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From Zero to Overwhelm: PANS and PANDAS as Culprits Behind Sudden OCD in Pediatrics

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Abstract

Pediatric autoimmune neuropsychiatric disorders (PANDAS) and patient neuropsychiatric syndrome (PANS) are psychiatric illnesses characterized by a rapid onset of symptoms, including obsessive-compulsive disorder (OCD), behavioral symptoms and poor motor functions in children. The rapid onset and severity of OCD symptoms prompted investigations to provide an evidence-based intervention. This case series investigates the causes, diagnosis and treatment of the disease among children presenting with neuropsychiatric symptoms and acute-onset OCD. The diagnostic procedures provided grounds for the indication of medication. Methods: Bacterial infections, autoimmune cases and viral infections among 12 children with PANDAS and PANS were retrospectively studied. Pre- and post-treatment symptomatology were examined to monitor the effectiveness of interventions, following laboratory diagnostic approaches, including the Cunningham panel, serology, stool sample analysis, polymerase chain reaction (PCR), and bacterial cultures to determine the cause of the disorder. Diagnostic results informed treatments like non-steroidal anti-inflammatory drugs (NSAIDs), intravenous immunoglobulin (IVIG), fluid therapy, antibiotics, antivirals, steroids, and selective serotonin reuptake inhibitors (SSRIs) in each child. Post-treatment diagnostic results revealed remarkably improved symptoms of PANDAS and PANS, like inflammation and viral or bacterial infection. A combined therapy of antibiotics and NSAIDs or steroids was used to clear bacterial infections and manage inflammation. SSRIs and antiviral or fluid therapy were indicated for OCD and viral infections, respectively. Conclusions: OCD is a common comorbid disorder among children with PANS and PANDAS. Despite the severity and prevalence, OCD in children raises health concerns. The case series demonstrated the effectiveness of antibiotic therapy, RRIs, cognitive behavioral therapy, IVIG, steroids and NSAIDs in managing OCD in PANDAS and PANS, with a unique rationale of indication to every child.

Keywords: *PANS, PANDAS, Sudden Onset OCD, Pediatric OCD, Autoimmune Neuropsychiatric Disorders*

1.0 Introduction

PANDAS and PANS are neuropsychiatric complications that implicate abrupt OCD handwriting disorientation, personality changes, emotional liability, separation anxiety, and somatic symptoms, including urinary frequency, insomnia and enuresis (K. D. Brown et al. 2017; Verrotti et al. 2021). The natural history and systematic incidence are yet to be described. The annual incidence of the disorder is approximately 1 out of 11, 765 among children aged 3 to 12 years (Cunningham et al. 2023). Cunningham et al.'s study established that the overall incidence of PANDAS and PANS ranges between 2% to 4% among children aged 10 years and below.

Today, PANDAS and PANS, even though they do not implicate a significant health burden among children and the global economy, remain thought-provoking as clinicians need to understand their etiology, pathogenesis, diagnostic approaches and effective treatments. Global health organizations and concerned research institutions have deliberated studies to unveil insights into the neuropsychiatric disorder.

The American Academy of Child and Adolescent Psychiatry recommends screening for familial history, tics, stereotypes, and unusual movements. It is recommended that psychiatrists examine parents for unusual movements before indicating particular medications like psychotropic drugs (American Academy of Child and Adolescent Psychiatry,2018). An evidence-based intervention follows DSM-V diagnostic criteria for rational intervention. Currently, the commonly used diagnostic approaches include the rapid tests polymerase chain reaction test for viral infections, metabolic test, and bacterial cultures (Carlo Giaquinto Supervisore et al. 2017). The specificity of these diagnostic methods regards the association of PANDAS and PANS with viral infections, bacterial infections and autoimmune or immunomodulation. However, the current practice expands the diagnosis by including multiple laboratory tests for comprehensive results. Recently, additional tests like serology, stool sample analysis, and polymerase chain reaction (PCR) tests have been adopted to test for viral infections associated with PANDAS and PANS.

