Neuropsychiatric Testing Provides Objective Insight Into Beneficial Effects Of Intravenous Immunoglobulins In Patients With Pediatric Acute-Onset Neuropsychiatric Syndrome

Poster #246

Eremija J, Daines M
Division of Allergy, Immunology and Rheumatology, Department of Pediatrics, University of Arizona, Tucson

INTRODUCTION

Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) is defined by acute onset of OCD and/or restricted eating, but other diverse neuropsychiatric manifestations are also commonly seen, presumably in the setting of underlying immune dysfunction [1-4]. Thus, immunomodulatory interventions have crucial therapeutic role, but objective post-treatment evaluations are scarce and challenging given disease complexity [5-7]. We used standardized neuropsychiatric testing to assess how intravenous immunoglobulin (IVIG) treatment impacts cognitive function in children with PANS.

METHODS

Retrospective 5-year record review was completed in Children's Postinfectious Autoimmune Encephalopathy Center at University of Arizona. We identified 12 children who were diagnosed with PANS based on well-established clinical criteria [1-3], underwent immunomodulatory IVIG therapy (1-7 courses of 2g/kg IVIG) and completed neuropsychiatric testing before/after treatment. Score improvement of 1 standard deviation in any tested domain/subdomain (e.g. intelligence, memory, learning, visual, motor, sensory, integrative functions) was considered significant and is represented as ↑ in Table 2.

Table 1: Demographic and laboratory patient characteristics

Characteristics	Mean (SD)
Age of diagnosis	8.5 (4.5)
Age at IVIG treatment	11.5 (3)
	Number (%)
Male gender	5 (42)
IVIG < 2 years from diagnosis	5 (42)
Preceding Streptococcal Infection*	7 (58)
Residence in Arizona	6 (50)
Total adverse effects on IVIG	4 (33)
Severe adverse effects on IVIG	1 (8)
Improvement on IVIG	11 (92)
Hypogammaglobulinemia**	5 (42)

*: based on positive throat swab and/or Antistreptolysin-O titers
**: low IgG levels on presentation, requiring substitution through IVIG infusion

RESULTS

Patient demographic characteristics are presented in **Table 1.** Individual test results are depicted in **Table 2**

Table 2: Individual test results

	Dg-IVIG delay (years)	Number of IVIG courses	KBIT-2	WASI-2	WISC-4/5	WRAML-2 CVLT-C	WRAT-4/5 WIAT-3	Beery VMI	WRAVMA Pegboard
Patient 1	7	3	n/a	↔	↔	↔	↔	↑	↑
Patient2	1	3	n/a	↔	n/a	↔	↔	↔	↔
Patient 3	2	4	n/a	↔	↔	↑	↔	↔	↔
Patient 4	6	1	n/a	↔	↔	↑	↔	↔	↔
Patient 5	2	7	n/a	n/a	↔	↑	n/a	↔	n/a
Patient 6	5	2	n/a	n/a	↑	n/a	n/a	↔	n/a
Patient 7	4	3	n/a	↔	↔	↔	↑	↔	↑
Patient 8	1	3	n/a	n/a	↑	↑	↔	↑	↔
Patient 9	0	3	n/a	↑	↔	↑	↔	↔	↔
Patient 10	6	2	n/a	↔	↔	↔	↔	↑	↑
Patient 11	1	3	↑	n/a	n/a	n/a	n/a	n/a	n/a
Patient 12	1	5	↑	n/a	n/a	n/a	n/a	n/a	n/a
Improved	n/a	n/a	2/2	1/7	2/9	5/9	1/8	3/10	3/8

n/a: testing not done, or not comparable ↑: significantly improved. ↔: no change

Dg-IVIG delay: delay from diagnosis to treatment
KBIT-2: Kaufman Brief Intelligence Test, 2nd edition
WASI-2: Wechsler Abbreviated Scale of Intelligence, 2nd edition
WISC-4/5: Wechsler Intelligence Scale for Children, 4th or 5th Edition
WRAML-2: Wide Range Assessment of Memory and Learning, 2nd edition
CVLT-C: California Verbal Learning Test Children's
WRAT-4/5: Wide Range Achievement Test 4th or 5th edition
WIAT-3: Wechsler Individual Achievement Test 3rd edition
Beery VMI: Beery-Buktenica Developmental Test of Visual-Motor Integration
WRAVMA Pegboard: Wide Range Assessment of Visual Motor Abilities Pegboard

CONCLUSIONS AND DISCUSSION

In our cohort, 11 of 12 patients showed significant improvement following IVIG. Treatment was tolerated well and showed efficacy in almost all participants, independently from time lapsed since disease onset, emphasizing impact of immunomodulation in PANS. Furthermore, patients benefited from different numbers of IVIG courses.

Although PANS diagnosis requires presence of hyperacute OCD and/or restricted eating, other psychiatric and neuropsychological manifestations can sometimes overshadow OCD [1-3]. Therefore, our study focused on those additional pertinent neuropsychological disorders commonly seen within PANS spectrum and provided a novel expanded insight into beneficial effects of IVIG comparing to other trials, while proving that standardized neuropsychiatric testing is a valuable tool to objectively quantify improvement in these patients. Significant presence of baseline hypogammaglobulinemia in children with PANS emphasizes the presumed role of immune dysfunction in disease pathogenesis, especially given known connection between immunodeficiency and autoimmunity [8,9].

LITERATURE

1. Swedo SE et al. Modifying the PANDAS criteria to describe PANS (pediatric acute-onset neuropsychiatric syndrome). Pediatr Ther 2012;2(2):1–8.
2. Chang K et al. Clinical Evaluation of Youth with Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS): Recommendations from the 2013 PANS Consensus Conference. J Child Adolesc Psychopharmacol 2015;25(1):3-13.
3. Rea I et al. Clinical Features in Patients With PANDAS/PANS and Therapeutic Approaches: A Retrospective Study. Front. Neurol 2021;12:741176
4. Shimasaki C et al. Evaluation of the Cunningham Panel™ in pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS): Changes in antineuronal antibody titers parallel changes in patient symptoms. J Neuroimmunol. 2020; 339:577138.
5. Murphy TK et al. Characterization of the Pediatric Acute-Onset Neuropsychiatric Syndrome Phenotype. J Child Adolesc Psychopharmacol 2015;25(1):14-25.
6. Perlmutter SJ et al. Therapeutic plasma exchange and intravenous immunoglobulin for obsessive-compulsive disorder and tic disorders in childhood. Lancet. 1999;354(9185):1153-1158.
7. Williams KA et al. Randomized, Controlled Trial of Intravenous Immunoglobulin for Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections. J Am Acad Child Adolesc Psychiatry 2016;55(10):860–867.
8. Agarwal S et al. Autoimmunity in common variable immunodeficiency. Ann Allergy Asthma Immunol 219;123(5):454-460.
9. Azizi G et al. Autoimmunity in Primary Antibody Deficiencies. Int Arch Allergy Immunol 2016;171(3-4):180–193.