Di Stefano M, et al., J Clin Stud Med Case Rep 2024, 11: 250
DOI: 10.24966/CSMC-8801/1000250

HSOA Journal of Clinical Studies and Medical Case Reports

Case Report

Could barrier injury and eosinophilic inflammation contribute to neurological damage in PANS?

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Abstract

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcical infection (PANDAS) and Acute-onset Neuropsychiatric Syndrome (PANS) are pediatric neurologic disorders clinically characterized by a spectrum of neuropsychiatric symptoms, including obsessive thoughts and compulsive behaviors. Both these entities have been associated with viral or bacterial infections but the pathogenetic mechanisms have not been completely defined.

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Citation: Di Stefano M, et al. (2024) Could barrier injury and eosinophilic inflammation contribute to neurological damage in PANS?. J Clin Stud Med Case Rep 11: 250.

Received: September 05, 2024; **Accepted:** September 18, 2024; **Published:** September 28, 2024

We describe a case of a 12-year-old boy affected by PANS, eosinophilia and asthma, who was successfully treated with mepolizumab and experienced PANS-associated neurological symptoms.

Background

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcical infection (PANDAS) and Acute-onset Neuropsychiatric Syndrome (PANS) are pediatric neurologic disorders clinically characterized by a spectrum of neuropsychiatric symptoms including obsessive-compulsive disorders (OCD), restricted food intake, tics, hyperactivity, mild choreiform movements, anxiety/depression, irritability, oppositional behavior.

PANDAS has been associated with group A β-hemolytic streptococcal infections. A symptom complex similar to PANDAS has been described in a group of patients without evidence of streptococcal infection, identified as PANS. PANS has been associated with H1N1 influenza, Epstein-Barr virus (EBV), *Borrelia burgdorferi* or other infective agents, without evidence of streptococcal etiology [1]. Limited evidence hypothesizes the association between *Mycoplasma pneumoniae* infection and OCD [2].

The pathogenesis of PANDAS/PANS is currently not completely known, however, the involvement of autoimmune processes has been recognized: antibodies directed against microorganisms cross-react with antigenic epitopes on selected brain nuclei with a molecular mimicry mechanism [3]. The autoimmune and inflammatory disruption of the cortico-striato-thalamo-cortical circuits is a feature of PANS [4].

Furthermore, neuroinflammatory, toxic, environmental, metabolic or endocrine factors and disorders are also presumed to be involved in PANS via the triggering of autoimmune responses [5].

Regarding PANS diagnosis, the diagnostic criteria modified for PANS were proposed by Swedo et al. [6] and include:

Abrupt onset of OCD or restricted food intake.

Presence of at least 2 of the following symptoms: anxiety; emotional lability and/or depression; irritability/aggression; behavioral regression; worsening of school performance; sensory or motor abnormalities; sleep disturbances/enuresis or urinary frequency.

Symptoms not better explained by another disorder, such as Sydenham chorea, Tourette disorder or others.

Case Report

We describe the case of a 12-year-old boy who, at the age of two, developed a *M. pneumoniae* pneumonia, resolved with antibiotic therapy. Three years later he presented motor stereotypies, compulsive behaviors and obsessive attention to hygiene and order, restriction in food intake, hyperactivity and irritability and he was diagnosed with PANS. Cognitive-behavioral psychotherapy was started with mild improvements in neuropsychiatric symptoms.

Since 2020, the patient has been affected by severe uncontrolled allergic and eosinophilic asthma with chronic rhinosinusitis (CRS).

Total serum IgE were 1985 UI/mL, serum specific IgE showed sensitization to house dust mite, pollen and *Alternaria alternata*. Absolute eosinophil blood count was 1,00 x10^9/L.

The patient has been treated with high doses of inhaled corticosteroid plus long acting beta-2 agonists (ICS/LABA) and leukotriene antagonists with suboptimal asthma symptoms control. During 2022, three pulses of oral corticosteroids (OCS) were required to control wheezing, dyspnea and cough. During OCS pulses, the patient had shown worsening in neuropsychiatric symptoms, in particular in hyperactivity and irritability that worsened compulsive behaviors, with wide impact on the patient's and parents' quality of life (QoL) and productivity.

