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Corticosteroid induced Hypothyroidism and Cushing's syndrome: A Case Report

"They say Cushing's is rare, it's not true it's just rarely diagnosed"

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Abstract

Background: Glucocorticoids are vital in the treatment of many inflammatory, allergic, immunologic, and malignant disorders. Cushing's syndrome describes the signs and symptoms associated with prolonged exposure to inappropriately high levels of the hormone cortisol. This can be caused by captivating glucocorticoid drugs. The clinical signs suggesting Cushing's disease, such as obesity, moon face, hirsutism, and facial plethora. Drug-induced hypothyroidism is an underactive thyroid gland due to a reaction from medication. Corticosteroids can sometimes cause hypothyroidism or make it worse. High doses of prednisolone can slow the conversion of the thyroid hormone to the more active form.

Aim and Objective: To describe a case of Corticosteroid (Prednisolone) Induced Hypothyroidism and Cushing's syndrome.

Case History: Here is a case of a 47 year old female patient who is suffering from Cushing syndrome and Hypothyroidism caused by chronic use of prednisolone. She had been taking prednisolone 5 mg once daily since 1 year for joint's pain and backache. She presented with moon face, backache, swelling of limbs, abdominal distension, muscle weakness and striae since 3 weeks. The prednisolone dose was tapered and withdrawn.

Conclusion: Physicians must be aware of these opposing effects and should be vigilant in prescribing and be prepared to manage them. This case report highlights the potent adverse effects of corticosteroids and the need forconsistent monitoring in patients on long term therapy.

Keywords

glucocorticoids; cushing's syndrome; cortisol; hypothyroidism

Introduction

Glucocorticoids (GCs), such as prednisolone, characterize the significant and recurrently used class of anti-inflammatory drugs. Currently, glucocorticoids are imperative in the management of many inflammatory, allergic, immunologic, as well as in allotransplantation and malignant disorders, and the harmfulness of glucocorticoids is one of the commonest causes of iatrogenic ailments linked with chronic

inflammatory disease. Numerous toxicities, have been attributed to glucocorticoids. Corticosteroids are a class of substances that embraces steroid hormones mainly produced in the adrenal cortex of vertebrates and correspondents of these hormones that are synthesized in laboratories. The corticoids have widespread actions. They maintain fluid and electrolyte balance, cardiovascular and energy substrate homeostasis and functional status of skeletal muscles and nervous system [1]. In spite of excellent efficacy, the clinical use of GCs is hampered bya wide range of side effects, which are dose and duration dependent. Persistent exposure to elevated levels of circulating GCs has been associated with metabolic derangements including the development of central adiposity, dyslipidaemia, insulin resistance, glucose intolerance, diabetes mellitus and skeletal muscle wasting. Both the anti-inflammatory and metabolic effects of GCs are mediated through their binding to the GC receptor, which is ubiquitously expressed in the human body. Upon ligand binding, the GC receptor translocates into the nucleus where it enables initiation (transactivation) or suppression (transrepression) of target gene transcription. However transrepression fundamentally accounts for the anti-inflammatory action of GC's, while; transactivation of target genes involved in the metabolism of glucose, lipids or proteins is mostly implicated in the adverse effects. It has therefore long been hypothesized that it should be possible to design selective GC receptor agonists, with preserved transrepression actions and reduced transactivation effects, allowing the preservation of beneficial effects while reducing adverse effects [2].

Corticosteroids induced Cushing's Syndrome:

Cushing's syndrome defines the signs and symptoms linked with prolonged exposure to improperly high levels of the hormone cortisol. This can be triggered by taking glucocorticoid drugs, or by diseases that result in excess cortisol, adrenocorticotropic hormone (ACTH), or Corticotrophin-releasing hormone (CRH) levels [3]. The most common systemic side effects of prolonged use of glucocorticoids includes Cushing's syndrome, cataract, hypertension, dyslipidaemia, skin atrophy, failure to thrive, hypothalamo-pituitaryadrenal axis (HPA) suppression, striae, glaucoma and a predisposition to life-threatening infections. Endogenous hypercortisolism is associated with an increased risk of cardiovascular and metabolic manifestations, as well as respiratory disorders, psychiatric complications, osteoporosis and infections, leading to high rates of morbidity and mortality[4].

Pathophysiology: The hypothalamus is in the brain and the pituitary gland sits just beneath it. The para ventricular nucleus (PVN) of the hypothalamus releases corticotropin-releasing hormone (CRH), which stimulates the pituitary gland to release adrenocorticotropin (ACTH). ACTH travels via the blood to the adrenal gland, where it stimulates the release of cortisol. Cortisol is secreted by the cortex of the adrenal gland from a region called the zona fasciculata in response to ACTH. Raised levels of cortisol use negative feedback response on the pituitary, which declines the amount of ACTH released from the pituitary gland. Strictly, Cushing's syndrome refers to excess cortisol of any etiology (as syndrome means a group of symptoms). Unique causes of Cushing's syndrome is a cortisol secreting adenoma in the cortex of the adrenal gland (primary hypercortisolism/ hypercorticism). The adenoma causes cortisol levels in the blood to be very high, and negative feedback on the pituitary from the high cortisol levels causes ACTH levels to be very low[1].

