A Case of Steroid Induced Mania

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Abstract
Background: Steroids have been widely used and prescribed for a variety of systemic diseases. Although they prove to be highly effective, they have many physical and psychiatric adverse effects. The systemic side effects of these medications are well known and well studied, in contrast to the psychiatric adverse effects which their phenomenology needs to be the focus of more clinical studies.

However, the incidence of diagnosable psychiatric disorders due to steroid therapy is reported to be 3-6%. Affective reactions such as depression, mania, and hypomania are the most common adverse effects, along with psychosis, anxiety and delirium.

Aim: We describe a case of corticosteroid induced mania, its unusual clinical picture, its course and management.

Case description: A 14-year-old female intermediate school student, with a recent diagnosis of Chron’s disease was brought to A&E department due to acute behavioral disturbance in form of confusion, visual hallucinations, psychomotor agitation, irritability, hyperactivity, talkativeness, lack of sleep, and physical aggression. Those symptoms have started few days following corticosteroid therapy which was Prednisolone 40mg PO OD. And she was diagnosed with steroid induced mania.

Discussion: This case illustrates the need for more understanding of the phenomenology and diversity of corticosteroids induced psychiatric syndromes.

Conclusion: The incidence of Steroid induced psychiatric symptoms ranging from 8-15% of adult patients, but there is no report of incidence in children and adolescence. Although the mechanism by which corticosteroids affect behavior is likely multi factorial, there is a well-documented relationship between the dosage of prednisone and the risk of developing acute psychosis. Pediatricians should be aware of this rare complication when administering corticosteroids for various medical illnesses.

Introduction
Steroid psychosis is a syndrome involving variable constellation of symptoms. Affective reactions such as depression, mania, and hypomania are the most common adverse effects, along with psychosis, anxiety and delirium [1]. Steroid-induced psychiatric disorders appear in 3-6% of the patients who were treated with these drugs [2]. 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, reported the incidence of steroid psychosis as 1.3%, 4.6% and 18.4% while taking less than 40 mg/day, 40-80 mg/d and more than 80 mg/d, respectively [3]. Hall reported female sex and past psychiatric history to be host-related factors, while high dose and long-term administration of prednisone was an agent-related factor, inducing steroid psychosis [4]. In fact, some other studies report that most patients developing steroid psychosis do not have underlying psychiatric disorders [5]. This article reviews case report of steroid induced mania, its memorable unusual clinical picture, and course of management.

Case Presentation
Sociodemographic and clinical details
Our patient was a 14 years old, Saudi, unmarried, intermediate school student from middle socioeconomic status. She was medically free until one month prior to her presentation when she was diagnosed with chron’s disease. And had been started on Prednisolone (corticosteroid) 40 mg PO OD, for one month duration.

History of presenting complain
Three weeks after being on Prednisolone, She presented to the A&E department with 5 days history of acute onset of irritability, incessant talk, hyperactivity. She was verbally and physically
violent. And she was noticed to have marked decrease need for sleep and significant diminished food intake. She was also easily distracted and had fluctuating confusion (disoriented to time, place and person). According to her mother, she behaved like if she is seeing invisible person.

**Physical examination:** Her vital signs were within normal range. The physical examinations, including a detailed neurological assessment, were unremarkable.

**Mental Status Examination:** Rapport couldn’t be established. She was extremely agitated, continuously shouting unclear words on everybody. Her limbs had to be tied to the bed.

**General appearance and behavior:** Young female, average built, limbs restrained to the bed, restless, potentially aggressive, psychomotor agitation. Poor eye contact

**Talk and abstract ability:** Talkative, loud, unclear and incoherent, with mostly irrelevant answers.

**Mood:** Had irritable mood and affect.

**Thought content:** She had paranoid delusions toward her family as she suddenly believed that her family belong to isis group. She was also having delusions of grandiosity, believed that she is the God; later on she believed that she is God’s messenger.

**Perception:** She had visual hallucinations.

**Cognitive function:** She seems confused and disoriented to time, place and person. Short and long term memory couldn’t be assessed. She clearly had poor insight.

**Other Details:** Our patient was pre morbidly well adjusting. There was no history of medical or neurological disorders. No Hx of any kind of medications (apart from Prednisolone) and substance use. There was no history to suggest infection in recent past.

**Investigations**
Laboratory studies, including complete blood picture, renal functions, plasma glucose, liver and thyroid functions, urine analysis, electrolyte, and electro- cardiogram, brain Computerized Tomography (CT) all did not reveal any abnormalities.

**Diagnosis**
After ruling out organic etiology. We believed it to be steroid induced mania vs. delirious mania. As she showed clear picture of mania, psychosis, and was delirious.