In October 2023 the patient was evaluated in a multidisciplinary context. The Children's Yale–Brown Obsessive–Compulsive Scales (CY-BOCS) was used to evaluate neuropsychiatric involvement and resulted in 27/40; moreover, the Clinical Global Impressions- Severity (CGI-S) was assessed resulting in a score of 4 (moderately ill). Motor stereotypes were present. No radiological examinations were allowed for patient claustrophobia.

Considering the restricted food intake, the microbiome test was performed showing dysbiosis, so therapy with probiotics was introduced. Moreover, a personalized dietary intervention was proposed. Rifaximin and metronidazole prophylaxis was started.

Laboratory data confirmed 1,0 x 10^9 eosinophils/L and serum eosinophil cationic protein (ECP) was >200 µg/L. Asthma control test (ACT) was 12/25 and Sinonasal Outcome Test 22 (SNOT-22) was 75/110; considering the poorly controlled asthma and CRS symptoms and the need of OCS-sparing treatment, treatment with mepolizumab 100 mg every 4 weeks was started.

After the third mepolizumab injection, the asthma and CRS symptoms improved (ACT was 22/25 and SNOT-22 was 42/110), eosinophil count and ECP decreased to 0,14 x 10^9 cells/L and 56 µg/L, respectively. No further pulses of OCS were required and no further asthma exacerbations occurred.

Moreover, improvements in neuropsychiatric symptoms were observed: both motor stereotypies frequency and obsessive thoughts/compulsive behaviors reduced, CY-BOCS was 16/40. The Clinical Global Impressions- Improvement (CGI-I) was employed to evaluate changes from baseline and resulted in a score of 2 (much improved). Data were confirmed six months after mepolizumab introduction: in April 2024 blood eosinophils were 0.08 x 10^9/L and serum ECP was 11.8 µg/L; ACT was 21/25, SNOT-22 was 38/110. No asthma exacerbations occurred and no OCS pulses were needed. The CY-BOCS confirmed the stability in clinical neuropsychiatric involvement. These results were confirmed after 9 months of mepolizumab treatment.

Discussion and Conclusion

OCD in childhood or adolescence is defined as an early-onset disorder and it could be associated with other psychiatric manifestations, such as mood disorders, disruptive behaviors, tics or tourette syndrome, speech disorders, nocturnal enuresis, Attention Deficit Hyperactivity Disorder (ADHD) [7].

The OCD etiology is unknown, however many genetic risk factors contribute to altering the neurotransmitters setting, involving the frontal-striatal-thalamic circuits.

Several analyses have focused attention on the SLC1A1/EAAT3 implication in the OCD pathogenesis: EAAT3 is a glutamate transporter, sequence variants in SLC1A1 gene could impact the glutamatergic neurotransmission increasing the OCD susceptibility [8]. Moreover, a role of the GRIN2B glutamate receptor gene has been also hypothesized [9].

A dysregulated immune response to bacterial infections, such as group A β-hemolytic streptococcus, has been linked to neuroinflammation in the basal ganglia, OCD, tics or ADHD [10]. The overregulation of immature monocytes-macrophages near the basal ganglia neurons, the release of pro-inflammatory cytokines and the alterations of cell metabolism are implicated in the neuroinflammatory process [11]. Similar mechanisms, triggered by molecular mimicry between bacterial-induced antibodies and antigenic epitopes on selected brain nuclei, have been associated with PANDAS/PANS and lead to the autoimmune disruption of the cortico-striato-thalamo-cortical circuits [3].

As regarding PANDAS/PANS, currently different scales for clinical evaluation of neuropsychiatric involvement are available and/or applicable: the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), the Yale Global Tic Severity Scale (YGTSS), Modified Overt Aggression Scale (MOAS), Columbia Impairment Scale (CIS), PANS Global Impairment Score (GIS), and Children's Global Assessment Scale (CGAS).

Recently, the PANS 31-Item Symptom Rating Scale has been developed to identify and measure the severity of PANS symptoms with encouraging preliminary results [12].

In this case, CGI scale has been used to evaluate clinical evolution. Moreover, we performed the children's Y-BOCS (CY-BOCS), considering that the OCD-related symptoms were the predominant and more severe ones.

