

Manic Episode Due to Steroid Use in Pemphigus Vulgaris Patient: Case Report

PEMFIGUS VULGARİS HASTASINDA STEROİD KAYNAKLI MANİK EPİZOD: OLGU SUNUMU

Uğur ERAY¹

¹Kars Harakani Devlet Hastanesi, Psikiyatri, Kars, Türkiye

ABSTRACT

Corticosteroids are used in the treatment of numerous diseases, primarily in the treatment of autoimmune diseases. They have various side-effects. Although the pathophysiology of psychiatric side-effects have not clearly been revealed, the various risk factors leading to these have been defined. In the treatment of psychiatric symptoms which emerge after steroid treatments, it is firstly advised to discontinue the use of the steroid and initiate the use of an antipsychotic medicine together with a mood regulator or single-handedly. It is aimed at discussing the manic attack which took place after corticosteroid use in our patient diagnosed with pemphigus vulgaris, the risk factors leading to this situation and the course of the disease only with olanzapine.

Key Words : Pemphigus vulgaris, Steroid, Mania

ÖZ

Kortikosteroidler başta otoimmün hastalıklar olmak üzere birçok hastalığın tedavisinde kullanılmaktadır. Bu ilaçların çeşitli psikiyatrik yan etkileri de bulunmaktadır. Psikiyatrik yan etkilerin patofizyolojisi tam olarak aydınlatılmamış olup, ortaya çıkmasında önemli olan çeşitli risk faktörleri tanımlanmıştır. Steroid tedavisi sonrası ortaya çıkan psikiyatrik belirtilerin tedavisinde öncelikli olarak kullanılan steroidin kesilmesi ve duygudurum dengeleyici ile birlikte veya tek başına antipsikotik başlanması önerilmektedir. Pemfigus Vulgaris tanılı vakamızda kortikosteoid kullanımı sonrasında ortaya çıkan manik atak, buna yol açan risk faktörleri ve tek başına olanzapin tedavisi ile hastalığın seyrinin tartışılması amaçlanmıştır.

Anahtar Kelimeler : Pemfigus Vulgaris, Steroid, Mani

Uğur ERAY

Kars Harakani Devlet Hastanesi, Psikiyatri,
Kars, Türkiye

E-posta: drugureray@gmail.com

<https://orcid.org/0000-0001-5417-3394>

HIGHLIGHTS

- Our case had a manic episode due to steroid use without having risk factors such as female gender, systemic lupus erythematosus,, hypoalbuminemia, liver or kidney disfunction and additional drug use.

- Among the risk factors in the literature, he has only pre-disease shy and withdrawn personality traits.

- Although psychiatric conditions occur in pemphigus patients in the literature, steroid-induced mania is rarely seen.

- Our case was treated with only olanzapine 10 mg without the need for mood stabilizers.

Glucocorticoids are important in the treatment of many inflammatory, allergic, immunological and malign disorders. Systemic (oral or parenteral) corticosteroids have powerful anti-inflammatory, immunomodulator and antineoplastic characteristics and are used in the treatment of numerous diseases, including autoimmune diseases, allergic reactions, asthma exacerbation and chronic obstructive lung disease.

Systemic corticosteroids are medications which are frequently used in the treatment of Pemphigus vulgaris, which is a dermatological disease, with success. In some patients, while Pemphigus vulgaris can simply be controlled with a low dose of corticosteroids, some patients may experience symptoms and exacerbation which cannot be controlled even with high dosages (1).

Despite the potentially beneficial clinical effects of systemic corticosteroids, their use in particular in high dosages is associated with serious risks. Among the well-known side-effects associated with systemic corticosteroids are; osteoporosis, cardiovascular disease, impaired immune response and wound healing, changes in glucose and lipid metabolism and psychiatric diseases (2).

Among the psychiatric side-effects, mood swings, insomnia, irritability, depression, anxiety, euphoria, hyperactivity, manic and psychotic attacks can be listed (3). The most important factor leading to the emergence of psychiatric side-effects is the steroid dosage used and the female gender is another factor which increases the risk. In addition, it seems that psychiatric disease history, psychiatric complication history related to steroid medication or the application method of the steroid medication increase the incidence of psychiatric symptoms related to steroid medications (4).

Although the dosage used is directly related to the incidence of side-effects, it is not related to the emergence time, severity or duration of these effects (5). It is suggested to reduce the dosage or discontinue the use of the steroid used for euphoria, hypomania or mania which emerge after steroid treatment and initiate a neuroleptic treatment together with a mood regulator or single-handedly (6). It is stated in the literature that olanzapine as a neuroleptic gives successful results in the treatment and that it is well-tolerated (7).

