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Risperidone Treatment in a Steroid-Induced Psychosis Case

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ABSTRACT

Risperidone treatment in a steroid-induced psychosis case

Steroids have been used effectively for many years to treat a wide variety of both acute and chronic medical conditions. Despite some well-known side effects, the association of psychiatric disorders with the use of these drugs has not been well established and documented. We describe a case of a 46-year-old man with a recent diagnosis of optic neuritis, who has psychotic symptoms which appear to be induced by steroids. Psychiatric symptoms emerged after the first dose of steroid and diagnosis of steroid-induced psychosis was made. After discontinuation of steroid therapy, psychiatric symptoms did not improve. But after four weeks of risperidone treatment, he recovered completely. This case adds to small but progressive body of evidence supporting the incidence of steroid-induced psychiatric symptoms in patients with optic neuritis. We suggest that the prevalence of this phenomenon might be considerably higher than what has been reported in the current literature.

Key words: Steroid, psychosis, optic neuritis, adverse effects, risperidone

ÖZET

Steroid ile tetiklenen bir psikoz olgusunda risperidon tedavisi

Steroidler, gerek akut gerekse de kronik, çok çeşitli tıbbi durumların tedavisinde uzun yıllardır etkin olarak kullanılmaktadırlar. Bu ilaçların kullanımı ile ruhsal bozukluklar arasındaki ilişki, bazı iyi bilinen yan etkilere rağmen, yeterince kurulmamış ve belgelenmemiştir. Yakın zamanda optik nevrit tanısı almış, steroid ile tetiklendiği düşünülen psikotik semptomlara sahip olan 46 yaşındaki bir erkek olguyu tanımlıyoruz. Ruhsal belirtiler steroidin ilk dozu sonrasında ortaya çıkmış ve steroid ile tetiklenen psikoz tanısı konulmuştur. Steroid tedavisi kesildikten sonra ruhsal belirtilerde düzelme olmamış, ancak 4 haftalık risperidon tedavisinden sonra hasta tümüyle iyileşmiştir. Bu olgu, optik nevritli hastalarda steroid ile tetiklenen ruhsal belirtiler görülmesine dair sayıca az, ancak giderek artmakta olan kanıtlara bir ektir. Bu görüngünün yaygınlığının güncel literatürde bildirilenden daha fazla olabileceğini düşünüyoruz.

Anahtar kelimeler: Steroid, psikoz, optik nevrit, istenmeyen etkiler, risperidon

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INTRODUCTION

For the last half-century, steroids have been widely used and prescribed for a variety of systemic diseases. Some systemic side effects of these medications such as diabetes, hypertension, peptic ulcers, osteoporosis, cataracts, immune suppression, weight gain, endocrine disturbances, glaucoma, and electrolyte imbalance are well known (1). However, psychiatric adverse effects are not uncommon during the systemic steroid administration (2). Therefore, this kind of effects of steroids concerns all physicians.

The incidence of diagnosable psychiatric disorders due to steroid therapy is reported to be 3-6%, but more patients suffer from mild symptoms which do not fulfil any diagnosis (3). Affective reactions such as depression, mania, and hypomania are the most common adverse effects, along with psychosis, anxiety and delirium. There is no clear mechanism model to explain steroid-induced psychiatric disorder, but the dose of the steroid administered has a clear relationship with patients' likelihood of developing a subsequent steroid psychosis. In the Boston Collaborative Drug Surveillance Study (4), it was reported that in patients treated with a mean daily dose of prednisone below 40 mg/day, the incidence of psychotic symptoms was 1.3%, while in patients treated with doses more than 80 mg/day of prednisone or its equivalent, the incidence of steroid psychosis was 18.4%.

In the present study, we reported a middle aged case that had a diagnosis optic neuritis attack and rapidly developed steroid-induced psychosis following methylprednisolone pulse treatment.

CASE

A 46-year-old previously healthy man presented with sudden loss of vision. Neurological examination and testing revealed that the patient had optic neuritis. Treatment was started with high-dose (1000 mg/day) systemic methylprednisolone. Following the first dose of methylprednisolone, he unexpectedly became anxious, agitated, and sleepless. On the second day, he had a dysphoric affect that he wished he had never been born and wanted to die. He also became suspicious of his relatives, including his children and thought that they were giving poisonous drugs to kill him and finally reported visual hallucinations as some unrecognized faces that appeared in front him. His positive psychiatric examination findings were suspiciousness, hostility, hypervigilance, visual hallucinations, disorganised speech/thinking, persecutory delusions, irritable affect, agitation, severe insomnia and anorexia, decreased libido, poor judgement and reality testing, lack of insight at the end of the 2nd day. He was always oriented, aware of the time, place, and the people around him for this period.

