Steroid-induced psychosis in an adolescent: treatment and prophylaxis with risperidone

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Steroid-induced psychotic disorder is one of the serious adverse effects of corticosteroid therapy and is characterized by hallucinations and delusions. While the mechanism is unclear, treatment of steroid psychosis involves dosage reduction or discontinuation of prednisone. In cases where this cannot be done, typical treatment involves an antipsychotic medication. Although it is a well-known complication in adulthood, literature about steroid-induced psychotic disorder in children and adolescents is lacking. Here we report a 12-year-old case of steroid-induced psychotic disorder who was treated with an atypical antipsychotic, risperidone, and in whom the antipsychotic therapy was maintained because of continuation of her corticosteroid treatment for nephrotic syndrome. Pediatricians should be aware of this rare problem when prescribing corticosteroids in this age group. To our knowledge, this is the first reported case of steroid-induced psychosis successfully treated with risperidone in an adolescent with nephrotic syndrome.

Key words: steroid psychosis, risperidone, nephrotic syndrome, albumin, adolescent.

Over the last 50 years, exogenous corticosteroids have been used in the treatment of various medical illnesses. A number of adverse reactions have been established, including disturbance of mental state. The average incidence of diagnosable psychiatric disorders due to steroid therapy is reported to be about 6%, but more patients suffer from mild symptoms which do not fulfill any diagnosis[1]. Affective reactions such as depression, mania and hypomania are the most common side effects, along with psychosis, anxiety and delirium[2]. There is no clear mechanism model for corticosteroid-induced psychiatric disorder, but it appears to be dose-dependent. In the Boston Collaborative Drug Surveillance Program, psychiatric side effects developed in 1.3% of the patients receiving 40 mg or less of prednisone and in 18.4% of those who received more than 80 mg[3]. The incidence seems to be even higher at megadoses of methylprednisone[4].

Although it is a well-known complication in adulthood, literature about steroid-induced psychotic disorder in children and adolescents is insufficient. In the following, we report a 12-year-old case of steroid-induced psychotic disorder who was treated with an atypical antipsychotic, risperidone, and in whom the antipsychotic therapy was maintained because of continuation of her corticosteroid treatment for nephrotic syndrome. To our knowledge, this is the first reported case of steroid-induced psychosis in Turkey.

Case Report

A previously healthy 12-year-old girl was referred to our pediatric nephrology department with a two-year history of nephrotic syndrome. She had received oral prednisone in several doses ranging from 16 mg/day to 48 mg/day during the past two years, but remission could not be achieved. Kidney biopsy was performed with the diagnosis of steroid-resistant nephrotic syndrome. The histopathological changes were considered as focal segmental glomerulosclerosis. At this point, high-dose methylprednisone (MP) pulse therapy (30 mg/kg every other day IV) was started on

an outpatient basis according to the protocol proposed by Mendoza et al.[5]. After the 5th pulse of MP, she developed some behavioral changes such as fears, anxiety and sleep disturbances at home. Her parents took her to the pediatric emergency department on the second day of her complaints.

On admission, she had visual and auditory hallucinations and persecutory delusions. She claimed to be seeing dead bodies running around the room and calling her to come with them. She had fears of being kidnapped and murdered by strangers, and had been calling her parents to continuously stand nearby for protection. She had exhibited bizarre behavior such as praying differently and talking to herself. For the last two days, she experienced insomnia. She was oriented, aware of the time, place and the people around her. Her mother reported that she had never exhibited psychological problems in the past, and there was no family history of mental disorders.

At the time of hospitalization, her vital signs, and physical and neurological examination findings were completely normal. Her weight was 38.5 kg (3-10%), height 137 cm (<3%) and blood pressure 120/70 mmHg. She was taking methylprednisone at more than 1 mg/kg per day at this presentation. All laboratory tests including complete blood count, coagulation tests, blood urea nitrogen (BUN), serum creatinine, electrolytes, liver enzymes, blood gases, and C-reactive protein (CRP) levels were in normal limits except for hypoalbuminemia (1.6 g/dl) with proteinuria (1.8 g/m^2/day). Her cranial magnetic resonance imaging (MRI) and electroencephalography (EEG) were also normal.

