An Uncommon Case of a Patient with CVID & PANDAS

A.T. Nguyen[1], Y. Shi[2], T. Zheng[1]

[1]Division of Allergy & Immunology, Department of Pediatrics, Alpert Medical School of Brown University, Providence, RI. [2]Lifespan Physical Group.

Introduction

- Pediatric autoimmune neuropsychiatric disorder associated with Streptococcus infections (PANDAS), a subset of pediatric acute-onset neuropsychiatric syndrome (PANS), is characterized by new onset neuropsychiatric symptoms temporally associated with Streptococcus infection.
- Some patients with PANS/PANDAS have also been found to have antibody deficiency (IgG, IgA and vaccine antibody to Streptococcal pneumoniae).
- However, PANDAS in patients with common variable immunodeficiency (CVID) has not been previously reported.

Case Description

- A 16-year-old male with CVID and psoriasis was diagnosed with PANDAS at 9 years-old after a febrile illness with group A streptococcus infection.
- Given his ongoing severe neuropsychiatric symptoms including obsessive compulsive disorder, he transitioned from intravenous immunoglobulin (IVIG) dosing for CVID to a higher-dose (2 gram/kg/month) for the treatment of PANDAS. He did not have additional major infections, and after approximately a year of higher-dose IVIG treatment, his neuropsychiatric symptoms of PANDAS improved.

Evaluation

Immune Evaluation	Result	Reference Range
CBC with differential	Normal except for WBC 3.9 mildly decreased	
IgG	1921 - on high dose IVIG for PANDAS	540-1822 mg/dL
IgA	14 (low)	63-484 mg/dL
IgM	83	22-240 mg/dL
IgE	<21	2-537 IU/mL
Natural Killer Function	NK Lytic Units 0.2 (low) - decreased NK Cell function	>=1.0

Table 1. Immune Lab Evaluation

Naïve & Memory B Cell Panel	Result	Reference Range
CD19+ B Cells	235	110 - 450 cells/uL
CD20+	229	110 - 450 cells/uL
Total Memory CD27+	33	23 - 110 cells/uL
Non-Switched CD27+IgD+IgM+	25	5 - 46 cells/uL
Class-Switched CD27+IgD-IgM-	3 (low)	11 - 61 cells/uL
Transitional CD38+IgM+	11	1 - 17 cells/uL
Plasmablasts CD38+IgM-	0 (low)	1 - 8 cells/uL
Activated CD21low CD38-	6	3 - 26 cells/uL

Table 3. Naïve & Memory B Cell Panel Evaluation

Lymphocyte Enumeration	Result	Reference Range
Absolute CD3	1278	570-2400 cells/uL
Absolute CD4	678	430-1800 cells/uL
Absolute CD8	517	210-1200 cells/uL
Absolute Natural Killer Cells	28 (low)	78-470 cells/uL
Absolute CD19	226	91-610 cells/uL
Absolute CD45RA	420	150-870 cells/uL
Absolute CD45RO	295	190-1050 cells/uL

Table 2. Lymphocyte Enumeration by Flow Cytometry

Additional Evaluation	Result	Reference Range
Complete Metabolic Panel	Normal	
ESR	9	0-15 mm/h
CRP	<0.20	0-10 MG/L
Hepatitis C Antibody	Non-Reactive	
Hepatitis B Antigen	Non-Reactive	
Hepatitis B Antibody	608.8	>12 mIU/mL protective
CT Chest, Abdomen, Pelvis with IV Contrast	Normal without evidence of malignancy, hepatosplenomegaly, or lymphadenopathy	

Table 4. Additional Evaluation Including Labs and Imaging

Next Steps in Evaluation and Management:

- Obtaining genetic testing to evaluate for underlying genetic defects and for consideration of targeted medical therapy
- Collaborating with rheumatologist who is managing PANDAS and consideration of decreasing high dose IVIG when able
- Using multidisciplinary approaches, including cognitive behavioral therapy and/or pharmacologic therapy, to best treat the patient's residual neuropsychiatric symptoms

Discussion

The prevalence of PANDAS in children with CVID is unclear. The mechanism of IVIG in the treatment of PANDAS has not been elucidated. Mechanisms may involve the binding and neutralization of autoantibodies by anti-idiotypic antibodies, and also the eradication and prevention of Streptococcal infection.

PANDAS should be considered on the differential for patients with CVID and antibody deficiency who develop new onset or suddenly worsening neuropsychiatric symptoms in the setting of an acute upper respiratory tract infection.

Prompt diagnosis, timely treatment of an underlying streptococcal infection, and appropriate doses of IVIG, especially in patients with immunodeficiency, may prevent the development of severe PANDAS and improve the quality of life of patients.

References

- Calaprice, D., Tona, J., & Murphy, T. K. (2018). Treatment of Pediatric Acute-Onset Neuropsychiatric Disorder in a Large Survey Population. *Journal of Child and Adolescent Psychopharmacology*, *28*(2), 92–103. https://doi.org/10.1089/cap.2017.0101
- Crow, A. R., & Lazarus, A. H. (2008). The Mechanisms of Action of Intravenous Immunoglobulin and Polyclonal Anti-D Immunoglobulin in the Amelioration of Immune Thrombocytopenic Purpura: What Do We Really Know? *Transfusion Medicine Reviews*, *22*(2), 103–116. https://doi.org/10.1016/j.tmrv.2007.12.001
- Galeotti, C., Kaveri, S. V., & Bayry, J. (2017). IVIG-mediated effector functions in autoimmune and inflammatory diseases. *International Immunology*, *29*(11), 491-498. https://doi.org/10.1093/intimm/dxx039
- Hardin, H., Shao, W., & Bernstein, J. A. (2023). An updated review of pediatric autoimmune neuropsychiatric disorders associated with Streptococcus/pediatric acute-onset neuropsychiatric syndrome, also known as idiopathic autoimmune encephalitis: What the allergist should know. *Annals of Allergy, Asthma, & Immunology*, *131*(5), 567–575. https://doi.org/10.1016/j.anai.2023.08.022
- Pincetic, A., Bournazos, S., DiLillo, D. J., Maamary, J., Wang, T. T., Dahan, R., Fiebiger, B.-M., & Ravetch, J. V. (2014). Type I and type II Fc receptors regulate innate and adaptive immunity. *Nature Immunology*, *15*(8), 707–716. https://doi.org/10.1038/ni.2939
- Schwab, I., & Nimmerjahn, F. (2013). Intravenous immunoglobulin therapy: how does IgG modulate the immune system? *Nature Reviews Immunology*, *13*(3), 176–189. https://doi.org/10.1038/nri3401