As treatment modalities rely on diagnostic approaches, the current research and developmental studies investigate gaps in the current intervention measures to determine evidence-based and effective interventions. The current practices indicate antibiotic treatments for streptococcal-induced PANDAS and PANS, SSRIs for OCD, NSAIDs to alleviate pain, fever and inflammation, antiretrovirals for viral infections, alongside intravenous immunoglobulins for autoimmune disorders (Katz et al. 2022a, 2022b; Kuo et al. 2014; Lim et al. 2023; Verrotti et al. 2021). The diagnostic approaches and unique interventions have indicated unique children in different settings. While the diagnostic measures have been deemed effective and accurate in some settings, they have been associated with inaccurate results in other settings. Similarly, the treatment approaches have been regarded as effective and ineffective in different settings.

Even though previous studies examined clinical features reported by PANDAS and PANS patients associated with streptococcal infects, viral infections or induced by autoimmune functions to enhance psychotherapy, pharmacological interventions through antipsychotics, antibiotics, NSAIDs, and to improve symptoms of OCD (Verrotti et al. 2021), there remain gaps that cannot be understated. This case series evaluates the clinical presentations, diagnosis and treatments implemented in five cases in a single psychiatric clinic.

2.0 Methods

Case Selection

This retrospective case series reviews the cases of children in a single psychiatric facility. The children diagnosed with ADHD and ASD included were cases from a single child psychiatry

clinic diagnosed using multiple diagnostic tools: the Cunningham panel to determine pre- and post-treatment symptomatology-associated alterations in ant-neuronal autoantibody titers (Shimasaki et al. 2020). This laboratory test examined levels of anti-dopamine D1 and D2L antibodies, anti-lysoganglioside-GM1 antibodies, anti-tubulin levels, and CaM kinase II levels to tell the patient's autoimmune dysfunction. Additional diagnostic procedures included complete blood counts (CBC), inflammation measurements C-reactive protein (CRP), and serology analysis for viral infections.

3.0 Case Presentations

Case 1

An 8-year-old female with no prior psychiatric history presented at the clinic with abrupt onset OCD and heightened anxiety following influenza infection (Supplementary Table 1). The initial symptoms include body aches, fever, and fatigue. After two weeks, her parents indicated that the girl developed sleep disturbance, anxiety, abrupt onset of compulsivity and poor concentration. A PCR test was performed to detect influenza virus RNA from her respiratory sample. The girl tested positive for the influenza virus and was put on ibuprofen 100mg/5mL and oseltamivir 75mg OD for two weeks. Additional treatments, including cognitive behavioral therapy, fluoxetine 40mg OD for two weeks and supportive education, were administered to alleviate compulsivity and obsessive behavior. The patient tested negative for influenza and was found with remarkable symptomatology improvements after two months of therapy.

Case 2

A 10-year-old male child was previously diagnosed with ADHD. Initially, he complained of swollen lymph nodes, sore throat, fatigue and fever. Two weeks later, the boy's hyperactivity and lack of concentration increased. Additionally, he displayed new obsessive-compulsive behaviors like hand washing and repetitive checking. An Epstein-Barr virus serology test was performed for IgG and viral capsid antigen. 1 gram of paracetamol TID was prescribed for eight weeks to alleviate symptoms of viral infections and inflammations. CBT, low doses of stimulants were administered to address symptoms of ADHD. Table 1 summarizes the comprehensive laboratory tests for the patient. Pre-treatment results indicate a positive test for EBV and elevated levels of white blood cells and c-reactive proteins.