A significant effect of treatment for OCD has been defined as a 35% reduction in Y-BOCS/CY-BOCS score combined with a CGI-I score of 1 or 2 (i.e., very much improved or much improved [13].

Elevated serum levels of Tumor Necrosis Factor (TNF)-alpha and IL-6 have been observed in OCD and PANS patients [14]. Even if key symptoms, such as anxiety and emotional lability, seem to be shared symptoms, a clusterization of PANS patients has been proposed with the identification of a cluster, operationally defined as "cytokine-driven/physiological symptoms", predominantly including cytokine-related behavioral symptoms such as food restriction, mydriasis, fatigue, depressive symptoms, psychotic symptoms and complex tics and more frequently associated to mycoplasma positive serology [15].

Recent evidence demonstrated the role of COVID-19 infection in worsening PANDAS/PANS, confirming the central role of cytokines setting in this disease [16].

Moreover, the folate receptor alpha autoantibodies (FRAAs) have been associated with cerebral folate deficiency and autism spectrum disorder (ASD). Both of these syndromes have overlapping characteristics with PANDAS/PANS, suggesting a potential role of folate metabolism abnormalities and autoimmunity in the development of the symptomatology [17]. The treatment with leucovorin has improved symptoms in ASD-FRAAs positive patients [18].

Evidence has demonstrated that PANS is not rarely associated with autoimmune or inflammatory diseases (or with a positive family history for autoimmune diseases): inflammatory back pain and arthritis were present in 21% and 28% of PANS patients, respectively, and 80% of these patients have autoimmune/inflammatory positive family history [19].

In our allergic, eosinophilic severe asthma and PANS patient dietary modifications, together with the introduction of probiotics and anti-IL5-directed monoclonal antibody treatment, have shown to improve neuropsychiatric involvement.

The dysbiosis contribution to neurological diseases should not be undervalued. Recent evidence has evaluated the association between gut dysbiosis and both neurological and psychiatric diseases such as Alzheimer's disease, Parkinson' disease, depression, anxiety, ASD, Schizophrenia and bipolar disorder [20].

The imbalance in intestinal microbiome impacts the nutrient availability and triggers the immune system, leading to a chronic inflammatory status.

Different factors contribute in causing gut dysbiosis, such as the use of antibiotics in early life and poor dietary habits and food choice. Moreover, the allergen proteases action gives a huge contribution to the epithelial barrier injury, directly involving the cellular junctions, inducing the activation of immune response and the chronic inflammatory damage [21].

Probiotics, prebiotics or the association of both are currently widely employed in the treatment of dysbiosis-related diseases. As regarding the employment of probiotics in patients diagnosed with neurological, psychiatric, or sleep disorders, promising results derive from RCTs in alleviating the neuropsychiatric symptoms [22].

The link between the microbiota and neuronal activity has been highlighted in recent years, leading to the concept of microbiota-gut-brain axis.

The connection between gut microbiota and the central nervous system is bidirectional, begins during intrauterine life and is affected by many intrinsic and extrinsic factors, such as the type of birth, lifestyle habits, living arrangements, dietary and medication intake [23].

Metabolic, endocrine, neural, and immunological pathways are all involved, with the contribution of the vagus nerve, the hypothalamic-pituitary-adrenal axis, bacterial metabolites, immune mediators and entero-endocrine signaling [24].

Gut pathogenic bacteria or toxic substances exposure induce the inflammatory response, modulating the neuronal activity via the release of neurotransmitters and cytokines [25].

Moreover, gut microbiota bacteria are involved in tryptophan metabolism (the indole, melatonin and serotonin precursor) and in short-chain fatty acid production, influencing the synthesis of neurotransmitters or their precursors, such as glutamate, GABA, dopamine and serotonin. Low levels of serotonin have been linked to neurological disorders.

The intestinal microbiota is responsible for synthesizing vitamins; in particular, the group B vitamins play a fundamental role in the development and maintenance of the neurological system trophism and function.

The role of gut microbiota in neurological function has been confirmed by the evidence of improvements in neurological disorders after fecal microbiota transplantation from a healthy control; moreover, the gut microbiota contribution in neurological dysfunction has been also proved by the appearance of neurological symptoms in healthy hosts after the fecal bacteria transplantation from donors with a neurological disorder [26,27]. The gut dysbiosis could be considered as a contributing factor in development of neuropsychiatric disorders and it could be also considered as a potential biomarker in a group of neurological diseases.

