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Case Report

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Vasculitis and Steroid Psychosis: A Case Report and Review of Literature

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Abstract

Corticosteroids have become the cornerstone of therapy for many pathologies such as vasculitis. Steroid psychosis is a known complication of corticosteroids therapy, although infrequent. We describe a case of psychosis secondary to corticosteroids in a 69-year-old man with large-vessel vasculitis without previous history of psychiatric pathology. He was diagnosed with large-vessel vasculitis and the treatment started with prednisone 1 mg/kg/day. One week later, the patient presented with behavior change: emotional lability, disorientation and aggressiveness. The symptoms worsened for hallucinatory activity and cognitive deficit. After exclusion of other causes, the diagnosis of psychosis secondary to corticosteroids was assumed. It was decided to wean corticosteroids and start new therapy with methotrexate and tocilizumab and introduction of antipsychotic therapy. The patient had a good outcome with disease remission and had no further neuropsychiatric symptomatology. Systemic corticosteroids are widely used, sometimes with a low concern of its potential adverse effects. So it is important that physicians are aware of the potential for their adverse effects and the need to monitor disease activity and drug toxicity.

Keywords: Vasculitis; Corticosteroids; Adverse effects; Psychosis

Introduction

Vasculitis (VC) is a heterogeneous group of diseases characterized by inflammation of the blood vessel wall. Affected vessels vary in size, type, and location depending on the specific type of VC presented. The prognosis is very variable and depends on organ involvement, the duration of the disease and the early start of treatment. Corticosteroids (CCs) are used in the treatment of VC, as well as in a wide variety of acute or chronic medical conditions. Despite being a powerful therapeutic option, CC is associated with several adverse effects, whether physiological or neuropsychiatric. Here we describe a case of CC secondary psychosis in a patient with large-vessel vasculitis (LVV) with no previous history of psychiatric pathology.

Case Report

We report a case of a 69-year-old man who was admitted to the hospital with a 2-month history of asthenia and anorexia, 1 month of night sweats and 2 weeks of evening fever with maximum axillary temperature of 38.5 °C. Physical examination showed skin pallor with no other remarkable findings. The blood analysis revealed anemia with hemoglobin (Hb) of 10.8 g/dL, elevation of inflammatory markers: erythrocyte sedimentation rate (ESR) of 108 mm/h and C-reactive protein (CRP) of 16.68 mg/dL, and hypoalbuminemia of 2.4 g/dL. Blood cultures, urine samples, bacteriological and mycobacteriological bronchial secretions were all negative as well as viral, serological and immunological studies. The imaging study with transthoracic echocardiography, thoracic, abdominal and pelvic computed tomography scans, and upper digestive endoscopy did not show any alterations, and neither did the myelogram and bone marrow biopsy that were obtained in a later stage. Following the investigation of fever of unknown origin, a positron emission tomography was performed, showing evidence of uptake in the aorta, subclavia, common carotid, iliac and femoral carotid arteries, thus confirming the diagnosis of LVV.

The patient started treatment with prednisolone 1 mg/kg/day, on a total of 90 mg/day, with clinical and laboratory improvement (ESR 21 mm/h, CRP 0.66 mg/dL and Hb 12.3 g/dL) and was discharged home. However, 1 week after the start of CC therapy, the patient presented to the emergency department with behavior change: emotional lability, disorientation and aggressiveness. He had no previous personal or family history of psychiatric pathology. After a negative screening for infection or metabolic or VC activity was obtained, this behavioral change was assumed as an adverse effect of CC and the therapeutic dose reduced to 60 mg/day. Despite the reduction in CC, the patient's neuropsychiatric symptoms worsened with disinhibition, disorientation, aggressiveness, hallucinatory activity with a paranoid persecutory theme, and cognitive deficit with

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affectation of several domains, namely language and memory, requiring rehospitalization. The patient was evaluated by a multidisciplinary team and it was decided to maintain CC weaning and simultaneously initiate methotrexate (MTX) as a CC sparing therapy, as well as antipsychotic therapy, given the severity of the condition, with olanzapine and quetiapine. His neuropsychiatric symptoms improved after therapeutic changes. For exclusion of VC central nervous system (CNS) involvement, a head magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) were obtained and showed no alterations.

Taking into account the temporal line relationship between the development of neuropsychiatric symptoms and the onset of high dose of CC therapy, as well as the absence of alterations in head MRI and MRA, the diagnosis of psychosis associated with CC was assumed.

Approximately 2 weeks after maintaining therapy with CC on sub-optimal dose and MTX, without the onset of the peak of action, there was recurrence of fever and increase of inflammatory markers. Since the patient needed rapid control of his disease, given the severe vascular involvement, it was decided to initiate tocilizumab (TCZ) therapy and maintain CC weaning. The patient was discharged with normalization of neuropsychiatric symptoms only maintaining emotional lability and cognitive deficit in the memory domain and medicated with TCZ 8 mg/kg monthly, MTX 20 mg/week, folic acid 10 mg/week, prednisolone 15 mg/day and quetiapine 25 mg/day.

The patient completed 6 months of TCZ therapy and MTX was maintained at a dose of 20 mg/week and then increased to 25 mg/week as prednisolone was reduced to 2.5 mg/day, thus achieving remission of the disease.

Currently, 3 years after the diagnosis, the patient is only under MTX 20 mg/week and quetiapine 50 mg/day, with disease in remission and without neuropsychiatric symptomatology.