Table 1: Laboratory test results for EBV

Test	Pre-treatment results	Post-treatment (7 weeks)
EBV VCA IgM	Positive	Negative
EBV VCA IgG	Positive	Positive
CBC	WBC: 13,500/µL	WBC: 6,800/µL
CRP	10.3 mg/L	2.1 mg/L

Case 3

A 9-year-old boy developed severe OCD and tics. After two weeks, the boy's condition worsened, and he was admitted to a psychiatric clinic. A nasopharyngeal swab PCR test was performed, confirming enterovirus infection. Further laboratory tests revealed elevated complete blood count and c-reactive protein, with a negative serology for enterovirus RNA, stool analysis and bacterial culture. Additionally, a bacterial culture indicated no streptococcal infection, as summarized in Table 2. The boy was placed under care for eight weeks. Mainly, he underwent body fluids replacement, and additional tests were performed to determine his health status.

Table 2: Pre-and post-treatment diagnostic results

Test	Pre-treatment results (14 days)	Post-treatment results (32 days)
Nasopharyngeal Swab PCR test	Positive for enterovirus RNA	Negative for enterovirus RNA
CBC	White Blood Cells: 12,600/µL	White Blood Cells: 6,400/µL
CRP	8 mg/L	2 mg/L
Enterovirus Serology	IgM: Positive	IgM: Negative
Stool analysis for Enterovirus (PCR)	Positive for enterovirus RNA	Negative for enterovirus RNA
Throat Swab (PCR and Culture)	Culture: No streptococcal bacterial growth	Culture: No streptococcal bacterial growth

After 8 weeks, a series of laboratory tests was performed. The nasopharyngeal swab PCR tested the patient negative for enterovirus: The CDC test found that the patient's WBC was 6400/µL, C-reactive protein had declined to 2mg/L, a negative serology test revealed IgM, whereas stool sample PCR tested negative for enterovirus protein. A throat swab culture did not reveal bacterial growth, signifying any streptococcal infections.