It is aimed at discussing the manic episode which took place after corticosteroid use in our case diagnosed with Pemphigus vulgaris, the risk factors leading to this situation and the course of the disease with olanzapine treatment single-handedly. We think that the emergence of a manic attack after the use of high dose of steroid medication in the patient who does not have any other chronic diseases other than Pemphigus vulgaris and a psychiatric disease history will contribute to the literature.

CASE REPORT

M.E.A. a 23-year-old male patient. He was single and living with his family. He graduated from the Faculty of Theology a year ago. The patient and his family had no known history of psychiatric illness or smoking, alcohol or substance use. It is understood from his story that he is an introvert, does not have many friends, but has very strong ties with his family. He was a shy and anxious person. Pemphigus vulgaris was diagnosed on 02.02.2022 and received 2*24 mg oral corticosteroid treatment (methylprednisolone) for 14 days at Erzurum Atatürk University Hospital. He stated that he started to use 3*32 mg "accidentally" after he was discharged.

The patient was not given any treatment other than steroids. After the 4th day of this treatment, complaints such as increased activity, acceleration in thinking, less sleep, increased energy, making new plans and experiencing anxiety started. The patient was examined at the Kafkas University Medical Faculty Hospital 2 days after the onset of these complaints. In the examination of the patient, it was observed that there was an increase in psychomotor speed, an increase in the speed and amount of speech, his speech was scattered and tangential, and there was a flight of ideas.

He was partially cooperative, his mood was high and he was nervous, distressed, anxious, his emotions were exaggerated, his thinking speed was accelerated, and his associations were scattered. He expressed his concern about using the drugs incorrectly and therefore the embarrassment he felt towards his family. He exhibited an erroneous perception similar to derealization. His reasoning ability was intact. His insight was poor.

In the physical examination, it was seen that he had lesions on his left arm and hand, right hand and the

oral region. These were continuing lesions of the patient due to *Pemphigus Vulgaris*. The neurological examination was at a normal level. There were no pathological findings in his brain radiology.

The biochemical test results were at a normal value interval. In addition, albumin was 45 g/L (ref:35-52 g/L) and total protein was 65 g/L (ref. 66-87 g/L). The microbiological and serological tests were normal. It was learned that the patient did not use drugs other than steroids.

The patient's thyroid function test results were normal. The urine substance scan was evaluated as negative. The Young Mania Rating Scale (YMRS) score was calculated as 36.

Naranjo's adverse drug reaction probability scale score was calculated as 5. According to this scale, 9 points and over is evaluated as definite, 5-8 points as highly likely, 1-4 points as likely and 0 point as suspicious (8). In our case, his total score of 5 points from this scale made us think that the side-effect is highly likely related to the steroid.

The case was evaluated as a manic attack due to steroid use according to DSM-5 criteria and the patient was hospitalized in the Psychiatry Clinic of Kars Harakani State Hospital.

The steroid the patient used was discontinued. 5 mg of olanzapine was initiated and it was increased to 2*5 mg 2 days later. The patient's manic symptoms started calming down on the 5th day of his treatment. His speech started to reach its purpose and his duration of sleep increased. The patient whose activities decreased, who did not talk about new plans and whose insight increased, was discharged on the 5th day of his hospitalization to be followed-up in an ambulatory manner with a treatment of 2*5 mg of olanzapine. In the examination done on the 1st week after being discharged, the Young Mania Rating Scale (YMRS) was calculated as 8. In the examinations done on the 3rd, 8th, 12th weeks and first year, it was seen that all of the manic symptoms of the patient diminutively disappeared. A new mood episode was not observed.

Our case was classified under "Medication/Substance Related Bipolar Disorder and Related Disorders" heading according to DSM-5 diagnostic criteria and the steroid treatment which led to the manic attack was discontinued and olanzapine treatment was

initiated. As a result, the symptoms of the patient were relieved and we think that not having a new mood attack after the olanzapine treatment was ended and in the follow-up examinations affirms our diagnosis and treatment.

DISCUSSION

In patients who use steroid medications, mood swings, anxiety symptoms, cognitive disorders, behavior disorders or psychotic characteristics can be seen on their own or in a combined manner (5). In a study, in which 2069 patients who used steroid medications for systemic diseases were analyzed, it was determined that 19 patients had mood disorders or psychosis due to steroids (9).