Discussion

The CC is widely used in clinical practice [1]. Although it is a powerful therapeutic option, CC is associated with several adverse effects, namely physiological and neuropsychiatric effects [2]. Approximately 20% of patients receiving high doses of CC develop psychiatric disorders [3]. The literature reports several cases of depression related to the use of CC, with an incidence of 40.5%. Symptoms of mania, psychosis and delirium are also common, with an incidence of 27.8%, 13.9% and 10.1%, respectively. Only a small percentage (3%) present with psychosis and hallucinations [4].

The most frequently identified symptoms include agitation, anxiety, distraction, fear, hypomania, indifference, insomnia, irritability, lethargy, unstable mood and restlessness [2]. The etiology and pathogenesis of CC neuropsychiatric effects remain poorly understood. CC receptors are expressed in different areas of the brain and their role is related to the regulation of various neurotransmitters, including serotonin and dopamine. The effect of CC at the CNS level is particularly relevant in the hippocampus region that provides the processing of emotional information and memory. Several studies have shown a correlation between high levels of endogenous cortisol and hippocampal atrophy, resulting in lesion and cognitive dysfunction. The incidence of neuropsychiatric effects due to CC ranges from 2% to 60%, reflecting dose variability, duration of administration and identified risk factors, including genetic predisposition [4].

The dose of CC is the most important risk factor for the development of psychiatric symptoms. Patients with a dose of 40 mg/day or less only present an incidence of 1.3% of psychiatric disorders compared to those who receive 41 to 80 mg/day who present an incidence of 4.6%. Patients receiving more than 80 mg/day had an incidence of 18.4%. However, the dose does not predict the onset, severity, duration or type of symptoms. Other risk factors for the development of CC-associated psychosis are female gender, hypoalbuminemia, and drugs that increase circulating levels of CC, such as inhibitors of the cytochrome P450 enzyme. A history of psychiatric illness does not condition a risk factor, nor does any specific age group seem to be at increased risk [5]. Psychiatric disorders may occur at any time during treatment, including almost immediately after initiation and even after cessation of CC [2]. In 86% of cases they occur within the first 5 days of treatment. Analysis of several studies leads to an average of 11.5 days after onset of CC until the onset of psychiatric symptoms. The duration of neuropsychiatric effects is highly variable and depends on severity, discontinuation of treatment and other instituted therapies [4].

Strategies for resolution of neuropsychiatric disorders are based almost entirely on case reports and a few small case series. Treatment should begin with suspension of CC or dose reduction. If the suspension is not an option, the dose should initially be reduced to 40 mg prednisolone per day followed by reduction of a physiological dose of prednisolone 7.5 mg/day [2]. This measure may be sufficient to improve neuropsychiatric symptoms without the need for additional medications. However, in severe cases of affective instability or psychosis or if the CC cannot be discontinued or reduced there is evidence from studies and case reports that support the use of antipsychotics and mood stabilizers, such as lithium and valproic acid [3]. Antipsychotics such as olanzapine and quetiapine may be used safely and effectively. The effect of antidepressants differs according to the type used: tricyclic antidepressants may lead to significant worsening of symptoms, whereas selective serotonin reuptake inhibitors such as fluoxetine may improve symptoms of depression during therapy with CC [6].

In last years, the use of lithium has been evaluated as prophylaxis of the neuropsychiatric adverse effects of CC, however, still without statistically significant results. It has also been ascertained whether the mode of administration of CC may be a form of prevention of neuropsychiatric adverse effects. To date there has been no evidence that a specific mode of administration decreases the incidence of neuropsychiatric complications, whether they are related to peak plasma (divided daily dose or pulse therapy) or related to the circadian rhythm model [1].

Any patient initiating treatment with systemic CC should be informed of possible adverse effects, including behavio-

ral changes. As adverse effects may arise at the start of treatment, the patient should be reassessed shortly after initiation of therapy, preferably within 1 week, and along with monitoring of weight, glucose and blood pressure, the patient should be asked about any changes in mood and symptoms of depression and mania [6]. In this context it is important that physicians are aware of the potential adverse effects of CC therapy; in this case it has been demonstrated in the form of psychosis, requiring intervention by a multidisciplinary team with readjustment of the therapeutic strategy.

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Conflict of Interest

The authors have no conflict of interest to declare.

Informed Consent

Informed consent was obtained from patient.

Author Contributions

EA is the physician who worked with patient and contributed to manuscript design and writing; MB and J Silva are the physicians who worked with patient and were involved in manuscript review; J Serodio and JC contributed to data collection and manuscript review.

References

1. Sirois F. Steroid psychosis: a review. Gen Hosp Psychiatry. 2003;25(1):27-33.
2. Warrington TP, Bostwick JM. Psychiatric adverse effects of corticosteroids. Mayo Clin Proc. 2006;81(10):1361-1367.
3. Gagliardi JP, Muzyk AJ, Holt S. When steroids cause psychosis. The Rheumatologist [Internet]. 2010 [cited 2019 Jul 14]. Available from: https://www.the-reumatologist.org/article/when-steroids-cause-psychosis/.
4. Ciriaco M, Ventrice P, Russo G, Scicchitano M, Mazzitello G, Scicchitano F, Russo E. Corticosteroid-related central nervous system side effects. J Pharmacol Pharmacother. 2013;4(Suppl 1):S94-98.
5. Menon VB, Sunny AA, Pereira P, Chikkaveeraiah S, Ramesh M. Steroid psychosis: a case series of three patients. Indian Journal of Pharmacy Practice. 2018;11(1):51-54.
6. Brown ES, Chandler PA. Mood and cognitive changes during systemic corticosteroid therapy. Prim Care Companion J Clin Psychiatry. 2001;3(1):17-21.