To our knowledge, the role of eosinophils and IL-5 in PANDAS/PANS has not been described in previous studies. The eosinophils' role in immunological type 2 (T2) diseases such as Eosinophilic granulomatosis with polyangiitis (EGPA) and hypereosinophilic syndrome (HES), in which the neurological involvement is common and mepolizumab has shown efficacy, is well known. However, less evidence is available about the potential contribution of T2 cytokines in autoimmune disorders that are characterized by a predominant type 1 (T1) inflammatory response. We have recently described a case of autoimmune hepatitis with liver eosinophilic infiltrate that showed good response to benralizumab [28].

The role of epithelial barrier dysfunction in allergic and autoimmune conditions such as asthma, atopic dermatitis, CRS, eosinophilic esophagitis, coeliac disease and inflammatory bowel disease, is well known. On the gut side, the leakiness of the gut epithelium has also been associated with autoimmune, metabolic and inflammatory diseases such as diabetes, obesity, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis and autoimmune hepatitis. Moreover, a 'leaky gut' and microbiome changes are suspected to contribute to inflammatory responses in Alzheimer disease, Parkinson disease, chronic depression and ASD [29].

Epithelial cytokines are released after the action of different types of stimuli such as allergen proteases, virus and bacteria, and toxic substances. The action of the IL-33/ST2 axis is not restricted as a promoter of T2 immune responses. IL-33 mediates activation of group 2 innate lymphoid cells (ILC2s), T reg cells, TH1 immune cells, CD8+ T cells, and NK cells as well as eosinophils, basophils, dendritic cells, iNKT cells, B cells, neutrophils and macrophage. IL-33 amplifies and stimulates the production of TNF-α, IFN-γ, IL-6, IL-17, and IL-2 by mast cells, basophils, NK and NKT cells [30].

Eosinophilic inflammation and epithelial dysfunction are strictly linked, being common features of many inflammatory diseases, including asthma, CRS with nasal polyps, EGPA, HES. Dysbiosis could be considered as one of the hallmarks of barrier damage similarly to the staphylococcal enterotoxins sensitization, which has been demonstrated to have a role in asthma and CRS phenotyping and evolution [31]. Allergen-induced epithelial barrier damage and eosinophilia could have contributed to development or worsening of neuropsychiatric symptoms in our PANS patient responsive to anti-IL5 and probiotic treatments. Although further studies are needed to confirm our hypothesis, the simultaneous treatment of both epithelial damage and eosinophilic inflammation led to the immunomodulation of injured barrier mechanisms and to changes in proinflammatory-anti inflammatory balance, favoring a better neurological outcome in our patient.

Moreover, the better asthma symptoms control, together with the OCS sparing, have undoubtedly contributed to the neurological improvements by favoring the reach of a better QoL in our patient.

Finally, waiting for further data of mepolizumab efficacy in PANS, we can sustain the safety of anti-IL5 treatment in PANS pediatric patients. If our results will be confirmed, targeting the barrier injury and the eosinophilic inflammation could be considered between the therapeutic options in PANS. Patient's parents consent has been obtained for publishing this case.

Abbreviations

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcical infection (PANDAS); Acute-onset Neuropsychiatric Syndrome (PANS); obsessive-compulsive disorders (OCD); Epstein-Barr virus (EBV); chronic rhinosinusitis (CRS); inhaler corticosteroid plus long acting beta-2 agonists (ICS/LABA); oral corticosteroids (OCS); quality of life (QoL); Children's Yale–Brown Obsessive–Compulsive Scales (CY-BOCS); Clinical Global Impressions- Severity (CGI-S); eosinophil cationic protein (ECP); asthma control test (ACT); Sinonasal Outcome Test 22 (SNOT-22); Clinical Global Impressions- Improvement (CGI-I); Attention Deficit Hyperactivity Disorder (ADHD); Diagnostic and Statistical Manual of Mental Disorders (DSM); Yale-Brown Obsessive Compulsive Scale (Y-BOCS); Yale Global Tic Severity Scale (YGTSS); Modified Overt Aggression Scale (MOAS); Columbia Impairment Scale (CIS); PANS Global Impairment Score (GIS), and Children's Global Assessment Scale (CGAS); Tumor Necrosis Factor (TNF); folate receptor alpha autoantibodies (FRAAs); autism spectrum disorder (ASD); type 2 (T2); Eosinophilic granulomatosis with polyangiitis (EGPA); hypereosinophilic syndrome (HES), type (T1); group 2 innate lymphoid cells (ILC2s).

