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Case Report

Steroid-Induced Mania in a 12-Year-Old Adolescent: A Case Report

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INTRODUCTION

Corticosteroids, known for their potent anti-inflammatory and immunosuppressive effects, are essential in treating a wide range of conditions, from autoimmune disorders to allergic reactions. Systemic corticosteroids, such as oral prednisolone and prednisone, commonly are used in pediatric respiratory illnesses.[1] Despite their therapeutic benefits, these medications have been associated with neuropsychiatric side effects in 2% to 60% of cases.[2] In a comprehensive review by Kenna and colleagues,[3] mania or hypomania was the most common presentation, observed in 54.5% (30/55) of adult cases. However, these complications remain underrecognized and often misdiagnosed in children.

Potential risk factors for steroid-induced neuropsychiatric symptoms, which are explored in this case, include recent viral infections (e.g., COVID-19), metabolic disturbances such as hypoalbuminemia, concurrent use of CYP3A4 inhibitors, and prior high-dose corticosteroid exposure, which may create a sensitization effect.

This case report describes steroid-induced mania in a 12-year-old male with a history of corticosteroid use and recent COVID-19 infection, illustrating the unique diagnostic and therapeutic challenges in pediatric populations. Alternative diagnoses, including pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and delirium, are considered. The case emphasizes the importance of maintaining a high index of suspicion for neuropsychiatric side effects in children undergoing corticosteroid therapy.

CASE REPORT

A 12-year-old male presented to the hospital with acute behavioral changes three days after initiating a treatment regimen of amoxicillin and a five-day course of prednisolone (50 mg daily) for group A streptococcal pharyngitis. His past medical history included expressive language disorder, speech delay, and reactive airway disease requiring intermittent corticosteroid inhalers. He also had experienced previous viral infections and a mild SARS-CoV-2 (COVID-19) infection five months prior to presentation.

The patient exhibited symptoms consistent with a severe manic episode with psychotic features, including hypersexuality, disinhibition, psychomotor agitation, decreased need for sleep, paranoia, and irritability, which escalated to aggression toward his dentist. Psychotic features included persecutory delusions. His affect was labile, alternating between inappropriate euphoria ("giddy and giggly") and irritability, along with pressured speech and motor restlessness (fidgeting). These symptoms marked a stark deviation from his baseline behavior.

Suspecting an allergic reaction, the pediatrician discontinued prednisolone and prescribed diphenhydramine 25 mg every four-six hours, which the patient took for two days prior to hospitalization. However, his mental status deteriorated, with increasing confusion, agitation, excessive laughter, unusual vocalizations, and socially inappropriate behavior. Due to concern for PANDAS, his pediatrician recommended hospital admission.

On the medical floor, the psychiatry consultation team noted disorganized, tangential, and illogical thought processes, as well as paranoid delusions directed at both family and hospital staff. He was distractible, intrusive, disinhibited, and exhibited self-stimulatory behaviors. The clinical picture strongly suggested an acute manic episode with psychotic features, likely triggered by corticosteroid use. However, steroid-induced psychosis and delirium also were considered in the differential.

A full medical workup to evaluate for PANDAS included a complete blood count, metabolic panel, thyroid studies, and a comprehensive autoimmune panel (antinuclear antibody, antinuclear antibody, anti-double-stranded DNA antibody, anti-extractable nuclear antigen, complement levels, anti-neutrophil cytoplasmic antibodies, anti-cardiolipin, lupus anticoagulant, anti-N-methyl-D-aspartate receptor, and anti-α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor antibodies). Inflammatory markers, including erythrocyte sedimentation rate (reference range: 0-15 mm/hr) and C-reactive protein (reference range: <0.3-1.0 mg/dL), also were obtained. All results were unremarkable.

Neuroimaging with non-contrast head computed tomography was normal. Lumbar puncture was not performed. A rapid strep test was positive, confirming recent group A streptococcal infection. Anti-streptolysin O (ASO) titer measured four days after a 1 g ceftriaxone dose, and approximately 10 days post-infection, was 186 (reference range: 0-199). Based on clinical findings and laboratory results, PANDAS was considered unlikely.

Collateral history from the patient's parents and grandmother confirmed a dramatic change from his typical behavior. Premorbidly, he was described as respectful, quiet, and academically successful, with no history of psychiatric disorders, behavioral issues, learning difficulties, or substance use. He alternated living with his divorced parents weekly and had a longstanding close relationship with his grandmother. Developmentally, he had experienced mild speech delays requiring therapy until fifth grade but otherwise met all milestones. Birth history was notable for severe maternal hemorrhage due to placenta accreta requiring a five-day hospitalization.