Patients with high serum steroid levels develop neurological deficits such as cognitive impairments, mood disorders and decrease in hippocampus volume. It is considered that stress and glucocorticoids change hippocampal neurogenesis and may contribute to the pathophysiology of mood disorders (10).

The type of these mood disorders may be related to duration. During the short-term use of high dosages of steroids, manic symptoms are seen more commonly compared to depression (11). Psychiatric symptoms related to corticosteroids emerge in an average of 11.5 days in most cases after the initiation of the treatment (12). In our patient, the symptoms started emerging on the 4th day of increasing the dosage and on the 18th day after the treatment was initiated.

In a study in which 29 studies were reviewed, it was stated that about 5 % of the patients treated with steroids had severe psychiatric syndromes and that the female gender, systemic lupus erythematosus, use of high dosages of prednisone might be risk factors for the development of psychiatric syndrome related to steroids (13). Our case was male, used methylprednisolone and was diagnosed with *Pemphigus vulgaris*, a systemic disease.

Dosage is an important risk factor in the emergence of side-effects related to corticosteroids; in dosages less than 40 mg per day, psychiatric side-effects are seen in 1.3 % of the patients and this rate reaches 18.4 % in 80 mg dosages (14). Our patient has used 48 mg/day of oral corticosteroid for 14 days and afterwards 96 mg/day for 4 days.

Besides dosage, other risk factors have also been mentioned in the literature. Since hypoalbuminemia is related to higher free and active glucocorticoid levels, it is another reported risk factor. In addition, the risk is increased as well in patients with synchronous use of medications such as Sitokrom P450 (CYP) enzyme inhibitors (for instance, clarithromycin) which increase circulating corticosteroid levels and in patients with liver or kidney function disorders (15). In our patient, there was no history of hypoalbuminemia, CYP enzyme inhibitor medication use and liver or kidney function disorder.

Additionally, there are publications which report that personality traits prior to diseases are related to risk as well and in particular being shy and withdrawn are underlined (16-18). As far as we have found out, our patient was a shy person who has strong ties with his family and was socially withdrawn.

In the literature, it has been mentioned that the combined use of lithium and olanzapine in the treatment of mania cases resulting from steroids have given successful results (19).

However, use of olanzapine single-handedly has given successful results as well. In a study, in which the effects of olanzapine on patients who developed psychiatric symptoms due to the use of steroids were analyzed, olanzapine was used alone and the dosage was titrated from 2,5 mg to 20 mg per day. It was seen that the psychiatric symptoms significantly regressed in all of the patients (10). In our case study, our patient has given a very good response to 10 mg/day olanzapine treatment and this supports the view that olanzapine alone as an antipsychotic might be sufficient.

In the light of the current data, although it is not clear whether there is a two way relationship between mental health and severity of Pemphigus vulgaris, studies show that the incidence of mental health problems in patients with Pemphigus vulgaris is much higher compared to both the general population and patients with other chronic skin disorders. Corticosteroids, which are one of the most important reasons for this, are currently the first-line treatment for Pemphigus vulgaris and they have been defined as a potential independent risk factor for mental health comorbidity in Pemphigus vulgaris (20).

Oral corticosteroid treatment is prescribed in high dosages and in general for long-term use for skin diseases. It is well-known that steroid treatments cause metabolic and organic side-effects such as osteoporosis, diabetes, high blood pressure. However, psychiatric side-effects are usually underestimated and may not be recognized since they are not specific symptoms. In the literature, manic attacks are seen in a limited number in Pemphigus vulgaris patients. Associations between bipolar disorder and autoimmune diseases have been studied before and in one study, a significant association was found between bipolar disorder and pemphigus (21). However, in our patient, manic episode started after steroid treatment. In the literature, we did not find any manic episode starting after steroid treatment in a patient with pemphigus.

Besides all the side-effects which may arise during corticosteroid use, psychiatric side-effects should also be followed carefully. Specific attention should be paid to patients who are given high dosages of steroids and have high risk factors. Therefore, we believe that increasing the awareness of physicians and patients about psychiatric side effects for patients who will be started on high-dose steroid treatment will increase the chance of early detection of possible side effects and early psychiatric treatment.