We considered the possibilities of delirium, drug intoxication 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. In drug intoxication patients have perceptual disturbances and intact reality testing. Our patient had impaired reality testing, normal cognitive functions, normal EEG, and her symptoms had begun after the initiation of mega doses of steroid. We thus diagnosed her as having steroid-induced psychotic disorder according to DSM-IV-TR criteria[6]. A regime of risperidone (1 mg at night) was initiated. Four days after starting the treatment, her symptoms dramatically improved and IV MP pulses were continued, to be given every other day for two weeks. Three weeks later, she had no psychiatric signs or symptoms. The only side effect was mild sedation at bedtime. Because her recent psychotic reaction had became a risk factor for further steroid therapy, we decided to continue with risperidone 1 mg as a prophylaxis. At the last visit, six months after beginning risperidone treatment, she remained free of psychiatric symptoms, despite the use of prednisone, and she was tolerating the medication well.

Discussion

The use of corticosteroids in various forms and doses has been known as the main therapeutic approach in childhood nephrotic syndrome. Children routinely receive high-dose corticosteroid therapy; as many as 45% will have a frequently relapsing course and some will be steroid-dependent[7]. Children with nephrotic syndrome often experience serious problems with depression, anxiety and increased aggression during high-dose prednisone therapy[8].

Female sex, past psychiatric history, prednisone dose of more than 40 mg/day and long-term administration are considered to be the major risk factors for steroid psychosis[9]. In our case, three of these risk factors - female gender, over 1 g prednisone and steroid treatment for more than two years - were present.

Steroid psychosis often occurs from a few days to two weeks after administration of this agent. Although our patient had been receiving prednisone for more than two years, she had not developed any psychiatric manifestations. When she experienced psychiatric symptoms, her albumin level was 1.6 g/dl and she had significant proteinuria. The explanation for this may be that synthetic steroids bind to serum albumin, at which point they are inactive. Therefore, higher levels of free and active fraction of steroids along with low plasma albumin levels will expose the patient to more adverse effects[10]. Interestingly, the incidence of psychosis in nephrologic patients is higher than other groups of patients treated with steroids (for example, those with chronic obstructive pulmonary disease)[11]. Thus, those patients with

disease causing low levels of serum proteins (as in those with nephrotic syndrome) would be predisposed to experience more adverse effects with steroids. Our case had normal serum albumin level (3 g/dl) with normal renal function in the period without psychiatric signs/symptoms.

The treatment of steroid psychosis is to taper the steroids to the lowest dose or to discontinue the medication. In this case, since corticosteroid therapy had to be maintained to prevent further relapses of her nephrotic syndrome, these interventions were not possible. In several reports, lithium[12] and antipsychotics including haloperidol[13], chlorpromazine[14], and risperidone[15] were offered for the treatment of steroid-induced psychosis in adults. There are only two case reports about the pharmacotherapy of steroid psychosis in children and adolescents, with promethazine[16] and risperidone[17].

Although most of the previous reports have suggested lithium for the treatment, it has many practical limitations, among which are its neurological, endocrinological and nephrological side effects, its low therapeutic index and drug-drug interactions.

Atypical and typical antipsychotics are comparable in their clinical efficiency to some extent, but they differ remarkably with regard to their side effect profiles. Typical antipsychotics have more risk for developing extrapyramidal side effects (EPS) including dyskinesias and dystonias (as a result of D2 receptor blockade) than atypicals. Moreover, younger patients particularly appear to be at a higher risk for developing EPS[18]. Therefore, atypical antipsychotics are currently preferred in the initial treatment of psychotic disorders in this age group[19]. Risperidone is an atypical antipsychotic that, unlike typicals, has a high binding ratio of serotonin (5 HT2) receptors to dopamine (D2) receptors. Side effects include somnolence and weight gain. This patient had a significant improvement in psychotic symptoms with risperidone treatment, and the medication was well tolerated.

The decision of whether to treat a patient prophylactically to prevent steroid-induced psychosis is problematic, as the predictability of this idiosyncratic reaction is difficult. Post et al.[20] drew a comparison between steroid-induced psychosis and the concept of behavioral sensitization, where continuation of a drug is associated with increased effects on behavior and apparent reverse tolerance. Nonetheless, we believe that certain cases such as the one presented, in which the clinician believes that the risk of a psychotic reaction is high, do merit prophylactic treatment.