Following psychiatric assessment, risperidone 0.25 mg orally twice daily was initiated; however, due to refusal, he was switched to intramuscular olanzapine 2.5 mg at bedtime. He also received a single dose of intramuscular penicillin to complete treatment for streptococcal pharyngitis. Despite treatment, the patient continued to exhibit

hypersexuality, disorganized behavior (e.g., attempting to drink from a remote control), and hallucination-like experiences (e.g., calling for deceased relatives), necessitating transfer to inpatient psychiatry.

On the adolescent psychiatry unit, the patient showed minimal engagement, poor insight, perseveration, anxiety, and restlessness. Risperidone 0.25 mg twice daily was resumed but led to minimal improvement. By Hospital Day 4, disinhibition and inappropriate behaviors worsened, requiring another intramuscular olanzapine dose. Risperidone was titrated to 0.25 mg in the morning and 0.5 mg at bedtime, which resulted in gradual symptom improvement and discharge on Hospital Day 9.

The patient had 12 outpatient follow-up visits over the course of one year (Appendix A). At the first visit, one-week post-discharge, hypersexuality, agitation, and impulsivity had resolved with medication adherence, although the patient had poor recall of the events surrounding hospitalization. Approximately six weeks later, his family tapered the medication without medical supervision, leading to symptom recurrence and an urgent follow-up visit. He presented with disorientation, distractibility, expansive affect, confabulation, and impaired insight. While hypersexuality did not recur, collateral sources reported belligerence, impulsivity, and behavior inconsistent with the patient's self-report. Risperidone was reinstated and titrated to 0.5 mg twice daily, leading to symptom resolution within two weeks.

In subsequent follow-ups, the patient remained stable. A cautious taper was attempted during winter break, reducing risperidone to 0.25 mg in the morning and 0.5 mg at bedtime. Another taper during spring break three months later was well tolerated. Over the next several months, two additional 0.25 mg tapers were completed, and risperidone was fully discontinued at the one-year mark. At his most recent visit, the patient remained stable off medication for one month.

DISCUSSION

Previously documented cases of steroid-induced mania in pediatric populations reveal a spectrum of presentations, ranging from mild symptoms resolving after steroid discontinuation to severe episodes requiring intensive psychiatric intervention (Appendix B). Several key patterns emerge from these reports: steroid-induced mania can occur in individuals without a personal or family history of psychiatric illness, and symptoms typically develop rapidly, often within the first week of treatment, regardless of the route of administration (inhaled, oral, or intravenous).[4-6] Our patient's progression from behavioral changes to frank mania with psychosis within three days of starting prednisolone aligns with this characteristic rapid onset, offering an important diagnostic clue.

Our patient's presentation illustrates several diagnostic pitfalls. Initial consideration of PANDAS was deemed unlikely for several reasons: the patient's age was outside the typical four - nine year range,[7] he lacked hallmark features such as tics or obsessive-compulsive behaviors, and, most notably, his symptoms emerged acutely within days of streptococcal infection, rather than the gradual onset (3 to 12 months) described in a large case-control study of 75,000 children.[8] Additionally, his ASO titer of 186 was not significantly elevated. According to diagnostic criteria, ASO titers should ideally be obtained at symptom onset (within two weeks) and repeated four - eight weeks later, with a fourfold rise considered supportive of a streptococcal trigger.[9] As Prato et al.[10] note, PANDAS typically is associated with marked elevations in ASO and anti-DNase B titers, along with inflammatory markers such as erythrocyte sedimentation rate and C-reactive protein (CRP), none of which were present in our patient. While a limitation of this case was the absence of repeat ASO testing, the normal one-time titers, absence of obsessive-compulsive disorder or tics, and rapid symptom onset collectively argued against a PANDAS diagnosis.

The diagnostic picture was further complicated by signs of possible superimposed delirium, including confusion and disorientation, potentially worsened by diphenhydramine's deliriogenic effects. In alignment with Kenna et al.,[3] who reported a mean resolution time of 9.6 days for steroid-induced delirium, our patient's confusional symptoms improved relatively quickly, while manic features persisted, supporting the presence of comorbid delirium and mania rather than either condition alone. This underscores the complexity of steroid-induced neuropsychiatric presentations.

Several risk factors likely contributed to our patient's psychiatric episode. His prescribed prednisolone dose (50 mg daily) exceeded the 40 mg threshold associated with increased risk for neuropsychiatric side effects.[11] Individual variability in steroid metabolism and distribution further may influence susceptibility, particularly in the presence of CYP3A4 inhibitors or hypoalbuminemia, which increase free corticosteroid availability (odds ratio 2.2).[12] While our patient had previously tolerated both inhaled and oral corticosteroids for respiratory illnesses, cumulative exposure may have contributed to vulnerability. Sullivan et al.[13] reported a 1.29-fold increase in the risk of new adverse effects with more than four corticosteroid prescriptions in a year.

