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Case Series

Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections-presentation and challenges to care in a Nigerian community

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ABSTRACT

To present a case series of paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), highlighting the clinical presentation, diagnostic process, and management strategies. PANDAS is characterized by the sudden onset of neuropsychiatric symptoms such as obsessive-compulsive disorder (OCD) or tic disorders following streptococcal infections. The condition poses diagnostic and therapeutic challenges due to its complex presentation and overlap with other neuropsychiatric disorders. This case series highlights three children in a Nigerian community diagnosed with paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). Presentations included the abrupt onset of obsessive-compulsive behaviour, tics, and neuropsychiatric disturbances linked to prior streptococcal infections. A detailed clinical evaluation, laboratory testing, timely diagnosis, and individualized multidisciplinary management approach, including antibiotics, immunomodulatory therapies, and psychosocial support, resulted in significant clinical improvement and successful management of PANDAS. These cases underscore the importance of considering PANDAS in children with abrupt neuropsychiatric symptoms post-streptococcal infection and illustrate the benefits of a comprehensive management approach to optimize outcomes.

Keywords: Autoimmune, Neuropsychiatric disorders, Children

INTRODUCTION

PANDAS is an acronym for paediatric autoimmune neuropsychiatric disorders associated with Streptococcal Infections. It is a subcategory of PANS (Paediatric Acute-onset Neuropsychiatric Syndrome). It is a rare condition that was first described by Swedo in a cohort of children describing five distinct criteria for its diagnosis, which include abrupt "overnight" OCD or dramatic, disabling tics; a relapsing-remitting episodic symptom course; young age at onset; the presence of neurologic abnormalities; and an association between onset of symptoms and Group A streptococcal infection.[1] After the description of PANDAS by Swedo, there were certain misconceptions about the mechanism of the disorder.[1-4]

However, with further research, more studies have substantiated PANDAS and described the pathophysiology as a cascade of autoimmune mechanisms triggered by molecular mimicry, leading to cross-reactivity between streptococcal antigens and basal ganglia neurons or cholinergic interneurons in the brains of affected children.[4-7] The neuropsychiatric symptoms of PANDAS in children are often frightening to caregivers due to their sudden onset in a previously normal child.[8,9] In addition to antibiotic therapy, management requires addressing the immune-mediated pathophysiology, as is

the case in Sydenham chorea (a neurological manifestation of rheumatic fever) and other post-streptococcal sequelae.[8,10,11]

Generally, demographic data on PANDAS is moderate and varies across different geographical locations.[12] Most available reports/studies are from the United States and Europe.[7,13,14] This is possibly due to greater awareness and availability of diagnostic and management facilities in these regions.[15] In contrast, despite high rates of streptococcal infections in low- and middle-income countries (LMICs), including Nigeria, there is minimal epidemiological data relating to PANDAS in these regions.[16,17] Plausible reasons for the low prevalence of PANDAS across different regions include lack of awareness of PANDAS among healthcare providers, poor access to specialized paediatric neurology or psychiatric services, paucity of confirmatory diagnostic tests, and cultural interpretations of neuropsychiatric manifestations of illnesses.[18,19]

Research to develop reliable test panels is ongoing, as some available ones, such as the Cunningham Panel, have demonstrated poor specificity.[15] The diagnostic process is challenging due to a lack of disease-specific biomarkers, clinical overlap with other symptoms, and scarcity of tools for monitoring the levels of autoantibodies like anti-neuronal antibodies.[8,9,15] The need for the standardization of screening methods and the developing of easy-to-administer tools to enhance the management of PANDAS in resource-poor regions cannot be overemphasized.

CASE SERIES

Case 1

A 4-year-old female presented with acute obsessive-compulsive disorder (OCD) symptoms, motor tics, and emotional lability. Her speech became difficult to comprehend as her words were no longer precise. There was associated emotional lability described as unusual and excessive crying, irritability, separation anxiety as well as abnormal oppositional behavior, which parents termed recent onset of stubbornness. The motor tics were severe enough to affect her gait, so she staggered and could not walk unassisted. The past medical history revealed a preceding pharyngitis episode (painful swallowing, refusal of food, drooling of saliva, purulent and bloody discharge from the throat for 1-2 weeks for which she was first treated by a nurse in her neighborhood and subsequently by a pediatrician who administered intramuscular medications.