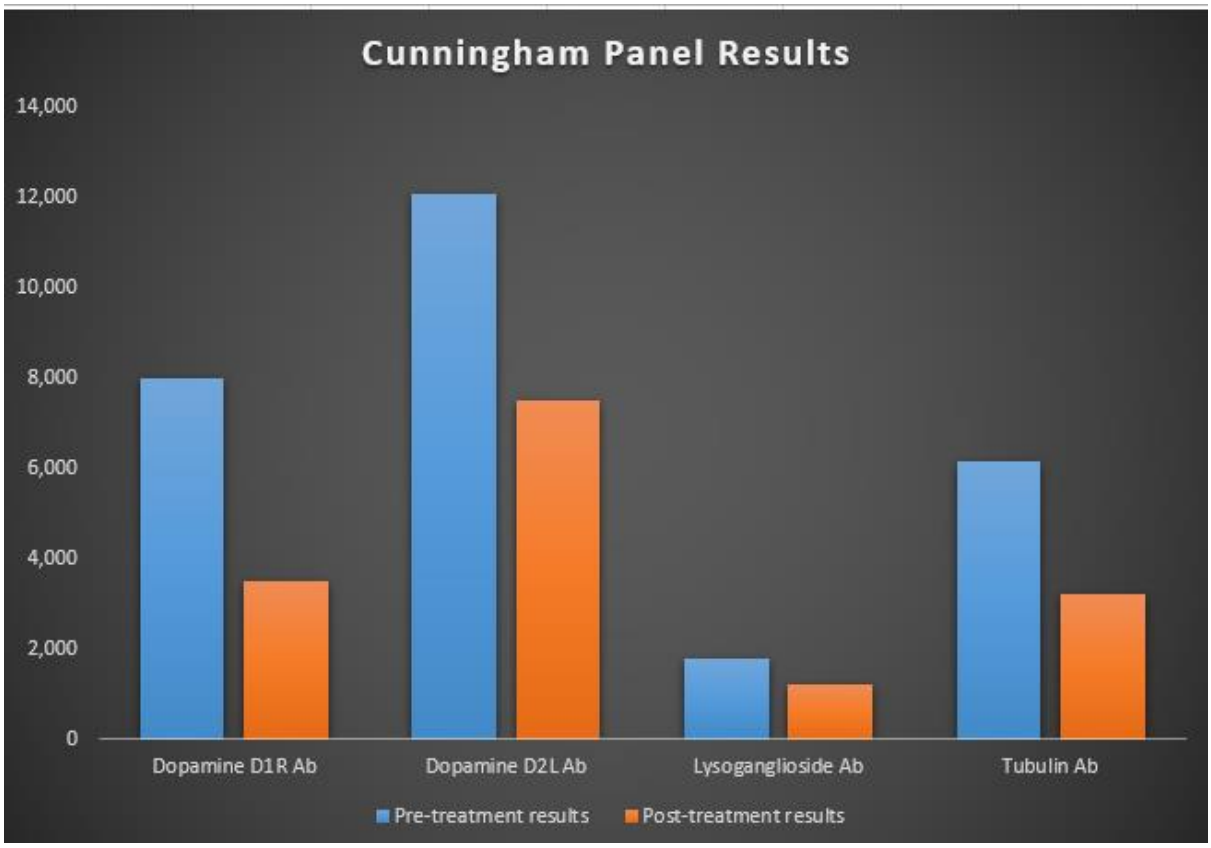
Case 4

An 11-year-old female patient reported at the clinic and presented severe obsessive-compulsive disorder, insomnia and sleep disturbances, mild anxiety, mood fluctuations, and symptoms of social withdrawal. The patient did not have a significant medical history. A polymerase chain test was performed for adenovirus DNA in her respiratory tract. A sterile swab was gently inserted in the patient's nasopharynx and swabbed around the nasopharynx for samples. The sample was analyzed, and she tested positive for adenovirus DNA. The 11-year-old patient was put on 1 gram of paracetamol TID for 8 weeks to reduce the inflammation. The patient's OCD symptoms were addressed through cognitive behavioral therapy and low doses of fluoxetine for three weeks. Additionally, the clinicians ensured the patient was hydrated.

Case 5

A 13-year-old male was admitted with autism and ADHD. The patient presented high levels of irritability, compulsivity, and impulsive behavior after a herpes simplex virus infection (HSV). The Cunningham panel tests confirmed PANDAS and treatment with Augmenting – 400mg/day for 4 weeks. Pre- and post-antibiotic intervention results suggested improved symptomatology after the treatment period. While CaM Kinase II activation reduced from 180% to 125% after the treatment, dopamine D1R – from 8000 to 3500 - and D2l – from 12050 to 7500 -, Ab reduced below the recommended thresholds (Figure 1). Likewise, the test revealed reduced lysoganglioside Ab from 1780 to 1200, whereas tubulin Ab reduced from 6133 to 3200. The patient was put on IVIG at a rate of 0.8 mL/kg/hour for 20 minutes to restore the desired concentration of immunoglobulins (Supplementary Table 2).

Figure 1: Pre- and post-antibiotic treatment results



Case 6

This case involves a 7-year-old female child presenting with an acute onset of severe OCD at the clinic. The child presented with symptoms like compulsive hand cleaning and obsessive fears of contamination. A bacterial culture confirmed that the beta-hemolytic streptococcus bacteria caused the symptoms. The child was put on amoxicillin 400mg/day, ibuprofen 100mg/5mL and CBT for 4 weeks. An assessment was performed, and the results showed remarkable improvement in symptomatology. Further, the child's symptoms improved in the next 8 weeks.

Case 7

This case involves a 10-year-old boy presenting with sleep disturbances, separation anxiety, depression, nervousness and OCD rituals. Clinicians took a swab on his laryngopharynx and

he tested positive for scarlet fever. Also, the boy tested positive for penicillin allergy, promoting the indication of 50mg/kg erythromycin body weight for 10 days, 1 gram of paracetamol TID for 10 days, and oral prednisone 2mg/kg for 30 days. The patient was scheduled for a follow-up after 30 days, after which CBT was indicated for another 30 days. The symptoms significantly improved.