The timing of our patient's psychiatric manifestations also suggests the role of preceding inflammatory insults. While he had previously tolerated corticosteroids, mania emerged only after sequential infections, a mild COVID-19 infection five months prior, followed by streptococcal pharyngitis. Emerging research indicates that COVID-19 may predispose children to psychiatric sequelae through elevation of pro-inflammatory cytokines such as interleukin-6, tumor necrosis factor-α, and CRP.[14,15] This inflammatory cascade may be particularly disruptive during periods of neurodevelopmental vulnerability in brain regions such as the amygdala, hippocampus, and prefrontal cortex.[16,17]

The glucocorticoid vulnerability hypothesis provides a potential mechanistic framework, positing that high densities of glucocorticoid receptors in limbic and prefrontal regions[18,19] render these areas susceptible to corticosteroid-induced changes. Chronic corticosteroid exposure has been associated with dendritic retraction in the hippocampus,[20] possibly extending the window of neuronal vulnerability. This may explain how prior inflammatory insults (e.g., viral and bacterial infections) and corticosteroid exposure culminated in a "perfect storm" for steroid-induced mania in our patient.

Understanding this pathophysiology informs therapeutic decision-making. While tapering corticosteroids is a standard first-line approach,

effective in 94% of cases in Lewis and Smith's series and half of those in Appenzeller's study,[3] our experience demonstrates that tapering alone may be insufficient. For steroid-induced mania specifically, Kenna et al.'s[3] systematic review highlights successful outcomes using antipsychotics and/or mood stabilizers, including haloperidol (with or without lithium), risperidone, quetiapine, olanzapine (alone or with valproate), carbamazepine, lithium, and lamotrigine plus clonazepam.

This is consistent with previously reported cases. Khan et al.[4] reported resolution with steroid discontinuation alone, while Couturier et al.[5] and Cassidy et al.[6] described patients requiring antipsychotics, mood stabilizers, and benzodiazepines. Notably, the patient who received inhaled corticosteroids alone had the shortest duration of symptoms (48 hours) and recovered with steroid discontinuation alone, likely due to lower systemic and central nervous system exposure.[4-6]

Our patient required prolonged treatment with risperidone, which may reflect the complexity of his case, including inflammatory priming from prior infections. Following a year of stabilization, he was successfully tapered off risperidone and remained symptom-free for one month without medication.

CONCLUSIONS

This case offers several important clinical takeaways:

1. Education: Patients and families should be thoroughly counseled about potential neuropsychiatric side effects of corticosteroids. Education should occur at treatment initiation, during therapy, and before any dose adjustments. In our case, lack of counseling led to symptom recurrence following unsupervised medication tapering.
2. Monitoring: Structured psychiatric monitoring protocols are essential, particularly during high-dose steroid treatment and dose changes. Follow-up should extend beyond corticosteroid discontinuation, as recovery may be delayed.
3. Risk Assessment: This case illustrates the need for a comprehensive risk assessment strategy. Our patient's episode was likely precipitated by a convergence of risk factors: recent viral and bacterial infections, high-dose steroid exposure, and anticholinergic use. Current monitoring guidelines for long-term corticosteroid use emphasize physical parameters, weight, glucose, blood pressure, lipids, and bone density, but do not adequately address neuropsychiatric monitoring.[21,22]

We propose the development of a standardized neuropsychiatric risk assessment tool to complement existing physical monitoring protocols. This tool should account for both non-modifiable (e.g., age, psychiatric history) and modifiable factors, such as concurrent medications (e.g., CYP3A4 inhibitors), albumin levels, sleep hygiene, psychosocial stressors, and substance use. Such a multidimensional approach could help guide clinicians in identifying high-risk patients and implementing timely preventive interventions.

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Keywords: glucocorticoids, mania, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections

