Steroid-induced Psychosis in a Patient without a Previous Psychiatric History

Carol Avila, Rio Bravo Family Medicine Residency Program, Clínica Sierra Vista; Raquel Horowitz, Family Medicine Residency, The Brooklyn Hospital Center; Hector Arreaza, Rio Bravo Family Medicine Residency Program, Clínica Sierra Vista

Corresponding Author

Carol Andreina Avila Hernandez, avilaca@clinicasierravista.org
Rio Bravo Family Medicine Residency Program , Clínica Sierra Vista

ABSTRACT

This is a 45-year-old Hispanic male with retinitis pigmentosa, no previous psychiatric history, and no known substance use disorder who was treated with 80 mg of oral prednisone, tapered off over 6 weeks before undergoing eye surgery. One week after completing the treatment, he went missing, and when he was found, he described visual and auditory hallucinations, as well as paranoid thoughts. He demonstrated a calm affect, flat mood, decreased expressiveness, poor eye contact, and fluent speech. The thought process was linear and goal-directed. Thought content was negative for hallucinations and paranoia, but delusional, with limited judgment and insight into his current situation. Negative suicidal or homicidal ideations. He was admitted to the hospital for further work up for encephalopathy. Images and laboratory results were irrelevant. The patient's encephalopathy completely resolved the following day, and no antipsychotic medications were administered. The psychiatric assessment was compatible with steroid-induced psychosis based on the acute onset, the brief psychotic episode with complete resolution of symptoms (5 days), precipitated by stressors (combined effects of an incapacitating disease). With this case presentation, we want to raise awareness among primary care physicians of the occurrence of steroid-induced psychosis and highlight the importance of patient education including their caregivers, as the cornerstone for an early recognition and prompt management of neuropsychiatric adverse events of glucocorticosteroids.

Keywords: *Steroids, Corticosteroids, Psychosis, Steroids related Delusions, Steroids related Hallucinations, Neuropsychiatric side effects, High-dose prednisone, Hispanic*

1. Case Presentation

This is a case of steroid-induced psychosis in a 45-year-old Hispanic male from Venezuela without a previous psychiatric history. His medical history is significant for a rare, hereditary eye disorder, that causes a gradual and complete vision loss called Retinitis Pigmentosa; currently, this disease has no known cure. He was undergoing an investigational gene therapy delivered by subretinal injection in the U.S.A. Prior to the surgery, a high dose of oral prednisone was given starting at 80 mg tapered down over 6 weeks. One week after completing the immunosuppressive treatment, he went missing. A day before going missing, he was reportedly not on his usual self. He blamed his sister for “hacking” his cell phone and moved out of his sister's house. He was found three days later. He described organized visual and auditory hallucinations not threatening in content, as well as paranoid thoughts. He endorsed beliefs such as: ‘doctors implanted a tracking device on my eye’, ‘cars belonging to gangs followed and harassed me’, ‘despite walking for hours, I kept hearing a voice telling me I wouldn't escape’. Additionally, he described hearing high-pitched sounds in both ears.

On admission to the hospital, he was afebrile and hemodynamically stable, but dehydrated, endorsing muscle aches in his legs. He denied any past psychiatric history including symptoms, diagnosis, medications, psychotherapy trials, hospitalizations, self-injurious behavior, self-harm, harm to others, as well as a negative history of neurologic or neurocognitive disorders, and no current or past substance use disorder. Information was confirmed by his sister. His mental status evaluation demonstrated a calm affect, cooperative, flat mood, decreased expressiveness, poor eye contact, low volume but fluent speech, and oriented in person, place, time, and date. His thought process was linear, and goal directed. His thought content was negative for hallucinations and paranoia, but he was delusional, with limited judgment and insight into his current situation. Negative suicidal or homicidal ideations. He was admitted with the initial diagnosis of encephalopathy.

A head scan ruled out acute or chronic intracranial hemorrhage, mass, infection, or infarct. Calf muscles were tender to palpation bilaterally with creatine kinase elevation (3381). Exertional rhabdomyolysis in the setting of walking for long hours was suspected and treated accordingly. Negative test results were obtained for alcohol levels, acetaminophen, salicylates, urine toxicology, HIV, and syphilis. Thyroid studies, cyanocobalamin, thiamine, folate, and ammonia levels were normal, excluding other potential diagnoses like substance use disorder, electrolyte imbalance, infection, and neoplasms; but medication-induced psychotic disorder remained among the possible cause of the patient's psychosis. The patient continued to be stable through the night and the encephalopathy completely resolved the next morning without administering antipsychotic medications.