The patient and his close relatives denied any past psychiatric history, including depressive, manic or psychotic symptoms. There was also no family history of psychiatric disorder. Nonetheless, the following premorbid personality traits were reported by family members: introversion, restriction in social relationships, stubbornness, and mistrust. At the time of positive psychiatric findings, his vital signs and physical examination, including neurological examination were completely normal, except for optic neuritis with reduced visual accuracy, a measurable change in peripheral vision, decreased perception of brightness in the affected eye, and a change in colour vision. All laboratory tests, including complete blood count, liver enzymes, blood urea nitrogen, serum creatinine, electrolytes, coagulation tests, blood gases, and C-reactive protein levels were in normal limits. His cranial magnetic resonance imaging and electroencephalography (EEG) findings were also normal. We considered the possibilities of delirium and steroid-induced psychotic disorder in the differential diagnosis. Patients with delirium have impaired consciousness, fluctuations in their symptoms, and their EEG shows a generalized slowing activity. Therefore, we diagnosed him as having steroid-induced psychotic disorder according to DSM-IV-TR criteria (5).

We preferred to stop the steroid treatment on the fourth day of medication but his symptoms did not improve. He was put on 2 mg risperidone daily. After two weeks, his was relieved from his symptoms and his thought form and content were normal with no evidence of overvalued ideas or delusions within a month. Eventually, his psychotic findings like agitation and visual hallucinations also completely disappeared. The patient recovered fully at the end of the month. Therefore, risperidone treatment was discontinued and thereafter, no more anti-psychotic drugs were needed.

DISCUSSION

The literature about the psychiatric symptoms associated with the use of steroids have been documented soon after their introduction in the 1950s and many clinical data confirmed that steroids are associated with major psychiatric disorders, including depression, anxiety, euphoria, increase in vigour, mania, and psychosis. Steroid-induced psychiatric disorders appear in 3-6% of the patients who were treated with these drugs (3). However, we suggest that, due to the transient nature of these symptoms, it is imaginable that many milder and more rapidly resolving cases do not come to medical attention and they are not reported.

As has been noted previously, steroids have different effects on cerebral blood flow, oxygen consumption, and brain excitability (6). There is a great number of specific research to understand the secondary effects of these drugs on monoamine levels. It is showed that psychiatric implications are caused by increase in dopamine levels exerted by high levels of steroids. On the other hand, steroids have a linkage with decreased peripheral and central serotonin secretions (7). Serotonergic afferent neurons are direct inhibitors of dopamine release at dopaminergic axons (8). Both these correlations may also have implications with regard to possible prophylaxis of steroid psychosis (9).

Wada et al. (10) identified 15 patients with mood disorder and 3 patients with psychotic disorder among 2069 patients who were referred from other departments. All three patients initially showed typical schizophrenic symptoms such as persecutory delusions, auditory hallucinations, and disorganized behaviours. This research showed that steroids tended to induce mood disorder and at a lower incidence, psychotic disorder. Steroids can affect various mental functions, including mood, cognition, and thought, and can induce different psychiatric syndromes based on the patient's vulnerability. An interesting feature of our case is that he had anxiety-depression symptoms at the beginning and then developed full-blown psychosis.

Psychiatric disorders usually occur early in the course of steroid therapy. Median time to the onset of psychiatric symptoms is 3-4 days (2). Besides, a case of a 75-year-old woman who developed paranoid delusions, visual and auditory hallucinations within 2 days after the steroid injection was reported in the literature (11). This situation was similar to that of our patient. The sudden onset of psychosis should lead the physician to look for another possible underlying psychiatric or non-psychiatric disorder as a cause. For this reason, comprehensive medical, physical, and psychiatric assessments were completed, but no evidence of any other psychiatric or non-psychiatric condition was detected, except from steroid-induced psychotic disorder in our patient. However up to now, the authors could not explain why the patients were very sensitive to steroids only at the initial stage of the treatment. We suppose that it may be related to some unknown mechanisms of adaptation or desensitization.