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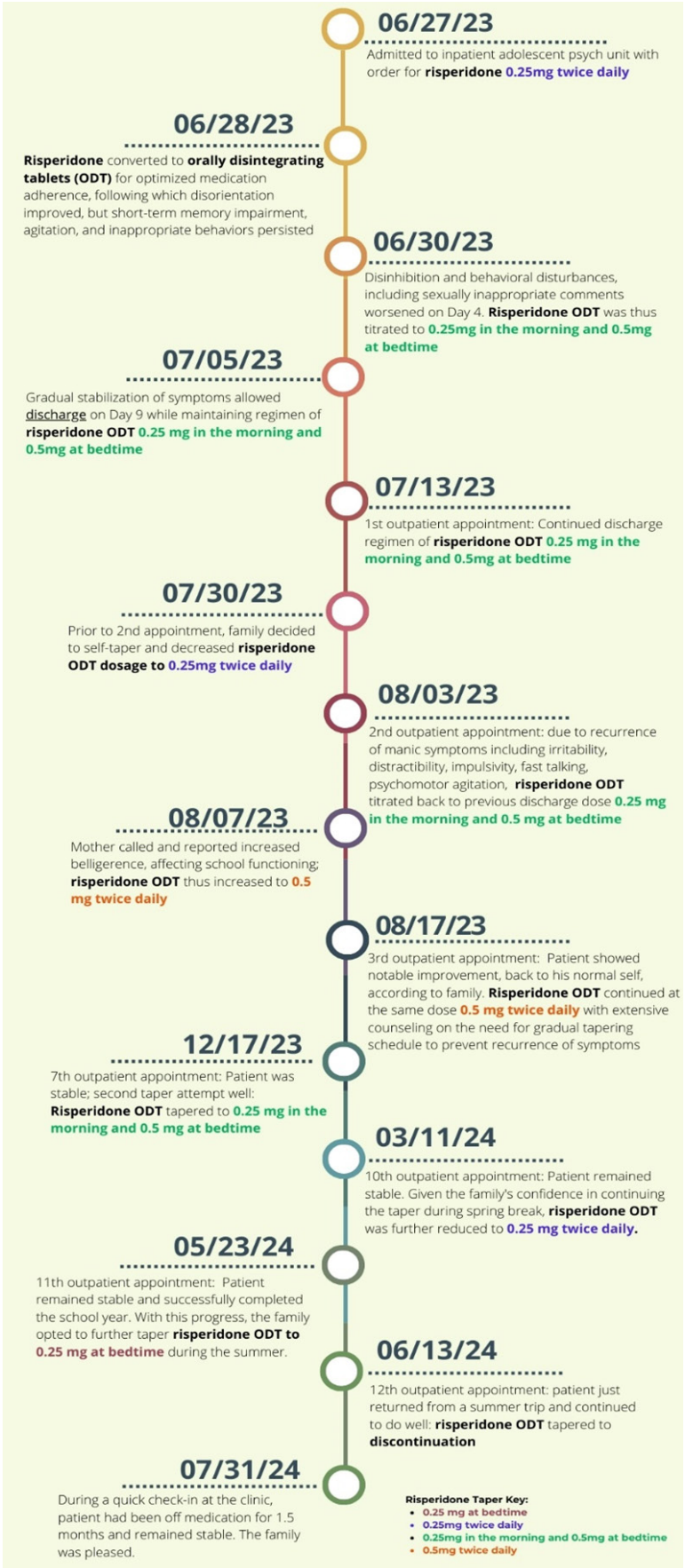
APPENDIX A

Timeline of Risperidone Taper



APPENDIX B

Comparative Table of Three Published Cases of Steroid-induced Mania in Pediatric Patients.

Case	Demographics	Medical & Substance History	Corticosteroid Info	Psychiatric Symptoms	Treatment & Response	Duration of Treatment
Couturier et al.[5]	Age: 15, Gender: F	Asthma; Weekly alcohol and marijuana use; Significant recurrent major depression (father, maternal grandfather)	Salbutamol, fluticasone, and prednisone 25 mg daily + clarithromycin 250 mg BID; Prednisone advanced to 50 mg daily for five days; Previous exposure: Short-term oral prednisone (30–50 mg daily); IV methylprednisolone 160 mg daily × three days => oral prednisone up to 80 mg daily	Elated mood, hyper-religiosity, pressured speech, auditory/visual hallucinations	Olanzapine was titrated from 5 mg to 10 mg at bedtime over five days, Valproic acid to 750 mg daily, and Lithium to 600 mg daily. Symptoms resolved in 7, 9, and 20 days and remained stable despite prednisone re-exposure (45 mg daily for seven days with clarithromycin 250 mg BID).	20 days of acute treatment and six months of planned maintenance therapy
Khan et al.[4]	Age: 16, Gender: F	Asthma; No substance or family history	Beclomethasone inhaler 42 µg one – two times each nostril twice daily; Previous exposure unknown	Euphoric mood, religious grandiosity, flight of ideas, impulsivity (self-mutilating behavior), racing thoughts, pressured speech, decreased need for sleep, increased energy	Discontinuation of inhaler. Mania resolved 48 hours after cessation of corticosteroid inhalers; no antipsychotics or mood stabilizers.	48 hours
Cassidy et al.[6]	Age: 17, Gender: M	Acute Lymphocytic Leukemia (ALL); No substance or family history	Dexamethasone 10 mg daily for 28 days; Previous exposure unknown	Affective lability, decreased need for sleep, increased energy, talkativeness, grandiosity	Risperidone 1 mg BID and Lorazepam 1 mg BID were titrated to a total of 4 mg daily. The patient was discharged on Risperidone 1 mg qam and 2 mg qhs, tapered to 0.25 mg at bedtime, remaining stable despite intermittent dexamethasone (up to 20 mg daily)	Three weeks of acute inpatient treatment; outpatient tapering duration not specified