Case 8

In this case, a 10-year-old female child is brought to the clinic by grandparents. They complained that the child does not eat, citing the risk of contamination, infection or poisoning. The girl also has noticeable intrusive thoughts. The clinicians indicated 25mg OD sertraline for 14 days and scheduled the patient for a follow up. During the follow-up, her grandparents reported remarkable improvement in symptoms.

Case 9

This case involves a 9-year-old female child presenting with severe onset of OCD. Her family complains that she fears coming home, thinking that she will be harmed. Clinicians attributed her condition to environmental triggers and prescribed IVIG and CBT. A 20-minute of 0.8 mL/kg/hour of IVIG was indicated for 8 weeks to alleviate the symptoms. After 8 weeks, the patient was assessed for symptoms and severity of OCD (Supplementary Table 3). The clinical results showed decreased intensity and frequency of intrusive thoughts, counts of rituals, low anxiety and improved sleep.

Case 10

This case involves a 9-year-old female presenting at the clinic. The girl had a history of severe OCD, with parents indicating that she is compulsive nail-cutting and fears sharp objects. These symptoms began after testing positive for streptococcus bacteria, but did not comply to the dose. The patient was put on amoxicillin 250mg and oral prednisone 2mg/kg for 10 days. After completion of the dose, the patient underwent further tests that revealed improved symptoms of OCD, normal range of CRP and anti-streptolysin O titer (Table 3). Additionally, the clinicians indicated weekly CBT sessions to address the patient's OCD symptoms.

Table 3: Pre- and post-treatment tests

Diagnostic test	Pre-treatment results	Post-treatment results
Throat culture	Positive for Group A streptococcus bacteria	Negative
CRP	Increased	Normal
Anti-streptolysin O titer	Increased	Normal
Cognitive evaluation	Acute and severe symptoms of OCD	Very low symptoms of OCD

Case 11

This case involves a 7-year-old male with a history of neuropsychiatric complications. On this day, he presented at the clinic with flu-like symptoms. A physical exam revealed viral infection, and he was put on antibiotics and antivirals - 400mg/day azithromycin for 3 days, 75mg Tamiflu OD for 10 days, and ibuprofen 100mg/5mL for 10 days. CBT was administered every 72 hours to check on his OCD symptoms. 15 days later, the boy was examined again for symptoms of the viral infection and severity of OCD symptoms. The boy was found with remarkable improvements.

Case 12

A 9-year-old male child is admitted to the psychiatric clinic with sudden onset of extreme anxiety, emotional liability, dissatisfaction and compulsive checking behavior. The clinicians swabbed his mouth and tested for Group A streptococcal bacteria, which produced positive results. Immediately, 250mg/day of azithromycin and 1 gram of paracetamol TID were prescribed and administered. On the third day, a physical exam was performed to check compulsivity and anxiety. The boy reported remarkable alleviation of symptoms and was ready to go back to school.

4.0 Discussion

This retrospective study sought evidence on the diagnostic approaches, symptoms, and potential interventions for children with PANDAS and PANS. The rapid onset of severe OCD, tics, high levels of irritability, compulsivity, impulsive behavior, and other symptoms characterizes this neuropsychiatric complication. The disorder has been associated with low quality of life and poor motor skills, including poor handwriting among children under the age of 12 years. Yet, the current clinical practices are questioning the legitimacy and effectiveness of antibiotic therapy, NSAIDs, IVIG, psychotherapy and cognitive behavioral therapy.

Previous investigations reveal that viral infections are commonplace in PANDAS and PANS. Influenza, adenovirus, EBV, HSV, and SARS-CoV-2 infections have been found among children with PANDAS and PANS (Lim et al., 2023). In the literature on PANDAS and PANS, these infections are associated with symptoms like tics, exacerbated obsession, mood instabilities, and anxiety. These results profoundly suggest that viral infections provoke immune responses, neuroinflammation and reactivation reactions in inflammatory processes.

