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RESEARCH ARTICLE

CORTICOSTEROID-INDUCED PSYCHIATRIC IATROGENIC DISORDERS: A CASE OF A STEROID-INDUCED PSYCHOTIC EPISODE

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Abstract

Introduction:-

Since their therapeutic use in the 1950s, corticosteroids have been prescribed in a wide range of medical disciplines. There are therapeutic uses in a wide range of allergic, neoplastic, inflammatory, and autoimmune conditions. Their therapeutic use is known to produce somatic and psychic side-effects.

The psychiatric side effects of corticosteroids have been described for over sixty years by Rome and Braceland[1]. These complications may occur shortly after the onset of steroid treatment, throughout the course of treatment, or even after treatment. Their onset and severity remain unpredictable. These steroid-induced disorders are highly varied and can cover an overly broad spectrum of psychiatric disorders, ranging from aggressive and violent behavior to mild mood swings, anxiety, depression, hypomania, or frank psychosis [2] [3]. Certain severe reactions occur in around 5% of patients [2] [4] [5].

Although relatively uncommon, they are estimated to occur in 5-18% of patients on corticosteroids [6]. Consequently, they are classified as a subset of substance- or drug-induced psychosis in the (DSM-5) [7]. Whilst the risk factors behind this remain elusive, they are often dose-dependent and observed at higher dosage levels, according to the Boston Collaborative Drug Surveillance Program. According to the BCDSP, psychiatric disorders were observed in 18.6% of patients taking >80 mg of either prednisone or methylprednisolone, while 4.6% of patients taking 41-80 mg/day and 1.3% of patients taking <40 mg or less per day [8]. While the exact cause remains obscure, exogenous steroid-induced stress on the hypothalamic-pituitary-adrenal (HPA) axis is the mechanism implicated. Current data show that progressive reduction or cessation of the responsible steroid is the first step in symptom management in most cases.While reducing or ceasing corticosteroid treatment may remedy these undesirable side effects, psychotropic drugs are often required due to the medical necessity of the corticosteroid or the severity of the psychiatric symptom.

Corticosteroids are pharmacologically active in the brain, affecting sleep-wake regulation, memory and mood [9]. The prevalence of steroid-related psychiatric disorders varies. They remain underestimated because they are rarely detected clinically, and the literature is sparse in studies concerning them [10] [11]. Estimation of this prevalence is even more difficult when corticosteroids are taken outside the usual therapeutic framework, as part of self-medication with no medical monitoring or control. Self-medication with corticoids concerns a population of women in certain regions of Morocco and is mainly aimed at weight gain. Unfortunately, this misuse of corticosteroids is

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not without serious health risks. In these regions, plumpness is considered a criterion of feminine beauty, and being overweight is a culturally accepted phenomenon.

Physicians and other healthcare professionals need to be aware of the potential for these side effects, possible means of prevention and effective treatments. They must be cautious and regularly assess patients on corticosteroids to minimize the risk of complications. Further research is needed to better understand the deleterious psychiatric effects associated with corticosteroids and the underlying pathophysiology.

Objectives and Methods:-

This is a case report of a young woman who experienced an acute psychotic episode following self-intake of corticosteroids for weight gain. The importance of early diagnosis and preventive care is discussed, particularly in view of the cultural aspects involved in the case presented. A review of the literature and published data on adverse psychiatric effects induced by corticosteroids is also presented, using the key words "corticosteroids," "steroids," and generic names of corticosteroid drugs with terms for psychiatric syndromes or symptoms, including psychosis, mania, hypomania, depression, apathy, anxiety, panic, depersonalization, delirium, confusion, hallucinations, delusions, psychosis and cognitive disorders, in the various search engines, googlescholar,PubMed, Embase, PsychLit and psychoInfo.

Clinical vignette:

The case is of a 23-year-old single female patient from an average socio-economic background with no previous medical or surgical history. She had no psychiatric or neuropsychiatric history. Nor was there any family history. Brought to the emergency room by her family for treatment of psychomotor agitation and hetero-aggression, she had become isolated, soliloquizing, distrustful of those around her, with bizarre behavioural patterns and verbalized delusions, while experiencing insomnia.

On her first visit to the emergency room, the patient was agitated, of average build, unsatisfactory corporal and clothing care, wearing a black djellaba with dirty patches, poorly coiffed, dynamic expression, approachable, basic psychic activities seemed preserved, with disorganized speech, off-key responses and unmotivated laughter. Upon examination, a delusional syndrome was noted, with a vague, poorly systematized delusion of persecution and bewitchment, with an intuitive and interpretative mechanism, reported with a low affective charge. A hallucinatory syndrome was also noted, with auditory hallucinations and attitudes in favor, impaired judgment, and insight. The diagnosis of a steroid-induced psychotic episode was adopted.