**Treatment details and course in hospital**

<table>
<thead>
<tr>
<th>Day 2</th>
<th>Olanzapine 5 mg Po</th>
<th>Still very disturbed, her sleep and appetite were improved</th>
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<tr>
<td>Day 6</td>
<td>Olanzapine 15mg PO</td>
<td>She was still agitated and had fluctuating attention, physically aggressive, restless</td>
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<tr>
<td></td>
<td>Haloperidol 5 mg IM (PRN)</td>
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<td>Day 7</td>
<td>D/C Haloperidol</td>
<td>She experienced muscle rigidity, bradykinesia</td>
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<tr>
<td>Day 12</td>
<td>Valproic Acid 500 mg PO</td>
<td>Still agitated and confused, walking naked in the corridors, defecating and urinating on the floor</td>
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<td></td>
<td>Olanzapine 20 mg PO</td>
<td>Over the time there was gradual improvement, she became oriented to time, place and person, but the clinical picture was evolving to full blown manic picture with irritable labile mood, hyperactivity, disinhibition, talkativeness and marked decreased need for sleep</td>
</tr>
<tr>
<td></td>
<td>Valproic acid 1000 mg PO</td>
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</table>

She was Discharged in a stable condition after total of two months stay in the hospital, on Olanzapine 20mg/day Po HS, and Valproic Acid 1000mg/day PO HS.

**Follow-Up period**
About two weeks after-discharge, she was maintained on Olanzapine 20mg/day Po HS, and Valproic Acid 1000mg/day PO HS. She maintained euthymic stable state at home. When she showed up in the follow up appointment, she was mute and had a flat affect. She was given another follow up appointment 1month later, and was stable. Her mood was euthymic with normal range affect, talking normally with no clear formal thought disorders. No evidence of any delusions or other abnormal thoughts, indicative that she is in state of remission. Olanzapine was tapered off and Valproic Acid continued one the same dose. Then she was lost to follow up.

**Discussion**
Our case represents severe form of Steroid induced mania in childhood. Moreover, the case is worth mentioning because of severe remarkable presentation, dramatic evolution of the clinical picture, long-lasting symptoms and priority of affective symptoms. Who responded wonderfully to treatment? A classical case of bipolar-I, but with an element of delirium.

Bipolar disorder (BD) is classically viewed as a condition characterized by periods of euphoric excitement and depressive retardation, which is easy to diagnose and treat, whose treatment is exclusively pharmacological, and whose outcome is generally favorable. However, it may have co morbidity with other psychiatric conditions which makes the diagnosis of BD becomes difficult when there is a variation of the classical picture.

Which brought us to think about Delirious mania (DM) a severe but under-recognized neuropsychiatric syndrome characterized by the rapid onset of delirium, mania, and psychosis, not associated with a prior toxicity, physical illness, or mental disorder. While
initially believed to be rare, recent reports suggest that 5-20% of all patients with acute mania show signs of delirium [6].

Klerman proposed staging of manic spectrum as follows: normal, neurotic, hypomanic, manic, and delirious [7]. In 1921, Kraepelin categorized mania into 3 types: acute, delusional, and delirious [8,9]. The transition of mania to DM is marked by emergence of confusion, more hallucinations, and a marked intensification of the manic symptoms. This condition still has no formal diagnostic classification. The syndrome was first described by Calmiel in 1832. In 1849, Luther Bell, who is credited with providing the first comprehensive description of the syndrome, reported 40 patients out of 1700 admissions to McLean Hospital, who had features suggestive of DM and 75% of these patients subsequently died [10].

Adolescents and children are particularly prone to the very rapid development of DM [11]. Studies found that DM is more likely to be seen in younger, female and with a prior diagnosis of bipolar disorder [12]. In 2008 R Karmacharya reviewed 16 cases admitted to McLean Hospital with delirium and mania and observed a series of symptoms rarely reported in manic or psychotic episodes, which they consider distinctive symptoms of delirious mania (Table 1), they are helpful guides in allowing clinicians to recognize the syndrome, In addition, to the severe forms of classic manic and psychotic symptoms typically seen [12].

<table>
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<th>Distinctive symptoms of delirious mania</th>
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<td>• Acute onset of severe symptoms (within days)</td>
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<td>• Incontinence/inappropriate toileting</td>
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<tr>
<td>• Denudativeness (disrobing/extended naked periods)</td>
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<tr>
<td>• larger lapses of episodic memory extending over many hours in comparison to manic patients</td>
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<td>• Pouring water (on own head/on the floor)</td>
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Table 1: Symptoms of delirious mania.

We believe that our patient is a challenging case; its initial presentation is best explained by DM vs. steroid induced mania. The first line treatment of steroid psychosis is to taper the steroids to the lowest dose or to discontinue the medication if possible. Supporting care is required, neuroleptic medications may be used if necessary.

So upon discussing the case with her medical team we agreed on stopping steroid as her chron’s is under control in the mean time. According to DSM IV (diagnostic and statistical manual of mental disorders, fourth edition) steroid induced psychiatric disorder subsides after discontinuing steroid by maximum period of one-month. Which doesn’t apply on our case as she continued with a picture of full-blown mania after discontinue steroid for two-month period. We propose that our patient showed a picture (DM) as severe form of extreme excitement during the manic phase of BP disorder.

**Conclusion**

Such patient needs aggressive management. In several reports, valproic acid lithium and antipsychotics including risperidone have been tried for treatment. Nicolato reported successful treatment of DM with a combination of Olanzapine and ECT [13]. ECT was considered but was kept as the last resort in case all pharmacological interventions were ineffective.

In conclusion, our case is one of the several reports documenting steroid-induced psychiatric disorder in childhood that need to be the focus of further studies. The fact remains that there is a separate entity of mania called Delirious mania has been reported is several studies, we suggest to be considered to be included in the new classification system with clear diagnostic criteria.

**References**