, James A. Haley Veteran's Administration Hospital, Moffitt Cancer Center, and Johns Hopkins All Children's Hospital, Tampa and St. Petersburg, FL, USA



Patient Presentation

A 58-year-old female diagnosed with alopecia universalis for five years presents for immunologic evaluation due to thrombocytopenia, neutropenia, and low globulin levels.

Her past medical history includes thyroid nodules with negative thyroid antibodies and joint pains with negative autoimmune serologies. She does not have a significant history of recurrent sinopulmonary infections.

Her past surgical history includes tonsillectomy, adenoidectomy, and septoplasty.

- Social and family history are unremarkable.
- She is not taking any medications associated with cytopenias or bone marrow suppression.
- Physical exam reveals alopecia universalis with absence of eyebrows and eyelashes but no splenomegaly or lymphadenopathy.

Treatment

- IVIG replacement is initiated at 400 mg/kg/month despite absence of recurrent infections, to prevent potentially severe future infections.
- IgG trough measured during treatment averages between 600-700 mg/dl.

Testing

TABLE 1: BASIC LABORATORY STUDIES

Reference Range	Patient Values
White Blood Cells: 3,800-10,800 cells/µL	3,500 (L)
Platelet Count: 140,000-400,000 cells/µL	130,000 (L)
Hemoglobin: 11.5-17.0 g/dL	5.7 (L)


TABLE 3: LYMPHOCYTE SUBSETS

Reference Range	Patient Value
Absolute CD19 Count: 880-3,040 cells/µL	722 (L)
Absolute CD4 Count: 400-1,740 cells/µL	602
Absolute CD8 Count: 180-1,170 cells/µL	127 (L)
Absolute CD19 Count: 110-640 cells/µL	96 (L)

TABLE 2: IMMUNOGLOBULIN LEVELS

Reference Range	Patient Values
IgG: 698-2,030 mg/dL	446 (L)
IgA: 81-416 mg/dL	117
IgM: 48-271 mg/dL	14 (L)

Patient Outcomes



6 months of treatment

9 months of treatment

18 months of treatment

- She begins to notice return of eyelashes and eyebrows.
- She experiences significant regrowth of scalp hair.
- IVIG replacement is stopped for several months due to unforeseen circumstances, and she again loses her scalp and body hair.
- When it is resumed, she notices complete hair regrowth within 8 months. It is maintained while she remains on IVIG.

Discussion

- This is an unusual case of CVID initially presenting as alopecia universalis with significant regrowth of hair following six months of IVIG therapy at a typical replacement dose.
- Reversible alopecia universalis is a potential autoimmune complication in a subpopulation of CVID patients.

Diagnosis

- She is diagnosed with common variable immune deficiency (CVID) with concomitant alopecia universalis.

