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Case Report

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Methyl-Prednisolone and Betamethasone Induced Iatrogenic Cushing Syndrome - A Rare Case Report

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ABSTRACT

Effects of supraphysiologic Glucocorticoid levels originating from exogenous administration of Glucocorticoids known as iatrogenic Cushing syndrome and endogenous overproduction by the adrenal gland (ACTH dependent) or by abnormal adrenocortical tissues (ACTH independent) known as ectopic Cushing syndrome. We report a case of a 50-year-old male patient with symptoms of abdominal distension, swelling of the face, fat deposition around the neck, buffalo hump, and loss of muscles in the upper limbs. The patient had a history of administration of Betamethasone 0.5mg for about 6 months and Methylprednisolone 16mg OD for 15 days. The patient was diagnosed with iatrogenic Cushing syndrome. The steroid dose was tapered gradually to bring back the adrenal function to a normal position. The co-morbid condition leads to the overall worsening of health condition. Therefore, strict control of the co-morbid condition must be a priority. Similar management strategies were adopted by slowly tapering the dose of steroids weekly along with the addition of Furosemide and Metformin to the treatment regimen to control the underlying co-morbid conditions. The case was well managed with appropriate guidelines followed by medication. Identification and diagnosis of this kind of clinical condition are not always clear and consistent. Hence, awareness of diverse forms of presentation of this disorder should be encouraged. Clinical pharmacists have to be aware of these rare syndromes and support the clinicians in whatever ability is required. Far outreach to all healthcare professionals in the form of such case studies can also be an additional tool to create awareness.

Key words: *Adrenocorticotropic hormone, Glucocorticoids, Methylprednisolone, Betamethasone*

INTRODUCTION

Cushing syndrome is caused by excessive activation of glucocorticoid receptors. The iatrogenic (exogenous) is the most frequent Cushing syndrome which is caused due to the prolonged administration of synthetic glucocorticoids such as prednisolone The endogenous Cushing syndrome is uncommon and is due to the overproduction of cortisol by adrenal glands because of an adrenal tumor, excessive production of ACTH by a pituitary tumor, or ectopic ACTH production by other tumors [1]. Iatrogenic Cushing syndrome (ICS) is presented with weight gain usually central obesity with redistribution of fat to truncal areas and the appearance of

dorsocervical and supraclavicular fat pads (buffalo hump) and the classic moon face. Osteoporosis, plethora, easy bruising, thin skin, abdominal striae, myopathy, and muscle weakness can also be seen. The psychological adverse effects include depression and psychosis. Patients are also susceptible to poor wound healing which increases the incidence of infections and atherosclerotic disease [2]. In healthy individuals, the pituitary gland secretes the ACTH that stimulates the adrenal glands to secrete cortisol. When the steroids are administered, suppression of this hypothalamic pituitary adrenal axis occurs [3]. Steroids induce gluconeogenesis and inhibit the uptake of glucose by the cells which results in hyperglycemia and hypertension The catabolic effects cause loss of collagen and reabsorption resulting in the development of osteoporosis and increased susceptibility to fractures. Patients with Cushing syndrome are at risk of various infections because glucocorticoid suppresses the immune system [4]. Certain features such as an increase in intraocular pressure, cataracts, benign intracranial hypertension, osteoporosis, and pancreatitis are more common in the ICS than in the exogenous Cushing syndrome [5]. The diagnosis of iatrogenic Cushing syndrome can be made by measuring 24-hour urinary free cortisol or serum cortisol or administration of 1mg Dexamethasone or late-night salivary cortisol and also by checking the past medical history of the patient for administration of steroids in any form [6]. Here, we report a case of a 50-year-old male with iatrogenic Cushing syndrome due to the administration of Tab. Methylprednisolone and Tab. Betamethasone.

Case presentation

A 50-year-old male patient was admitted to the department of general medicine on 24/12/20 with complaints of abdominal distension for 2 months, swelling of the face for 2 months, and shortness of breath (SOB) for 2 months (grade 1). On clinical examination, his vitals were found to be 150/90 mm of Hg and increased blood sugar levels of 193 mg/dl. He also had fat deposition around the neck (increased supraclavicular fat) and buffalo hump. The patient also presented with a loss of muscle mass in the upper and lower limbs. An X-ray of the pelvic region showed decreased bone density which indicated osteoporosis. The patient's past medical history reveals pain in the abdominal region and SOB after intake of alcohol. His past medication history revealed the usage of Tab. Betamethasone 0.5mg for about 6 months and Tab. Methyl-prednisolone 16mg OD for about 15 days. His day-wise progress and prescription are shown in **Table 1**. The endocrinologist report is listed in **Table 2**. Moreover, the patient underwent various diagnostic tests during the hospital stay which are listed in **Table 3**.