REFERENCES

1. Fernandes, N. C., & Perez, M. Treatment of pemphigus vulgaris and pemphigus foliaceus: experience with 71 patients over a 20 year period. *Revista do Instituto de Medicina Tropical de Sao Paulo* 2001; 43: 33-36
2. Rice, J. B., White, A. G., Scarpati, L. M., Wan, G., & Nelson, W. W. Long-term systemic corticosteroid exposure: a systematic literature review. *Clinical therapeutics* 2017; 39(11): 2216-2229.
3. Grando, S. A. Pemphigus autoimmunity: hypotheses and realities. *Autoimmunity* 2012; 45(1): 7-35.
4. Parasher, A., & Bez, J. Steroid induced psychiatric adverse effects: an overview of risk factors, clinical features and management. *International Journal of Research in Medical Sciences* 2020; 8:23-65

5. Warrington, T. P., & Bostwick, J. M. Psychiatric adverse effects of corticosteroids. In *Mayo Clinic Proceedings* 2006;81:10, 1361-1367.
6. Sirois, F. Steroid psychosis: a review. *General hospital psychiatry* 2003; 25(1): 27-33.
7. Brown, E. S., Chamberlain, W., Dhanani, N., Paranjpe, P., Carmody, T. J., & Sargeant, M. An open-label trial of olanzapine for corticosteroid-induced mood symptoms. *Journal of affective disorders* 2004;83(2-3): 277-281
8. Naranjo, C. A., Busto, U., Sellers, E. M., Sandor, P., Ruiz, I., Roberts, E. A., ... & Greenblatt, D. J. A method for estimating the probability of adverse drug reactions. *Clinical Pharmacology & Therapeutics* 1981; 30(2):239-245.
9. Wada, K., Yamada, N., Sato, T., Suzuki, H., Miki, M., Lee, Y., ... & Kuroda, S. Corticosteroid-induced psychotic and mood disorders: diagnosis defined by DSM-4 and clinical pictures. *Psychosomatics* 2001;42(6): 461-466
10. Kino, T. Stress, glucocorticoid hormones, and hippocampal neural progenitor cells: implications to mood disorders. *Frontiers in physiology* 2015;6:230.
11. Brown, E. S., & Chandler, P. A. Mood and cognitive changes during systemic corticosteroid therapy. *Primary care companion to the Journal of clinical psychiatry* . 2001; 3(1): 17.
12. Ciriaco, M., Ventrice, P., Russo, G., Scicchitano, M., Mazzitello, G., Scicchitano, F., & Russo, E. Corticosteroid-related central nervous system side effects. *Journal of pharmacology & pharmacotherapeutics* 2013;4:94.
13. Lewis, D. A., & Smith, R. E. Steroid-induced psychiatric syndromes: a report of 14 cases and a review of the literature. *Journal of affective disorders* .1983;5(4): 319-332.
14. Goldstein, E. T., & Preskorn, S. H. Mania triggered by a steroid nasal spray in a patient with stable bipolar disorder. *American Journal of Psychiatry* 1989;146:1076-1077
15. Lu, Y., Ann, L., & McCarron, R. Steroid-induced psychiatric symptoms: What you need to know. *Current Psychiatry* 2021; 20(4): 33
16. Garner, H. H., & Falk, M. A. Toxic psychosis: pemphigus and psychiatric disease. *Psychosomatics* 1967; 8(3): 133-137
17. Demir, B., Kocamer Sahin, S., Guneyusu, E., Elboga, G., & Altindag, A. Two Manias Triggering with Only Prednisolone: A Case with Immune Thrombocytopenia. *Psychiatria Danubina* 2021;33(1): 67-68.
18. Bolu, A., Erdem, M., Yalçın, F. Y., & Günay, H. Steroid kullanımına bağlı ortaya çıkan mani olgusu. *Journal of Mood Disorders* 2013;3(2): 74-76.
19. BALIBEY, H., Yaşar, H., & Tekeli, H. Periferik yüz felci geçirmiş olan bir hastada kısa süreli kortikosteroid kullanımı sonrasında ortaya çıkan karma mani atağı: Bir olgu sunumu. *Journal of Mood Disorders* 2012; 2(1):17-20.
20. Matthews, R., & Ali, Z. Comorbid mental health issues in patients with pemphigus vulgaris and pemphigus foliaceus. *Clinical and Experimental Dermatology* 2022; 47(1): 24-29.
21. Kridin, K., Zelber-Sagi, S., Comaneshter, D., & Cohen, A. D. Bipolar disorder associated with another autoimmune disease—pemphigus: a population-based study. *The Canadian Journal of Psychiatry* 2018, 63(7), 474-480.