During the psychiatric evaluation, the patient explained that having vision problems affected his job performance leading to feelings of sadness and frustration. The psychiatric assessment was compatible with steroid-induced psychosis based on the acute onset, complete resolution of symptoms after 5 days, precipitated by stressors (combined effects of an incapacitating disease). There were no indications to start psychotropic medications, and the patient was advised to discuss the episode of steroid-induced psychosis with providers to start antipsychotic medications if future immunosuppressive therapies were needed.

Discussion

There is not much knowledge on the pathophysiology of the neuropsychiatric complications of corticosteroids, however, there is an established correlation between corticosteroids and impairment in cognitive function.[1,2,3,4,5] It is thought to be related to abnormalities of the hypothalamic-pituitary-adrenal axis, particularly glucocorticoid negative feedback dysfunction.[1,2,3,5]

The most common and expected side effects of corticosteroid use are an increased risk of infections, leukocytosis, hyperglycemia, gastritis, and weight gain, among others.[3] Less frequently, neuropsychiatric manifestations may occur, including steroid-induced psychosis (delusions and hallucinations) as well as, mania, depression, anxiety, insomnia, and irritability.[3,6,7,8] Individuals may exhibit overt aggression and violence, posing a danger to others; and in the most extreme situations, suicide attempt.[3,6,9]

Steroid-induced psychosis involves the acute onset of delusions or hallucinations related to corticosteroid therapy causing functional impairment with complete resolution of symptoms within days and up to three or more weeks.[2] It is considered a substance-induced psychotic disorder by the Diagnostic and Statistical Manual of Mental Disorder, 5th edition (DSM-5).[3] A history of neuropsychiatric conditions, drug use disorder, electrolyte imbalance, infections, and neoplasms, is required to be ruled out before making the diagnosis of Steroid-induced psychosis because this is a diagnosis of exclusion.[2]

The Boston Collaborative Medication Surveillance Program monitored 10,062 hospitalized patients receiving glucocorticoids and identified acute psychiatric reactions in 2.9% of prednisone recipients.[1,7,11] None of these patients disclosed any prior psychiatric history, and they all experienced complete remission followed by a decrease in the dose of corticosteroids or a brief course of psychopharmacological medication.[11]

A dose-response correlation was observed in the same study. Individuals who experienced neuropsychiatric side effects received a mean dose of 59.5 mg/day of prednisone, which was greater than the mean dose for patients who did not develop neuropsychiatric complications.[11] The incidence of acute psychiatric reactions statistically significantly rose with increasing average daily dosages of prednisone.[11] The likelihood of developing steroid-induced psychosis, however, is not predicted by the presence of past psychiatric history.[3,11]

Multiple investigations indicate that high doses of glucocorticoids (prednisone above 80 mg/day, dexamethasone above 12 mg/day), as well as, a prior history of a glucocorticoid-induced neuropsychiatric disease increase the likelihood that these outcomes would occur.[1,7,8] However, patients on a daily dose of prednisone above 40 mg should be considered at risk.[6] Contrary to other study results, the potential risk depends on both the dose and the duration.[3,7] There is no correlation between the presentation of the glucocorticoid, or the onset of symptoms.[3,4,5,7,10]

In patients receiving glucocorticosteroids, mania, and delirium are more common among men, while depression is more

likely in women.[10] The chance of developing psychiatric symptoms is decreased overall with subsequent glucocorticosteroid exposure, but individuals who had symptoms during a previous course of glucocorticosteroids are more likely to develop psychiatric symptoms during a second course.[10] In patients older than 70 years of age there is a tenfold increased risk of delirium, mania, and depression; whereas the risk of suicide attempts and panic disorder decreases with age.[1,10]

The incidence rates of suicidal behaviors and severe neuropsychiatric disorders were studied by Fardet et al., in over 350,000 patients receiving glucocorticoids in primary care settings.[1] The likelihood of committing suicide or suicide attempt during the first course of corticosteroid increased five to sevenfold compared with patients who did not receive corticosteroid.[1]

The development of neuropsychiatric effects with corticosteroid use varies between less than 24 hours following the first dose, and up to two years following chronic steroid use.[3] According to Lewis et al., in a review of a series of cases of steroid-induced psychiatric complications, 93% of the patients experienced symptoms within 6 weeks of treatment,[4] with a median treatment time of 11 days.[4,5,7] However, symptoms can appear at any point during the corticosteroid therapy and may persist even after the drug has been stopped.[7]

The approach to the management of neuropsychiatric side effects of corticosteroids is patient specific. The initial step is the reduction of dosage or therapy withdrawal if feasible, followed by a first-generation antipsychotic (e.g. haloperidol), second-generation antipsychotics (risperidone, olanzapine, quetiapine), lithium, or SSRI in severe cases.[2,3,5,7]