As data suggest a rapid onset of psychiatric side effects, the patients should be seen soon after the initiation of steroid therapy, preferably within a week. Along with monitoring weight, blood glucose and blood pressure, the patient should be asked about mood swings and symptoms of depression and mania. As a minimum, the pediatrician should warn parents at the beginning of the course of steroid therapy that their child might experience behavioral, cognitive and affective changes. The information and appropriate warning given to parents may allow them to be better prepared for such problems.

Referring to the described case above, we suggest that psychotic reaction should be taken into account as a possibility in all children who develop behavioral changes during corticosteroid treatment; atypical antipsychotics such as risperidone may be considered not only as a part of the treatment but also as a prophylactic agent.

REFERENCES

1. Lewis DA, Smith RE. Steroid-induced psychiatric syndromes: a report of 14 cases and review of the literature. J Affect Disord 1983; 5: 319-332.
2. Patten SB, Neutel I. Corticosteroid-induced adverse psychiatric effects: incidence, diagnosis and management. Drug Saf 2000; 22: 111-122.
3. The Boston Collaborative Drug Surveillance Program: Acute adverse reactions to prednisone in relation to dosage. Clin Pharmacol Ther 1972; 13: 694-698.
4. Wollheim FA. Acute and long term complications of corticosteroid pulse therapy. Scand J Rheumatol 1984; 54: 27-32.
5. Mendoza SA, Reznik VM, Griswold W, et al. Treatment of steroid resistant focal segmental glomerulosclerosis with pulse methyl prednisolone and alkylating agents. Pediatr Nephrol 1990; 4: 303-307.
6. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (4th ed). Text Revision Washington, DC: American Psychiatric Association; 2000: 338-343.
7. Neuhaus TJ, Fay J, Dillon MJ, Trompeter RS, Barratt TM. Alternative treatment to corticosteroids in steroid sensitive idiopathic nephrotic syndrome. Arch Dis Child 1994; 71: 522-526.

8. Soliday E, Grey S, Lande MB. Behavioral effects of corticosteroid in steroid-sensitive nephrotic syndrome. Pediatrics 1999; 104: e51.
9. Hall RC, Popkin MK, Stickey SK, et al. Presentation of the steroid psychosis. J Nerv Ment Dis 1979; 167: 229-236.
10. Lopez-Medrano F, Cervera R, Trejo O, Font J, Ingelmo M. Steroid induced psychosis in systemic lupus erythematosus: a possible role of serum albumin level. Ann Rheum Dis 2002; 61: 562-563.
11. Niewoehner DE, Erbland ML, Deupree RH, et al. Effect of systemic glucocorticoids on exacerbations of chronic pulmonary disease. N Engl J Med 1999; 340: 1941-1947.
12. Siegel FP. Lithium for steroid psychosis. N Engl J Med 1978; 299: 155-156.
13. Ahmad M, Rasul FM. Steroid-induced psychosis treated with haloperidol in a patient with active chronic obstructive pulmonary disease. Am J Emerg Med 1999; 17: 735.
14. Bloch M, Gur E, Shalev A. Chlorpromazine prophylaxis of steroid-induced psychosis. Gen Hos Psychiatry 1994; 16: 42-44.
15. DeSilva CC, Nurse MC, Vokey K. Steroid induced psychosis treated with risperidone. Can J Psychiatry 2002; 47: 388-389.
16. Lee KM, Lin YZ, Huang FY. Steroid-induced acute psychosis in a child with asthma: report of one case. Acta Paediatr Taiwan 2001; 42: 169-171.
17. Kramer TM, Cottingham EM. Risperidone in the treatment of steroid-induced psychosis. J Child Adolesc Psychopharmacol 1999; 9: 315-316.
18. Findling RL, McNamara NK, Gracious BL. Antipsychotic agents: traditional and atypical. In: Martin A, Scahill L, Charney DS (eds). Pediatric Psychopharmacology. New York: Oxford University Press; 2003: 328-340.
19. Sikich L, Hamer RM, Bashford RA. A pilot study of risperidone, olanzapine, and haloperidol: a double-blind, randomized, 8-week trial. Neuropsychopharmacology 2004; 29: 133-145.
20. Post RM, Rubinow D, Ballenger JC. Conditioning, sensitization and kindling. In: Ballenger JC, Post RM (eds). The Neurobiology of Mood Disorders. Baltimore: Williams and Wilkins; 1984: 1673-1684.