Availability statement

The study materials could be obtained upon reasonable request to the corresponding author.

Conflicts of interest

The authors declare they have no conflicts of interest.

Acknowledgement

Not applicable.

Funding

Not applicable.

Author's contribution

All the authors approved the submitted version of manuscript.

All authors have contributed to the manuscript production. MDS and IB focused on manuscript writing; SC, CC, AP, AG, RM and MAZ focused on manuscript revision.

References

1. Caruso JM, Tung GA, Gascon GG, Rogg J, Davis L, et al. (2000) Persistent preceding focal neurologic deficits in children with chronic Epstein-Barr virus encephalitis. J. Child Neurol. 15: 791-796.
2. Fallon BA, Kochevar JM, Gaito A, Nields JA (1998) The underdiagnosis of neuropsychiatric Lyme disease in children and adults. Psychiatr. Clin. North Am 21: 693-703.
3. Ercan TE, Ercan G, Severge B, Arpaozu M, Karasu G (2008) Mycoplasma pneumoniae infection and obsessive-compulsive disease: A case report. J. Child Neurol. 23:338–340.
4. Müller N, Riedel M, Blendinger C, Oberle K, Jacobs E, et al. (2004) Mycoplasma pneumoniae infection and Tourette's syndrome. Psychiatry Res 129: 119-125.
5. Williams KA, Swedo SE (2015) Post-infectious autoimmune disorders: Sydenham's chorea, PANDAS and beyond. Brain Res 1617: 144-154.
6. Kumar A, Williams MT, Chugani HT (2015) Evaluation of basal ganglia and thalamic inflammation in children with pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection and tourette syndrome: A positron emission tomographic (PET) study using 11C-[R]-PK11195. J Child Neurol 30:749-756.
7. Garvey M, Jay G, Swedo S (1998) Topical review: PANDAS: The search for environmental triggers of pediatric neuropsychiatric disorders. Lessons from rheumatic fever. J. Child Neurol 13: 413-423.
8. Swedo SE, Leckman JF, Rose NR (2012) From research subgroup to clinical syndrome: Modifying the PANDAS criteria to describe PANS (pediatric acute-onset neuropsychiatric syndrome) Pediatr Ther 2: 113.
9. Peterson BS, Pine DS, Cohen P, Brook JS (2001) Prospective, longitudinal study of tic, obsessive-compulsive, and attention-deficit/hyperactivity disorders in an epidemiological sample. J Am Acad Child Adolesc Psychiatry. 40: 685–695.
10. Zike ID, Chohan MO, Kopelman JM, Krasnow EN, Flicker, et al. (2017) OCD candidate gene SLC1A1/EAAT3 impacts basal ganglia-mediated activity and stereotypic behavior. Proc Natl Acad Sci U S A 114: 5719-5724.
11. Kohlrausch FB, Giori IG, Melo-Felippe FB, Vieira-Fonseca T, Velarde LG, et al. (2016) Association of GRIN2B gene polymorphism and Obsessive Compulsive disorder and symptom dimensions: A pilot study. Psychiatry Res 243: 152-155.
12. Cosco TD, Pillinger T, Emam H, Solmi M, Budhdeo S, et al. (2019) Immune Aberrations in Obsessive-Compulsive Disorder: a Systematic Review and Meta-analysis Mol Neurobiol 56: 4751-4759.
13. Wohleb ES, McKim DB, Sheridan JF, Godbout JP (2015) Monocyte trafficking to the brain with stress and inflammation: a novel axis of immune-to-brain communication that influences mood and behavior. Front Neurosci 8: 447-450.
14. Bernstein GA, Khan MH, Freese RL, Manko C, Silverman M, et al. (2024) Psychometric Properties of the PANS 31-Item Symptom Rating Scale. J Child Adolesc Psychopharmacol 34: 157-162.
15. Mataix-Cols D, Fernandez de la Cruz L, Nordsletten AE, et al. (2016) Towards an international expert consensus for defining treatment response, remission, recovery and relapse in obsessive-compulsive disorder. World Psychiatry 15: 80-81.
16. Walls A, Cubangbang M, Wang H, Raiji M, Knight J, et al. (2015) Pediatric autoimmune neuropsychiatric disorder associated with streptococcus immunology: A pilot study. Otolaryngol. Head Neck Surg 153: 130-136.
17. Murphy TK, Patel PD, McGuire JF, Kennel A, Mutch PJ, et al. (2014) Characterization of the pediatric acute-onset neuropsychiatric syndrome phenotype. J Child Adolesc Psychopharmacol 25: 14-25.
18. Pallanti S, Di Ponzio M (2023) PANDAS/PANS in the COVID-19 Age: Autoimmunity and Epstein-Barr Virus Reactivation as Trigger Agents? Children (Basel) 10: 648.
19. Wells L, O'Hara N, Frye RE, Hullavard N, Smith E (2024) Folate Receptor Alpha Autoantibodies in the Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) and Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) Population. J Pers Med 14: 166.
20. Frye RE, Delhey L, Slattery J, Tippett M, Wynne R, et al. (2016) Blocking and Binding Folate Receptor Alpha Autoantibodies Identify Novel Autism Spectrum Disorder Subgroups. Front. Neurosci 10: 80.