According to the family, the patient, in order to gain weight, had been taking corticosteroids (one prednisone 40 mg tablet per day) for two weeks. Blood tests, serologies, urine toxicity tests and a cerebral CT scan all proved normal.The patient was treated with a risperidone-based antipsychotic in progressive doses up to 4mg per day, combined with an anxiolytic (temesta 1mg) for the first few days. This treatment was well received and led to an improvement in psychiatric symptoms after one week. On regular outpatient follow-up, the antipsychotic was maintained at the same dosage for six weeks, then reduced to 2mg per day for one year. The patient responded well to this treatment, with good improvement in symptomatology. It was paired with supportive psychotherapeutic and psycho-educational intervention.

The occurrence of an acute psychotic episode calls into question the role of corticosteroid therapy.The rapid onset of psychotic symptoms after the corticosteroid was taken, the early respite from psychotic symptoms after the corticosteroids were stopped, and the absence of any psychiatric history or notion of intoxication by another substance all point to a direct link between the occurrence of this episode and the introduction of corticosteroids. The hypothesis of the iatrogenic origin of psychosis due to corticosteroids in this episode therefore seems highly probable.

Discussion:-

Since the 1950s, corticosteroids have been widely used and are frequently associated with both systemic benefits and side effects. They are commonly prescribed as anti-inflammatory/immunosuppressive drugs. They affect T-cell-mediated inflammation by suppressing cytokines and impairing the immunostimulatory function of monocytes and macrophages [7]. According to the DSM-5, for a patient to be diagnosed with substance- or drug-induced psychosis, such as steroid-induced psychosis, there must be a psychotic symptom often after exposure to the drug, causing

significant functional impairment. It is therefore more a diagnosis of exclusion after ruling out all other causes, such as organic psychiatric disorders, drug use, intoxication, metabolic disorders, infections, and neoplasms.

The psychic side-effects of corticosteroids range from clinical anxiety, sleep disturbance and severe mood symptoms such as depression, hypomania, and mania, to acute psychotic disorders and, in some cases delirium. They typically manifest shortlyafter steroid intake, usually after a median of three to four days, but can occur at any time during treatment or even after cessation[12]. In short-term treatment, thymic disorders primarily manifest as euphoria and hypomania, whereas depression is more frequently observed during long-term treatment. The rate of Steroid-induced psychosis occurrence is in around 5% of cases [13] [14].

Reports of steroid-induced psychiatric adverse effects began to appear in the literature shortly after the introduction of these drugs in the 1950s. Regrettably, early studies relied on informal classification and measurement procedures, and tended to use descriptive, non-specific terminology (such as “steroid psychosis”). A growing number of contemporary studies have begun to address these issues. Nonetheless, the literature remains surprisingly underdeveloped from a pharmaco-epidemiological point of view, consisting largely of case reports and case series.

The dosage of the corticosteroid administered seems to be the most decisive risk factor, especially at higher dosages (40 mg or more of prednisone or equivalent): the Boston Collaborative Drug Surveillance Program reports in its study that psychiatric disorders were observed in: a) 1.3% of patients treated with less than 40 mg/d of prednisone; b) 4.6% of patients receiving between 40 and 80 mg/d; c) 18.4% of patients receiving more than 80 mg/d. The dose of corticosteroid does not, however, predict the nature of the psychiatric reaction, nor its severity or duration. The type of corticosteroid molecule does not appear to be a determining factor [15]. In their study, Barrami et al. underline female predominance. In this respect, women are more likely to have depressive episodes, while men are more likely to have manic episodes. Although the female sex predisposes to psychosis, it would seem that this factor is more closely related to the more frequent prescription of corticosteroids in women. A psychiatric history is not a predictive factor in the development of psychosis, nor is previous use of corticosteroids. The period between the start of corticosteroid treatment and the onset of psychosis varies from study to study, ranging from 1 to 54 days for Lewis et al. and from 2 to 23 days for Hall et al. These studies found no evidence of a pre-morbid personality or predisposing psychological factors [9].