There is a statistically significant increase in the incidence of psychiatric disorders with increasing daily doses of steroid. The average daily dose of steroids for patients who developed psychosis was 59.5 mg/day of prednisone or equivalent as compared with 31.1 mg/day for patients who did not develop adverse psychiatric effects (4). The incidence seems to be even higher at mega doses of methylprednisone. These results also confirm our patient's condition who takes high-dose methylprednisolone treatment and rapidly developed a psychotic episode.

Minimal data were found on the treatment of steroid-induced psychiatric disorders. The first-line treatment should begin with dose reduction and discontinuation. In some patients this has not proven adequate in reversal of symptoms, as happened in our case. In cases with severe psychiatric symptoms, antipsychotic therapy should be initiated. The treatment of steroid-induced psychosis has not been well studied. Because of the previously mentioned effects of steroids on serotonin level, it is interesting that a selective serotonin reuptake inhibitor has been used as a therapeutic agent in one case. Beshay and Pumariega (7) reported successful use of sertraline in the treatment of a 12-year-old boy who presented with psychosis and depression following high-dose prednisone treatment. Anecdotal data suggest that tricyclic antidepressants can lead to a significant worsening of psychiatric symptoms. Hall et al. (12) found that tricyclic antidepressants were associated with increased agitation and psychosis in 4 patients using steroid therapy. Patten and Neutel (3) suggested that some of the cases described by Hall et al. as worsening with tricyclic antidepressants treatment of the steroid psychosis might be occurrence of a worsening delirium aggravated by the anticholinergic effects of such drugs. So, antidepressants should probably be avoided as first-line treatment for mood symptoms likely secondary to steroids. If an antidepressant is used, physicians should prefer prescribing a selective serotonin reuptake inhibitor rather than a tricyclic agent.

Goggans et al. (13) described a case in which lithium may have prevented a relapse of prednisone-related psychosis in a patient who required steroid therapy for severe pulmonary disease. The efficiency of valproate as a prophylactic agent against steroid-induced psychosis has also been documented (14). Although mood stabilizers such as lithium and valproate appear to be effective, carbamazepine should probably be avoided as this medication induces the metabolism of some steroids, potentially lowering plasma levels of them and increasing the symptoms of the underlying disease process (15).

Steroid-induced psychosis has also been successfully treated with typical and newer atypical antipsychotic

agents like risperidone (16). Kramer and Cottingham (17) have reported a case who developed psychosis after taking high-dose (24 mg/day) dexamethasone for acute lymphoblastic leukaemia intensification regimen and treated with risperidone successfully. In addition, we also reviewed the Turkish literature on this subject. Similarly, both typical (18,19) and atypical antipsychotics (20,21) have been used to treat steroid psychosis cases successfully. Hergüner et al. (21) reported a 12-year-old case of steroid-induced psychotic disorder who was treated with risperidone successfully and in whom the antipsychotic therapy was maintained because of continuation of her steroid treatment for nephrotic syndrome. According to this case report, risperidone also proved to be an easily tolerable and effective antipsychotic drug in prophylaxis of steroid psychosis.

Once a diagnosis is made and treatment instituted, the literature suggests that complete recovery is likely to occur in 90% of patients. Three percent of patients with steroid psychosis commit suicide. The remaining 5-7% will have an ongoing psychotic or depressive disorder or develop recurrent psychiatric symptoms. Ninety two percent of patients who have steroids tapered fully recover, while 84% of patients who are maintained on steroids but treated with antipsychotic medicines show full recovery of symptoms. Electroconvulsive therapy, in the 11 cases reported in the literature has been universally effective in reversing the course of steroid psychosis (22).

CONCLUSION

The effects of steroids on mental status have not been entirely documented in the literature. The case report presented here adds to small but growing evidence supporting the existence of steroid-induced psychiatric symptoms. It is conceivable that subtle mood disturbances and mild psychotic symptoms are often unreported due to both their rapid reversal and seemingly benign nature of many behavioural outbursts. Since the disturbances explained here are iatrogenic and often quite preventable with cautious use of these agents, it would entail clinicians to be aware of this complication in clinical practice. Further research is certainly needed to study the relative efficacy of various treatments in the event of occurrence of steroid-induced psychiatric disorders.

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