21. Chang K, Frankovich J, Cooperstock M, Cunningham MW, Latimer ME, et al. (2015) From the PANS Collaborative Consortium Clinical evaluation of youth with pediatric acute-onset neuropsychiatric syndrome (PANS): Recommendations from the 2013 PANS Consensus Conference. J. Child Adolesc. Psychopharmacol 25: 3-13.

22. Naufel MF, Truzzi GM, Ferreira CM, Coelho FMS (2023) The brain-gut-microbiota axis in the treatment of neurologic and psychiatric disorders. Arq Neuropsiquiatr 81: 670-684.

23. Baglivo I, Quaranta VN, Dragonieri S, Colantuono S, Menzella F, et al. (2024) The New Paradigm: The Role of Proteins and Triggers in the Evolution of Allergic Asthma. Int J Mol Sci. 25: 5747.

24. Mitrea L, Nemeş SA, Szabo K, Teleky BE, Vodnar DC (2022) Guts imbalance imbalances the brain: A review of gut microbiota association with neurological and psychiatric disorders. Front. Med 9: 813204.

25. Góralczyk-Bińkowska A, Szmajda-Krygier D, Kozłowska E (2022) The Microbiota-Gut-Brain Axis in Psychiatric Disorders. Int J Mol Sci 23: 11245.

26. Houser MC, Tansey MG (2017) The gut-brain axis: is intestinal inflammation a silent driver of Parkinson's disease pathogenesis? NPJ Parkinsons Dis 3: 3.

27. Zhu F, Tu H, Chen T (2022) The Microbiota-Gut-Brain Axis in Depression: The Potential Pathophysiological Mechanisms and Microbiota Combined Antidepression Effect. Nutrients 14: 14.

28. Xiao L, Yan J, Yang T (2021) Fecal Microbiome Transplantation from Children with Autism Spectrum Disorder Modulates Tryptophan and Serotonergic Synapse Metabolism and Induces Altered Behaviors in Germ-Free Mice. mSystems 6: 6-8.

29. Ponziani FR, Caruso C, Baglivo I, Macagno F, Gasbarrini, et al. (2023) Autoimmune hepatitis with eosinophilic infiltration responsive to anti-interleukin-5 receptor treatment: a case report and literature review. Italian Journal ofMedicine 17.

30. Akdis CA (2021) Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions? Nat Rev Immunol 21: 739-751.

31. Caruso C, Colantuono S, Ciasca G, Basile U, Di Santo R, et al. (2023) Different aspects of severe asthma in real life: Role of Staphylococcus aureus enterotoxins and correlation to comorbidities and disease severity. Allergy 78: 131-140.

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