Complete recovery is expected, in most cases of corticosteroid-induced neuropsychiatric complications.[3,4,5] In the review of a series of cases by Lewis et al., 93% of the patients had a full recovery, 4% had recurrent psychiatric symptoms, and 3% committed suicide.[4] The resolution of symptoms is expected within 24 hours after corticosteroid withdrawal, the longest time documented was 8 weeks. Patients who were able to stop taking their steroids experienced a faster remission.[3]

Although psychosis is considered a multifactorial polygenic disorder, it has also been associated with environmental factors, and it is connected to the onset and progression of stress. [12] In our patient, the stress caused by the impairment of his quality of life resulting from a disabling eye disease along with the high dose immunosuppressive therapy could have affected the hypothalamic-pituitary-adrenal axis, specifically the dysfunction of glucocorticoid negative feedback causing this brief episode of psychosis.[1,2,3,5]

As a result of their complexity, and unpredictability, corticosteroid-induced neuropsychiatric problems may go undiagnosed, or concealed by other disorders. Acute psychiatric reactions could also be underestimated due to the rapidly self-resolving, mild episode that could result in a failure to diagnose by clinicians. However, psychotic episodes can also be severe and lead to risky behaviors resulting in injury to self or others. In the worst cases, patients could potentially commit suicide as a consequence of their severe symptoms.

There are limited studies on the best practices to prevent negative neuropsychiatric consequences of corticosteroids, however, with this case presentation, we want to raise the awareness of primary care physicians to be cognizant of the potential neuropsychiatric outcomes of the glucocorticoid treatment, including delusions, hallucinations, mania, and suicidality[3,6,7,8] to provide a comprehensive care.

The authors also want to highlight the importance of patient education including caregivers, as the cornerstone for an early recognition of potential complications of corticosteroid use. Prompt identification of steroid psychosis can lead to expeditious management by primary care physicians in collaboration with other medical professionals like psychiatrists to provide holistic care to their patients including the reduction of dosage or therapy withdrawal if feasible, as well as the administration of a short course of antipsychotic medications in severe cases.[2,3,5,7]

References

1. Fardet L, Petersen I, Nazareth I. Suicidal behavior and severe neuropsychiatric disorders following glucocorticoid therapy in primary care. Am J Psychiatry. 2012;169(5):491-497. doi:10.1176/appi.ajp.2011.11071009
2. Janes M, Kuster S, Goldson TM, Forjuoh SN. Steroid-induced psychosis. Proc . 2019;32(4):614-615. doi:10.1080/08998280.2019.1629223
3. Huynh G, Reinert JP. Pharmacological Management of Steroid-Induced Psychosis: A Review of Patient Cases. J Pharm Technol. 2021;37(2):120-126. doi:10.1177/8755122520978534
4. Lewis DA, Smith RE. Steroid-induced psychiatric syndromes. A report of 14 cases and a review of the literature. J Affect Disord. 1983;5(4):319-332. doi:10.1016/0165-0327(83)90022-8
5. Ali S, Paul S, Yakkali S, et al. Glucocorticoids-Induced Neuropsychiatric Disorders in Patients With Inflammatory Bowel Disease: A Systematic Review. Cureus. 2022;14(9):e28981. doi:10.7759/cureus.28981
6. Naber D, Sand P, Heigl B. Psychopathological and neuropsychological effects of 8-days' corticosteroid treatment. A prospective study. Psychoneuroendocrinology. 1996;21(1):25-31. doi:10.1016/0306-4530(95)00031-3
7. Kazi SE, Hoque S. Acute Psychosis Following Corticosteroid Administration. Cureus. 2021;13(9):e18093. doi:10.7759/cureus.18093
8. Dubovsky AN, Arvikar S, Stern TA, Axelrod L. The neuropsychiatric complications of glucocorticoid use: steroid psychosis revisited. Psychosomatics. 2012;53(2):103-115. doi:10.1016/j.psym.2011.12.007
9. Borman MC, Schmallenberg HC. Suicide following cortisone treatment. J Am Med Assoc. 1951;146(4):337-338. doi:10.1001/jama.1951.63670040004007b
10. Brown ES. An epidemiological approach to "steroid psychosis." Am J Psychiatry. 2012;169(5):447-449. doi:10.1176/appi.ajp.2012.12020181
11. The Boston Collaborative Drug Surveillance Program. Acute adverse reactions to prednisone in relation to dosage. Clin Pharmacol Ther. 1972;13(5):694-698. doi:10.1002/cpt1972135part1694
12. Georgiades A, Almuqrin A, Rubinic P. et al. Psychosocial stress, interpersonal sensitivity, and social withdrawal in clinical high risk for psychosis: a systematic review. Schizophr 9, 38 (2023). https://doi.org/10.1038/s41537-023-00362-z