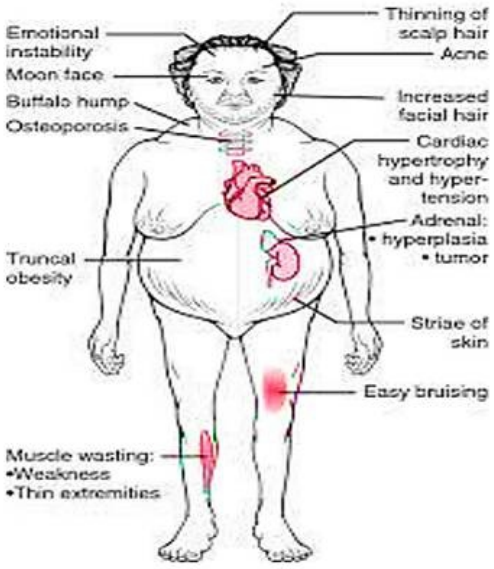

Figure 1: General Presentation of Cushing's syndrome

Corticosteroids induced Hypothyroidism:

Drug-induced hypothyroidism is an underactive thyroid gland due to a response from a medicine. "Drug-induced" means triggered or brought on by medication. Prednisone or other corticosteroids can sometimes cause hypothyroidism or make it worse. Here are a couple of diverse ways in which prednisone produces this. First, normal doses of prednisone can stop TSH secretion, leading to less thyroid hormone in the body. Second, the thyroid hormone comes in two forms. The less active form, T4 is released from the thyroid. It is then converted in the body to the more active form T3. High doses of prednisone can slow the conversion of the hormone to its more active form.

AIM: The main aim of this article is to present a case of Corticosteroid (Prednisolone) Induced Hypothyroidism and Cushing's syndrome. It is important for clinicians to be aware of its presentation. It is critical to detect the causative agent as early as possible and its withdrawal is necessary for critical management.

We report a case of Corticosteroid (Prednisolone) Induced Hypothyroidism and Cushing's syndrome in a 47 year old female patient who was prescribed Prednisolone for joint's pain and backache. The following case report demonstrates the necessity of prompt recognition and initiation of appropriate therapy to reduce the potential sequelae of Cushing's syndrome.

Case Presentation

A 47 year old female patient visited the outpatient department of general medicine department of the Mandya Institute of Medical Sciences and Teaching Hospital, Mandya, Karnataka, India. She presented with chief complaints of easy fatigability since 6 months, weight gain since 1 year and moon face, backache, swelling of limbs, abdominal distension, muscle weakness and striae since 3 weeks. Past Medical History revealed that she is known case of hypertension since 1 year, on Rχ Tablet Envas (Enalapril) 5 mg OD. She gives history of taking Prednisolone 5 mg OD since 1 year for joint pains and backache.

Investigations: General Physical examination of the patient on day-1 reveals an obese patient, with moon face (Figure 1), swelling of limbs, abdominal distension (Figure 2), striae, thinning of hair

(Figure 3) and a heart rate of 96 beats/minute, respiratory rate of 22cpm and blood pressure of 170/100mmHg. The patient was conscious, well-oriented and appeared uncomfortable but not in distress. The laboratory investigations are mentioned in Table 1.

Figure 1: Moon Face in Cushing's syndrome

Figure 2: Abdominal distension and Obesity

Figure 3: Striae and thinning of hair

No other significant past medical history or drug allergies. No focal deficits were identified on neurological examination. The patient was admitted to hospital with a presumptive diagnosis of drug-inducedor Corticosteroid Induced Cushing's syndrome.

Table 1: Patient laboratory investigations

LABORATORY INVESTIGATIONS				
Haemoglobin	10.9 gm %			
White Blood Cells	8,900 cells/cmm			
Differential Count	**N**	**L**	**M**	**E**
	71%	23%	4%	2%
Platelet Count	2.69 lakh cells/cmm			
AEC	140 cell/cmm			
RBS	179 mg/dl			
Blood Urea	24 mg/dl			
Serum Sodium	135.3 mmol/l			
Serum Potassium	4.03 mmol/l			
Serum Chloride	100.5 mmol/l			
Serum Creatinine	1.1 mg/dl			
Total Bilirubin	1.3 mg/dl			
Direct Bilirubin	0.5 mg/dl			
Total Protein	6.2 g/dl			
Serum Albumin	4.5 g/dl			
Serum Globulins	3.9 g/dl			
SGOT	47 U/L			
SGPT	45 U/L			
ALP	48 U/L			
Total Cholesterol	220 mg/dl			
Triglyceride	139 mg/dl			
HDL	42 mg/dl			
LDL	127 mg/dl			
VLDL	37 mg/dl			
Free T3	1 .96 pg/ml			
Free T4	0.61 ng/dl			
TSH	7. 2 µIU/ml			
1-mg overnight dexamethasone suppression test	> 50 nmol/L			

Prednisolone was withdrawn and the patient was monitored for signs of clinical recovery. On the day of admission patient's condition worsened with increased easy fatigability.