Teaching Points

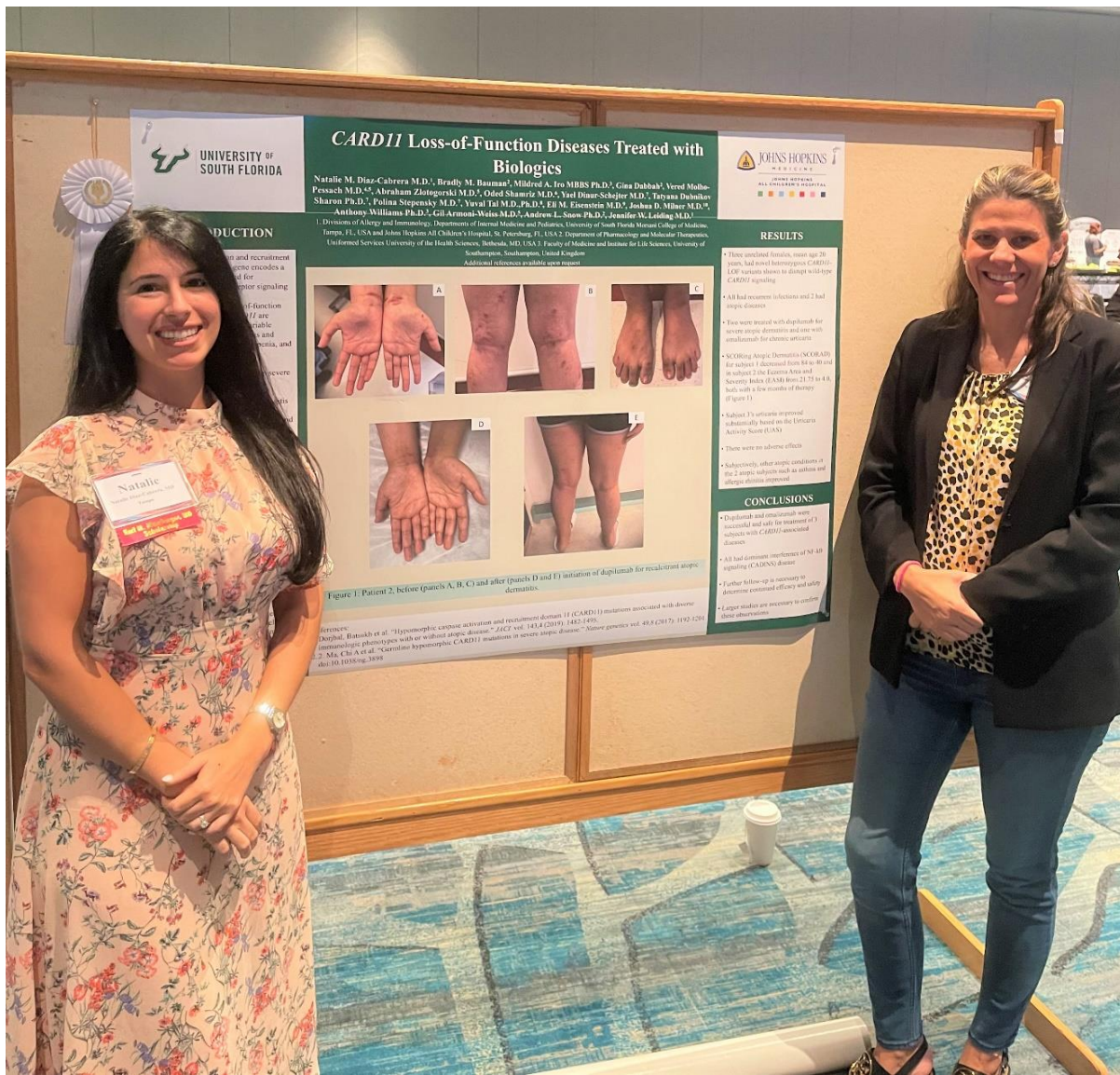
- CVID is associated with autoimmunity in approximately 20% of cases [1].
- Alopecia universalis has been reported in 1.6% of patients with CVID [2].
- The exact mechanism by which IVIG is beneficial in the treatment of alopecia universalis is unknown, but modulation of cytokines including IL-1, TNF, and IFN-γ may play a role [2, 3, 4].

References

1. Araki H, et al. Response to intravenous immunoglobulin, tacrolimus, and alopecia totalis: response to antioxygation and intravenous immunoglobulin therapy. *Cytological Endocrinology* 2014; 30(3): 388-392.
2. Bhatnagar S, et al. Effect of IVIG on Hair Regrowth in a Common Variable Immune Deficiency Patient with Alopecia Universalis. *Asian Pacific Journal of Allergy and Immunology* 2019; 37: 33-42.
3. Cohen JL, et al. Alopecia totalis and areata responding to intravenous IgG with varying responses to different preparations. *Br J Dermatol* 1991; 125: 175-4.
4. Niekirk G, et al. Alopecia totalis and areata in common variable immunodeficiency. *Postgrad Med J* 1995; 67: 255-4.

Awards

2ND PRIZE



Natalie M. Diaz-Cabrera, MD, 2nd year fellow, Division of Allergy and Immunology, Department of Internal Medicine, wins 3rd prize for her poster entitled "CARD11 Loss of Function Diseases Treated with Biologics" at the 2021 Annual Florida Asthma & Immunology Society (FAAIS) Meeting, Orlando, FL, July 16 – 18, 2021.

L to R: Natalie M. Diaz-Cabrera, MD, Jeniffer Leiding, MD.

With warm regards,

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 Distinguished University Health Professor
 Joy McCann Culverhouse Chair in Allergy
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