Clinical examination revealed inflamed tonsils with purulent exudates, bilateral convergent squint and ataxic gait. Elevated antistreptolysin O (ASO) titers 6400IU/ml (normal limit <200 IU/ml) and Anti-DNAse 620.8µ/l (normal limit <250 µ/l) confirmed recent streptococcal infection. Subsequent assays showed a steady decline till the ASO titre was within normal limits. The requested Cranial CT scan was not done due to financial constraints. Treatment included amoxicillin-clavulanate, a short course of corticosteroids, clonidine, and pyridoxine. The symptoms gradually resolved over eight weeks, and follow-up assessments up to one year showed no recurrence of symptoms.

Case 2

An 11-year-old boy presented with a sudden onset of vocal tics (repeating sounds and phrases) and complex motor tics (shrugging of the shoulder and repetitive brief jerks of different muscle groups) such that the patient could not stand without support. Abnormal behavior included aggression, excessive eating, undue fixation on a previous altercation with a classmate and anxiety about possible harm which was initially considered to be a bipolar disorder by the referring doctor and patient was given a stat dose of Chlorpromazine and then a one-week course of fixed combination of Tabs Fluoxetine/Olanzepine 25/3 before referral to a Paediatric Neurologist.

Further review revealed a preceding history of sore throat and painful swallowing as well as Peptic ulcer disease with an elevated Helicobacter Pylori assay for which he received the triple therapy regimen consisting of Amoxicillin, Clarithromycin, and Omeprazole. The ASO titre was markedly elevated (1600 IU/ml compared to the normal limit of < 200 IU/ml) while the White blood cell count was within normal range (7.3x109/L) with neutrophilia. Cranial CT scan reported no significant cranio-cerebral abnormality. Management included Amoxicillin-Clavulanate, Cognitive Behavioural Therapy (CBT), and family counselling, resulting in progressive recovery over three months.

Case 3

An 11-year-old female experienced a sudden onset of ocular tics (eyelid blinking, eye rolling, and staring) and motor tics (jerking of the body, broad-based gait, and a tendency to stumble or trip if not well-supported). The patient had episodic visual hallucinations described as reaching out to pick up things that did not exist. She also had intermittent episodes of clouded/blurry vision and staring with eyes wide open, but was unable to see or touch the examining doctor.

At other times, she was able to see clearly and identify the people around her as well as the colour of their clothes. She was hyperactive, constantly on the move, and unable to sit still (akathisia). She had choreiform movements in distal muscles (hands), a change in her handwriting (dysgraphia), and a decline in school performance. The patient could hear and sing well, and her speech was not slurred. She was often observed trying to demonstrate the songs she sang without being prompted to do so. There were episodes of heightened anxiety and agitation followed by unexplainable crying

(emotional lability). Streptococcal pharyngitis was identified as the throat swab yielded heavy growth of β-hemolytic streptococcus, and the ASO titre was markedly elevated. Computerized tomography of the brain reported no focal orbital pathway mass lesion or anomaly, as well as no focal intracranial mass lesion. Treatment measures included antibiotics, corticosteroids, Olanzapine, Piracetam, and family counseling with close observation.

Cognitive behavioural therapy and immunotherapy were later introduced, achieving substantial symptom improvement within four weeks. The cost of Human immunoglobulin (IVIG) was out of reach of the parents. Furthermore, the patient's treatment was intermittently interrupted by her parents' perception of the cause of the illness and their search for alternative healing methods. She was later discharged against medical advice as her parents cited financial constraints and their decision to address the spiritual cause of the illness by taking her to a prayer house for spiritual healing.

In all three cases, there was no family history of neuropsychiatric or autoimmune diseases, no family history of OCD and no previous history of tics. Their immunizations were up-to-date. Consent was obtained as well as ethical approval from the Federal Medical Centre, Onitsha, FMC/OSHA/ETH.C/073/011

DISCUSSION

This case series provides important insights into the presentation, diagnosis, and management of Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) in a resource-limited setting in Nigeria. It highlights the underdiagnosed nature of PANDAS in Sub-Saharan Africa, its clinical heterogeneity, and the challenges to care in communities where cultural beliefs and limited resources impact health-seeking behavior and therapeutic decisions.