In this case series, case 3 showcased enterovirus in PANDAS and PANS through a series of laboratory tests. After eight weeks of management at the clinic, the patient's CRP declined from 8mg/L to 2mg/L, whereas WBC increased from 12600/µL to 6400/µL. Similarly, case 2 produced a positive test for EBV virus with a complementary reduction in white blood cells, from 13500/µL to 6800/µL, and CRP from 10.3 mg/L to 2.1 mg/L. The positive tests for IgM and IgG indicated a recent viral infection.

Physiologically, the normal range of white blood cell count is 4500 to 1100 cells per microliter (Katz et al. 2022b). A decline in cell count corresponds with immunological response to the infection. Likewise, a positive test for immunoglobulins and reduced CRP represents a recent viral infection and associated inflammation.

These outcomes are aligned with reports from previous studies where enterovirus infections were associated with an increase in CRP and CBC beyond homeostatic levels (Kuo et al. 2014). Fundamentally, the nasopharyngeal swab and stool PCR test confirmed a negative test for enterovirus after eight weeks of fluid therapy. The patient had tested positive for the virus upon admission. On the other hand, the throat swab, both PCR and culture, did not find streptococcal

infection in pre-and post-treatment. The 9-year-old boy's symptoms, tics and severe OCD declined after the eight weeks of treatment, marking a major health improvement.

On the other hand, the pathogenesis of PANDAS and PANS, and the co-occurrence with OCD, features viral infections. Often, severe obsessive-compulsive disorder, insomnia and sleep disturbances, mild anxiety, mood fluctuations, and symptoms of social withdrawal characterize the disorder among children. Particularly, social withdrawal and tics are common among school-going children (Murphy et al. 2013), as witnessed in the fourth case. The American Academy of Child and Adolescent Psychiatry recommends differential diagnosis for comorbid disorders and combined therapy, including selective serotonin reuptake inhibitors.

Murphy et al. asserted the importance of rapid viral tests. Viral infections result in inflammation and provoke immune functions, which are synonymous markers of PANDAS and PANS. Nasopharyngeal swabs are ideal for collecting tissues and mucus containing viral DNA (Gamucci et al. 2019). The girl tested positive for adenovirus, justifying the indication of paracetamol and fluoxetine.

The interventions at addressing the inflammation and symptoms of OCD. Looking at the literature on NSAIDs and SSRIs establishes extensive efficacy and safety. Previous studies strongly associate infections, especially viral infections, with psychiatric complications. Adenovirus and SARS-COV2 are commonly associated with psychiatric symptoms (Verrotti et al.,(Verrotti et al. 2021). In response to the inflammations, NSAIDs have been indicated to combat the fever and inflammation. In cases 1 and 2, 100mg/5mL effectively reduced inflammation. On the other hand, 1 gram of paracetamol effectively managed the inflammation in case 4 and case 7. This evidence emphasizes the importance of NSAIDs in inflammation and fever management in PANDAS and PANS. The low dose of fluoxetine reduced symptoms of OCD in cases 1, 2, and 4, proving the effectiveness of SSRIs in managing OCD symptoms. Other studies reported that NSAIDs are given within 30 days as prophylactic (K. D. Brown et al. 2017). This treatment shortens the onset of flares among patients with remitting or relapsing PANDAS and PANS.

Apart from viral infections, investigations enumerated streptococcal infections as a trigger of PANDAS and PANS (Hesselmark and Bejerot 2019; Wells et al. 2024). Previously, researchers declared the immunomodulatory interventions inconclusive. Antibiotic therapy draws from the immunomodulatory effects of bacterial infections. This prompted further studies to establish the most appropriate interventions.

