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Case Report

Steroid sensitive nephrotic syndrome as a potential contributor to pediatric-onset psychosis: a case-based hypothesis

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ABSTRACT

Steroid-sensitive nephrotic syndrome (SSNS) is a type of primary glomerulopathy that results in multiple complications, including edema and hyperlipidemia. Most existing studies indirectly attribute psychiatric manifestations in SSNS to corticosteroid therapy, while its etiological role in neuroinflammation remains rarely discussed. This article aims to explore this association through a unique case report. An investigation of available English-language literature providing insight into pathophysiology of SSNS, neuroinflammation, and psychosis was done. Information collected was reviewed and analysed for quality and relevance. We present a rare case of a 13-year-old male with SSNS, who exhibited escalating oppositional behavior, emotional dysregulation, and aggression, resulting in a parental request for discontinuation of steroids and immunosuppressants. Despite cessation of medication, symptoms progressed to worsening of psychosis with multiple psychiatric hospitalizations, raising concerns for a potential link between SSNS and neuropsychiatric origin. Collateral history revealed discontinuation of immunosuppressant therapy in early childhood, indicating its limited significance in the current presentation. This case elucidates the potential correlation between SSNS and psychosis in pediatric patients from a pathophysiological and neuropsychiatric point of view, necessitating further investigations into its underlying mechanism.

Keywords: Steroid-sensitive nephrotic syndrome, Psychosis, Neuroinflammation, Cytokines, Case report

INTRODUCTION

Nephrotic syndrome (NS) is a clinical syndrome characterized by massive proteinuria (>40mg/m^2) and hypoalbuminemia (<30 g/L) leading to hyperlipidemia, edema, and various other complications.[1] SSNS, also called idiopathic nephrotic syndrome, is identified by responsiveness to 4-6 weeks of corticosteroid therapy.[2] Despite the limited understanding of its pathophysiology in current literature, remission of symptoms in response to use of immunosuppressants like corticosteroids indicates predominant involvement of the immune system in disease pathogenesis.

Psychosis can be broadly identified by a distorted perception of reality that interferes with basic daily functioning. It comprises a collection of symptoms, including hallucinations and delusions, which may co-occur with formal thought disorders. Psychosis may present as a part of a psychiatric disorder, as commonly seen in schizophrenia, schizoaffective disorders, and bipolar disorders (during manic episodes) amongst others, or as a consequence of an underlying medical condition.[3,4]

In existing reports regarding SSNS patients presenting with psychosis, there is a substantial amount of evidence supporting corticosteroid use as a causative factor.[5,6] Meanwhile, literature directly correlating SSNS, and the mechanisms behind this disease, to the development of psychosis is sparsely available. This paper documents a rare case of a pediatric patient with chronic history of SSNS, presenting with worsening psychiatric manifestations despite having ceased corticosteroid use in the distant past. This creates an opportunity for further investigations into the pathophysiological and neuropsychiatric basis for psychosis in SSNS.

CASE REPORT

We report the case of a 13-year-old male diagnosed with SSNS during early childhood. At age 3, he was initiated on a combination of corticosteroids and mycophenolate mofetil for management. The patient continued this treatment for three years, during which the parents observed that he was exhibiting increasingly aggressive behaviors, emotional dysregulation, and oppositional attitudes. Steroid therapy was discontinued due to the parents' concern regarding its possible side effects. SSNS was stabilized and mycophenolate mofetil was also discontinued.

The patient later experienced a relapse of NS and was restarted on mycophenolate mofetil, which was continued for approximately two more years. During this period of relapse, the patient demonstrated worsening oppositional behavior, severe aggression, and emotional instability. Parents requested to stop mycophenolate out of concern that it may have contributed to the patient's deterioration. Medication was stopped but the patient's symptoms continued to intensify as he began to have paranoid delusions and auditory hallucinations.

The patient had undergone eight psychiatric hospitalizations due to multiple severe episodes of psychosis prior to presenting at the clinic. His behavior was unpredictable and unmanageable. His daily functioning was severely impaired. Available documentation on clinical management from previous hospitalizations was limited, but parents stated that the patient's symptoms did not improve despite having undergone trials of risperidone and other antipsychotics. Presently, the patient has been initiated on Aripiprazole 400 mg, a once-a-month injection. His symptoms have stabilized, and he is regularly reevaluated.

DISCUSSION

It is becoming increasingly evident that neuroinflammation plays a significant role in the development of psychiatric conditions. Cytokines are common mediators of inflammation. In a study assessing the role of cytokines in NS, varying levels of 13 cytokines were observed in SSNS prior to initiation of corticosteroid therapy. Furthermore, levels of IL-5, IL-7, IL-13, IFN-γ, and TNF were suppressed following treatment with immunosuppressants, implying their significance in disease pathology.[7] Other literature has also correlated increased levels of IL-1β, IL-8, and IL-6 with relapse in SSNS.[8]

Certain proinflammatory cytokines like IL-1α, IL-6, and TNF-α are known to rapidly cross the blood-brain barrier, either through simple diffusion (in areas where the blood-brain barrier is insufficient) or via a retrograde axonal transport system. Some evidence suggests that cytokines also damage the blood-brain barrier, increasing permeability to other molecules that can also cause inflammation.[9,10] Existing studies linking psychiatric manifestations to cytokine-mediated neuroinflammation suggests that mania may be associated with a surge in cytokines, specifically IL-2, IL-6 and IL-4.[11]

In addition to cytokine-associated neuroinflammation, nephrotic syndrome may also be linked to certain neurological complications like posterior reversible encephalopathy syndrome (PRES). PRES is a rare disorder affecting the central nervous system and is characterized by vasogenic edema in the white matter of the parietal and occipital regions of the brain.[12-14] This contributes to neurotoxicity which may also lead to the presentation of psychiatric symptoms as seen in some reports.[15]

In the case discussed, it is interesting to note that the patient exhibited persistent symptoms of psychosis regardless of discontinuation of corticosteroids and mycophenolate mofetil. While this does not entirely rule out the possibility of medication-induced psychosis, it calls to attention the role of neuroinflammation in the pathogenesis of psychosis symptoms. Presently, the mainstay treatment for SSNS is steroids, however, it is frequently implicated as a causative factor for psychosis.[5,6] Further research is essential to create improved treatment strategies for mitigating psychiatric symptoms that arise from underlying medical conditions. Moreover, there is a substantial scope for exploring the diverse etiological factors leading to neuroinflammation which may provide a breakthrough for more targeted and effective interventions.

CONCLUSION

This case highlights the previously overlooked pathophysiological basis for psychiatric symptoms in steroid-sensitive nephrotic syndrome, necessitating further research into alternative and more etiology-specific

treatment methods. The unique presentation of this child, in which he exhibited worsening symptoms despite cessation of medication and subsequent absence of pharmacological influence, underscores the potential correlation between pathophysiology and neuropsychiatry. This analytical perspective encourages deeper investigations into the mechanisms of neuroinflammation and pathogenesis of psychosis with the intention of discovering more effective therapeutic approaches.

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