Clinical presentation and diagnostic challenges

The cases demonstrate the hallmark features of PANDAS, including the abrupt onset of obsessive-compulsive disorder (OCD), motor and vocal tics, emotional lability, and other neuropsychiatric symptoms. These findings align with Swedo et al.'s diagnostic criteria, and subsequent literature emphasizing the episodic nature of symptoms triggered by Group A Streptococcal (GAS) infections, elevated antistreptolysin O (ASO) titers and anti-DNAse levels observed in all three cases further support a streptococcal etiology.[20,21]

The absence of a family history of neuropsychiatric or autoimmune conditions in these patients suggests the role of environmental triggers and individual susceptibility, reinforcing the role of molecular mimicry and autoimmune mechanisms. On the other hand, Lougee et al reported that the rate of tic disorders and OCD in first-degree relatives of children with PANDAS were higher than those reported in the general population.[22] Recent studies suggest a multifactorial aetiopathogenesis for PANS and PANDAS, characterized by an interaction between environmental and genetic factors.[23]

The absence of specific biomarkers and reliance on clinical criteria complicates PANDAS diagnosis. Misdiagnoses, as seen in one case initially labeled as bipolar disorder, highlight the overlap of PANDAS symptoms with primary psychiatric conditions. In addition, although magnetic resonance imaging (MRI) is the gold standard for assessment of basal ganglia changes and is preferred to Computerized Tomography (CT scan), none of the patients' caregivers could afford it. Limited access to such advanced diagnostic tools and autoantibody assays further hampers diagnosis in low-resource settings like Nigeria. These findings underscore the importance of clinical acumen and microbiological confirmation in diagnosing PANDAS.

Barriers to care in resource-limited settings

The management of PANDAS in Sub-Saharan Africa is hindered by several factors. Lack of awareness among healthcare providers often results in PANDAS going unnoticed or misdiagnosed resulting in delays in treatment in many parts of the world. Untreated or unrecognized PANDAS has been associated with an increased risk of OCDs during adulthood.[24-26]

Additionally, cultural beliefs attributing neuropsychiatric symptoms to spiritual causes frequently lead families to seek traditional or alternative therapies, as seen in one case where treatment was interrupted for spiritual healing. Similar trends have been reported in other studies across rural communities in Nigeria, where traditional practices are often the first point of care for mental health conditions.[27-29]

Financial constraints also pose significant challenges. The high cost of immunomodulatory therapies such as intravenous immunoglobulin (IVIG) makes them inaccessible for most patients, as demonstrated in one case where the family could not afford IVIG despite its potential benefits. These barriers necessitate the development of cost-effective, locally adaptable diagnostic and treatment protocols.

Management and therapeutic interventions

All three cases in this series were successfully managed with a combination of antibiotics, corticosteroids, cognitive behavioral therapy (CBT), and family counseling. Antibiotics, such as amoxicillin-clavulanate, played a key role in eradicating GAS and reducing symptom severity. These findings align with evidence supporting the efficacy of antibiotics in managing streptococcal infection-associated neuropsychiatric symptoms. However, antibiotics alone may not fully

resolve neuropsychiatric manifestations, necessitating adjunctive therapies.[30-32]

Oral corticosteroids were used in severe cases to modulate inflammation and autoimmunity, resulting in significant symptom improvement. Immunomodulatory therapies such as plasmapheresis and IVIG, though effective in severe, refractory cases.[11, 33] were not feasible due to their prohibitive costs. Complementary evidence suggests that alternative therapies, such as azithromycin or NSAIDs, may provide affordable options in resource-limited settings, though the adverse effects of prolonged use should be considered.[34–36]

Cognitive behavioural therapy and family education were instrumental in improving patient outcomes and addressing misconceptions about PANDAS. In communities where supernatural attributions for illnesses are common, culturally sensitive counseling is essential to promote adherence to biomedical treatments.

Implications for practice and recommendations

This case series underscores the need for increased clinical awareness of PANDAS among healthcare providers in Nigeria. Early recognition and intervention are critical to improving outcomes, especially given the relapsing-remitting nature of the condition. Efforts should focus on training healthcare workers to identify PANDAS, integrating its diagnosis into routine paediatric care, and developing standardized management protocols tailored to resource-limited settings.

Collaboration between pediatricians, neurologists, psychiatrists, and immunologists is vital for comprehensive care. Public health interventions, such as routine screening for GAS infections and community-based education, may help reduce the burden of PANDAS. Future research should explore the epidemiology, pathophysiology, and cost-effective management strategies for PANDAS in Sub-Saharan Africa.

CONCLUSION

A diagnosis of PANDAS, though not commonly made in the study area, significantly affects children and their families. This case series highlights the presentation of PANDAS in a Nigerian community, emphasizing its diagnostic challenges, clinical variability, and management barriers. Despite these challenges, early recognition, combined with appropriate antibiotic therapy, immunomodulation, and psychosocial support, can lead to substantial symptom improvement. A multidisciplinary approach and sustained efforts to raise awareness are essential for optimizing care for children with PANDAS, particularly in resource-limited settings. Continued research and awareness are essential to optimise the diagnosis and management of PANDAS in resource-limited settings.

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