Despite limited evidence, previous studies demonstrate the efficacy of antibiotics against streptococcal infections in PANDAS and PANS (Burchi and Pallanti 2018). This evidence aligns with the previous studies on the efficacy and safety of antibiotic therapy against streptococcus infections in PANDAS and PANS, especially the beta-hemolytic streptococcus bacteria. The case series found that Augmentin 400mg/day eradicated bacterial infection and improved key symptoms like inflammation and pain, as reported in the fifth case in this series. Additionally, the finding supports study outcomes reporting 250mg/day of azithromycin or orally administered 250mg penicillin BID as effective approaches to eradicating bacterial infections.

Antibiotic therapy has been reported to be an effective intervention against neurological symptoms (Verrotti et al. 2021). Antibiotics clear the streptococcal strains that induce immune responses that characterize PANDAS and PANS through inflammation, and compulsive and obsessive behaviors. Significantly, the Cunningham panel test revealed that the 13-year-old's auto-antibodies, dopamine D1R and D2L, tubulin, and lysoganglioside reduced below the threshold. Pre-treatment test results revealed levels higher than the homeostatic limits. Thus,

antibiotic treatment significantly improves neuronal functioning, alleviating symptoms associated with blocking antibodies' binding sites. Hesselmark et al.'s investigation reported that antibiotic therapy produces higher patient satisfaction than cognitive behavioral therapy, NSAIDs and SSRIs. These findings align with the previous investigations as patients treated with antibiotics – azithromycin, amoxicillin, and Augmentin - reported remarkable alleviation of symptoms, including compulsivity and anxiety.

This case series established the effectiveness of fluoxetine and sertraline in OCD management. Particularly, 25mg sertraline produced remarkable symptomatology improvement within 14 days, as reported in case 8. Clinically, the girl reported improved symptoms during the follow-up period, making sertraline a better option for managing OCD symptoms. This offers multiple choices when making a clinical decision.

Antibiotic therapy takes care of penicillin allergy that may affect the indication of this class of medication. In case 7, erythromycin substituted penicillin due to allergy. A higher dose was indicated as erythromycin is not a drug of choice in upper respiratory tract infections (Parasrampuria et al. 2016). In cases 7 and 10, prednisone was indicated to complement the antibiotics, mainly treating inflammation. This medication was indicated to alleviate the inflammation in the brain and symptoms. Corticosteroids have been regarded as effective interventions for rapid onset and relapsing PANDAS and PANS. This is justified by the improved symptoms by the end of the second month of treatment (K. Brown et al. 2017).

IVIG therapy has been deemed an effective alternative for children who do not benefit from antibiotic therapy, steroids, psychotherapy and NSAIDs. In this series, IVIG therapy restored the optimal IVIG pooled concentration in the blood, restoring immune functions. The 20-minute infusion of 0.8 mL/kg/hour IVIG restored physiological levels of immune cells, as demonstrated in case 5. The therapy substantially reduced the severity of symptoms (Carlo Giaquinto Supervisore et al. 2017). The rationale of IVIG treatment is to reduce PANDAS' and PANS' symptomatology to improve the patient's quality of life. Nonetheless, this intervention is unsuitable for children with ongoing infections.

In addition to this, case 9 demonstrates the effectiveness of IVIG therapy after a treatment period of 8 weeks. The first and foremost impact of this intervention is remarkable sleep improvement, and alleviation of anxiety, alongside obsessive and compulsive behaviors. The patient's intensity and frequency of obsessive behavior on harm to her family was alleviated. This impacted on her overall quality of life. When the stress and anxiety on potential harm to her family was alleviated, the patient's quality of life improved. Lastly, the CBT intervention marked a significant improvement in symptomatology in case 9 and 10. The patient's panic attacks and social behavior significantly improved following the intervention. CBT imparts coping skills (Thienemann et al. 2017), hence, improving quality of life.

5.0 Conclusion

Even though PANDAS and PANS were defined in 1998, the diagnosis, treatment and symptomatology remain unclear and less understood among clinicians. Psychiatrists and researchers have been seeking evidence on causes and effective treatments to address the acute onset of compulsivity and other motor symptoms. Yet, the findings have not been convincing.