Treatment: On day-1 the patient was treated with following measures and medications- Back Rest, Oxygen Inhalation-2 ltr/min, Inj.Ceftriaxone1 gm IV BD, Furosemide 20 mg IV stat and OD, Tablet Enalapril 5 mg 1-0-1, Oral Atorvastatin 10 mg 0-0-1, Tablet Thyronorm 200 µg, Oral Ecoaspirin 150 mg 0-1-0 , Oral Tramadol 50 mg 1-0-1, TabletMetopirone 1000 mg HS, Oral Paracetamol500 mg 1-1-1, Diclofenac 3 cc IM stat; SOS.

On day-2, the physician dechallenged the drug and subsequently that patient was recovered from the presenting symptoms. In this patient, medical attention was not sought immediately and the patient continued on Prednisolone even after the occurrence of symptoms. The key prognostic marker in Cushing's syndrome is the prompt identification and withdrawal of the causative drug.

Outcome and Recovery: After 7 days of stay in the hospital muscle weakness was decreased and patient was discharged. During the discharge, the following medications such as Tablet Enalapril 5 mg 1-0-1, Oral Atorvastatin 10 mg 0-0-1, Tablet Thyronorm 200 µg, Oral Ecospirin 150 mg 0-1-0, Tablet Metopirone 1000 mg HS were prescribed.

Adverse Drug Reaction Analysis: After collecting the past and current medication history from the patient it was suspected that the patient had developed Prednisolone-induced Hypothyroidism and Cushing's syndrome. After analysing the ADR profiles of the drugs that were administered to the patient, it was found that prednisolone was the most likely suspect producing Hypothyroidism and Cushing's syndrome. We have further analysed to establish the relationship between the drug and the observed ADRs, through causality assessment by using Naranjo's scale, WHO-UMC ADR assessing scale as well as Hart wig's severity assessment scale, results were shown in Table 2. The Naranjo's criteria and WHO probability scale were applied to determine the causality for suspected ADRs. The causality assessment with both scales revealed that adverse reaction due to prednisolone in this case was probable and possible (Naranjo overall score: 7). The severity of ADRs were evaluated using Modified Hartwig and Siegel, based on which it was categorized as severe level 4 reaction.

Table 2: Causality assessment of suspected ADRs

Suspected drug	Consequence of suspected drug (ADR)	Naranjo's scale	WHO-probability scale	Hart wig's scale
Prednisolone	Hypothyroidism and Cushing's syndrome	Probable	Possible	Moderate

Severity: Severe level 4
Predictability: Unpredictable
Preventability: Probably preventable

Management of Adverse Drug Reaction: Generally, management of ADR includes withdrawal/suspension, dose reduction of suspected drug and administration of supportive therapy. Here in this case report the suspected drug Prednisolone was discontinued.

Fate of suspected drug: Dose Tapered and Drug withdrawn
Treatment Given: Specific
Outcome: Recovering

Discussion

Many drugs and medications can affect thyroid function, but only a small subset (glucocorticoids, dopamine agonists, somatostatinanalogs and retinoids) suppress TSH at the level of the hypothalamus or pituitary. Cushing's is a challenging disease to diagnose. The diagnosis is often delayed because Cushing's is frequently masked by its overlap with more common medical problems such as diabetes, high blood pressure, obesity, and polycystic ovary syndrome. Because of the damage hypercortisolism does to the body including muscles, joints, and bones, recovery is often painful and challenging. Treatment includes depending upon the symptoms, alteration or deletion of the causative drug. In the present case, the patient showed improvement with the help of certain other supportive measures once the dose of drug was tapered and stopped. Early diagnosis with the prompt recognition and withdrawal of all potential causative drugs is essential for a favourable outcome.

Conclusion

Chronic use of synthetic corticosteroids such as prednisolone is the most common cause of Cushing syndrome. Irrational administration of glucocorticoids is most common particularly in chronic therapies which leads to many side effects. Physicians must be aware of these adverse effects and should be cautious in prescribing and be prepared to manage them. The entire health care professionals should be aware of the iatrogenic disease management. Early detection of these disorders can reduce the duration of hospital stay and increase the quality of life. This case report highlights the potent adverse effects of corticosteroids and the need for regular monitoring in patients on long term therapy. There is also need for regular follow-up to assess compliance and response to therapy. Monitoring of ADRs should be done even when there are doubts of early toxic effects. It is important to obtain a history of allergy also as it was missed in this patient before prescribing the causal drug.

This report also highlights the importance of educating patients and their caregivers about the clinical manifestations of Corticosteroid adverse effects, so that it can be recognized early and treated appropriately. Hence, this case report serves to alert clinicians to remain clinically vigilant for such manifestations in patients with active cognitive lifestyles who are on long term steroid therapy. Immediate withdrawal of the causative drug is mandatory to avoid a possible fatal outcome.

A robust ADR monitoring system with a feedback to and the education of the prescribers can help prevent, identify and manage this life threatening condition much more effectively. Early diagnosis helps the clinician to elude secondary infection and subsequent complications. The offending drug should be discontinued and never be rechallenged.

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