In the present case, it was difficult to specify the dose of corticosteroid ingested. The intense quest for rapid weight gain and the severity of the disorder suggests the use of high doses of corticosteroid. However, the nature of the patient's female sex may have favoured the onset of symptoms.The pathophysiological mechanisms of iatrogenic corticosteroid side effects remain poorly established. Certain hypotheses consider the effect of corticosteroids on the central dopaminergic and cholinergic systems, or suggest a decrease in the secretion of serotonin, which is largely involved in the regulation of mood and behavior [16] [17]. Other hypotheses posit a neurotoxic effect on the hippocampus, with a reduction in its volume. The Brown et al. study of 17 patients showed a reduction in hippocampal volume in patients on corticosteroids, compared with the control group [18].The exact pathophysiology remains unclear, but exogenous steroid-induced stress on the HPA axis is the mechanism involved. It causes a decrease in levels of corticotropin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) as well as cortisol levels through preferential activation of glucocorticoid receptors in the adrenal glands. This imbalance can trigger neurocognitive and emotional disorders such as delirium, mania and mood disorders [19] [20]. Furthermore, in animal models, corticosteroids have been shown to cause an increase in tyrosine hydroxylase and, in turn, an increase in dopamine, which can induce psychosis [20].

The approach to the psychiatric care of steroid-induced psychiatric disorders has not been codified. In general, the first step is to gradually reduce the corticosteroid dosage to a minimum effective dose, or even stop corticosteroid therapy altogether. This approach alone can bring about the disappearance of psychiatric symptoms. However, this reduction is not always possible because of the underlying corticosteroid-treated condition and may prove insufficient because of the intensity or persistence of the disorders. In such cases, a specific treatment should be prescribed [21]. Some publications have shown the efficacy of classic neuroleptics such as haloperidol or chlorpromazine. However, among second-generation antipsychotics, olanzapine remains the most well-documented molecule, with efficacy in both manic and mixed symptoms. Risperidone also appears to be effective for psychotic symptoms such as delusions and hallucinations, as well as hypomanic symptoms [22]. Clinical improvement is seen within a few days to a few weeks for both molecules. The use of other antipsychotics, such as quetiapine and aripiprazole, has also been reported[9]. In addition, some authors have proposed the therapeutic use of mood-

regulating molecules such as lamotrigine, sodium valproate or phenytoin. For Falk et al., prescribing lithium in conjunction with corticosteroid therapy would prevent the onset ofsteroid-induced psychiatric side-effects. With regard to antidepressants, it seems that SSRIs and SNRIs such as sertraline, fluoxetine and venlafaxine have a beneficial effect on depressive symptoms. This symptomatology would, however, be aggravated by tricyclic antidepressants [9] [22].In this case, the decision to cease corticosteroids was not a problem, since corticosteroids were not part of a therapeutic framework. However, the intensity of the disorder necessitated the use of an antipsychotic, risperidone, initially combined with an anxiolytic. This therapeutic approach proved effective, improving symptoms within a week, in line with results reported in the literature. Indeed, the efficacy for steroid-induced psychosis is very good, with recovery achieved in 90% of cases, whereas 5-7% will develop recurrent psychotic symptoms or depressive disorders [16] [22].

Conclusion:-

Steroid-induced psychiatric disorders are extremely diverse, affecting a very large proportion of patients on corticosteroid therapy. The severity of some reactions potentially requires multidisciplinary therapeutic action involving psychiatrists and somatic specialists. Ensuring that healthcare teams, patients and their families are aware of the possibility of psychiatric side-effects linked to corticosteroids would enable early detection and care and prevent the onset of serious disorders. Clinicians must therefore exercise caution when prescribing corticosteroids, given their potential neuropsychiatric side effects. Appropriate assessment and early detection are essential to minimize the risk of complications.

Although there is a lack of in-depth research in the field of steroid-induced psychosis due to its unpredictable nature, it is essential to recognize its importance as it can be distressing and dangerous for patients. Current data have shown that progressive reduction or discontinuation of the responsible steroid is the first step in controlling symptoms in most cases. Nevertheless, if they persist, additional antipsychotic coverage may be indicated.

In this particular case, the clandestine use of corticosteroids, underpinned by cultural dimensions, calls for much more serious measures, involving not only healthcare professionals, but also social workers and the media, with the aim of informing the public about the risks, both somatic and psychiatric, of this self-medication. The role of doctors can be complemented by that of pharmacists, who can play a decisive role in providing information, given their more regular contact with patients and their families. There are no clear recommendations nor preventive strategies in place at present. Larger-scale surveys are needed to measure the extent of this cultural phenomenon and implement appropriate measures.

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