The case series unmasks solid evidence of expanding pediatric care through evidence-based management of PANDAS and PANS. Strong evidence of the effectiveness of NSAIDs, low doses of SSRIs, fluid therapy, psychotherapy, IVIG, and antibiotic intervention emerged in the retrospective investigation. To justify the treatment measures, the diagnostic criteria established that autoimmune, streptococcal, viral infections like adenovirus, influenza and

EBV alter immune functions, provoking neuropsychiatric symptoms. Thus, the interventions seek restoration of the immune system within the homeostatic limits.

The pharmacological interventions addressed particular complications associated with OCD, PANS, and PANDAS. Antibiotics are administered to clear bacterial infections whereas the antivirals clear viral infections. Clearing these pathogens restores immune functions. The NSAIDS and steroids mitigate inflammation as the infections are associated with immune modulation, hence, elevation of the inflammatory pathways. CBT was administered to address the rapid and new onset of psychiatric complications associated with OCD.

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Supplementary Table 4: Overview of Patient Symptoms, Viral Triggers, and Treatment Responses

Patient	Age	Previous Conditions	Viral Trigger	Key Symptoms	Treatment	Outcome
1	8	None	Influenza	OCD, Anxiety	Antibiotics	Significant Improvement
2	10	ADHD	Epstein-Barr Virus	Worsening ADHD, OCD	Antibiotics	Marked improvement
3	9	None	Enterovirus	OCD, Tics	Antibiotics	Significant improvement
4	11	Mild Anxiety	Adenovirus	Severe OCD	Antibiotics	Marked Improvement
5	13	Autism, ADHD	Herpes Simplex	Irritability, OCD, Impulsive Behavior	Antibiotics, IVIG	Significant Improvement
6	7	None	Scarlet fever	Compulsive hand-cleaning, and obsessive fears of contamination	Antibiotics, NSAIDS, and CBT	Significant symptom improvement.
7	10	None	Bacterial infection	Sleep disturbances, separation anxiety, depression, nervousness, and OCD rituals	NSAIDS, antibiotics, and steroids	Significant symptom improvement.
8	10	None	Environmental stressors	OCD, fear or going home and thoughts of being harmed	SSRIs	Alleviated symptoms
9	9	None	Environmental triggers	OCD	CBT, IVIG,	Improved sleep, low anxiety, decreased counts of rituals, intensity and frequency of intrusive thoughts.
10	9	Severe OCD, compulsive nail-cutting and fear of sharp objects	Environmental triggers, streptococcus infection	Severe OCD, compulsive nail-cutting and fear of sharp objects	Antibiotics and steroids	Normal CRP, anti-streptolysin O titer, negative Group A streptococcus, and very low symptoms of OCD.
11	7	Neuropsychiatric complications	Flu: viral infection	Flu-like symptoms, OCD	NSAIDs, antibiotics and CBT	Improved symptoms of OCD
12	9	none	Bacterial infection	Extreme anxiety, emotional liability, dissatisfaction and compulsive checking behavior	NSAIDs, antibiotics	Symptom alleviation

Supplementary Table 5: Pre- and post-treatment laboratory tests

Test	Pre-treatment results	Post-treatment results	Reference Range
Dopamine D1R Ab	8,000	3500	< 4,000
Dopamine D2L Ab	12,050	7500	< 8,000
Lysoganglioside Ab	1,780	1200	< 1,280
Tubulin Ab	6,133	3200	< 4,000
CaM Kinase II Activation	180%	125%	53-130%

Supplementary Table 6: Pre- and post-treatment assessment

Measurement Tool	Pre-treatment outcomes	Post-treatment outcomes
Yale-Brown Obsessive-Compulsive Scale	**29**	**10**
Children's Global Assessment Scale	**43**	**72**
Clinical Global Impressions-Severity score	**7**	**1**
Clinical Global Impressions-Improvement Score	**7**	**2**