Table 1. Day-wise progress and prescription

Day	Drugs and formulation	Dose and schedule
Day 1 22/12/2020 Admission	Upon admission, he was prescribed with Tab. Prednisolone Tab. Fludrocortisone Tab. Ranitidine Albumin powder Tab. Furosemide Tab. Metformin He was also advised bed rest and high protein diet	 5mg - 0 - 2.5 mg 0.1mg OD 150mg OD 1 spoon in 100ml milk 20mg OD 500mg OD
Day 2 23/12/2020 Complaints of abdominal distension and facial puffiness	Along with the previous day's prescription following medications were added Tab. Multivitamin Tab. Calcium and vitamin D3 Tab. Vitamin C Stop Tab. Fludrocortisone	 P/O OD P/O OD P/O OD
Day 3 - 7 24/12/2020 -28/12/2020	No fresh complaints. The same treatment was continued	
Day 8 29/12/2020 discharged	Tab. hydrocortisone Tab. Theophylline Tab. calcium and vitamin D3 Tab. Multivitamin Salmeterol inhaler	15mg – 0 -5 mg for 1 week 12.5 mg – 0 - 5 mg for 1 week 10mg -0 – 5 mg for 1 week 10mg- 0- 2.5 mg for 1 week 7.5 mg -0- 2.5 mg for 1 week 400mg OD P/O OD P/O OD 2 puffs BD

	Tab. Furosemide	20mg OD
	Tab. Metformin	500mg OD

Table 2. Endocrinologist report

Clinical parameters	Outcome
Moon face	Positive (**Figure 1**)
Dorsocervical fat pad	Positive (**Figure 2**)
Facial plethora	absent
Lipomastia	Positive (**Figure 3**)
Thin limbs	positive
Abdominal striae	absent
Cataract	positive

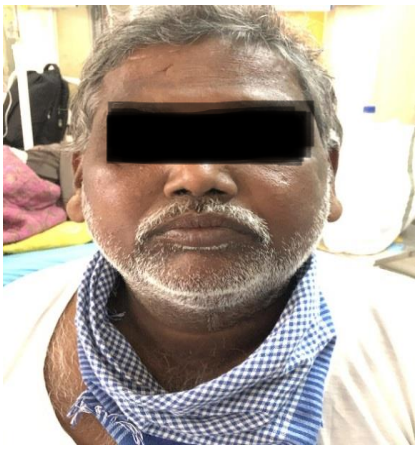

Figure 1. Image of the patient depicting the moon face

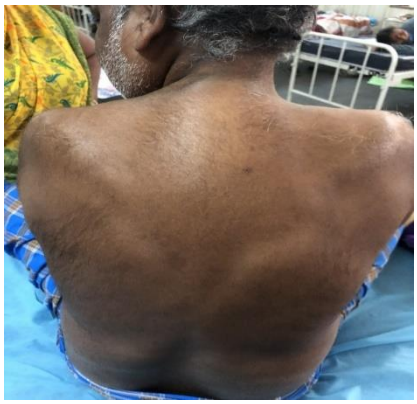

Figure 2. Image of the patient's Dorsocervical fat pad (Buffalo's Hump)

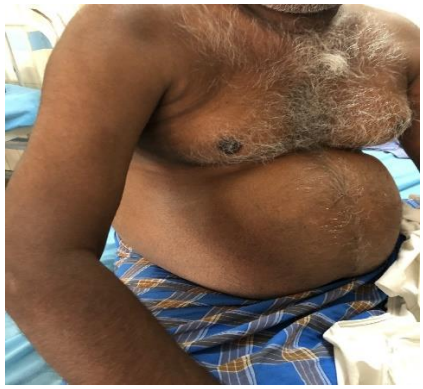

Figure 1. An Image of the patient chest region depicting lipomastia and central obesity

Table 3. Laboratory tests and diagnostic test results during the hospital stay

Date	Tests	Result	Reference range
23/12/2020	White blood cells	13.82	4-11 × 10^9/L
	Neutrophils	77%	50-70%
	Lymphocytes	14.2%	20-40%
	Monocytes	8.4%	3-12%
	Eosinophils	0.4%	0.5-5%
	Basophils	0.00%	0-0.1%
	IMG	0.60	0-999.99
	RBC	3.07	3.5-5.5×10^{12}/L
	Hb	10.1	11-16 g/dL
	MCV	97.7	80-100fL
	HCT	30%	37-54
	MCH	33	27-34
	Platelets	197	150-450×10^9/L
23/12/2020	pH	7.365	7.350-7.450
	PCO2	50.8	32-45 mm Hg
	PO2	54.8	83-108
	HCO3	28.3	22- 28 mEq/L
23/12/2020	USG Abdomen	Grade II fatty liver	
	ECG	Normal	
	Chest X-ray	Normal	
25/12/2020	Serum cortisol (morning)	41.26	185 – 624 nmol/L
26/12/2020	Blood Urea	20.98	15-40mg/dL
	Serum cholesterol	299.1	< 200mg/dL
	Serum creatinine	0.36	0.6-1.2 mg/dL
	Triglycerides	294.2	< 150mg/dL
	HDL	64.5	> 55mg/dL
	LDL	175	< 130mg/dL
	VLDL	58	2-30 mg/dL
	Direct Bilirubin	0.10	0.3mg/dL
	Total serum Bilirubin	0.83	1.2mg/dL
	Albumin	3.68	3.4-5.4g/dL
	ALP	84.1	44-147IU/L
	Serum electrolytes		
	Na	141	135-150 mEq/L
	K	4.1	3.5-5.0 mEq/L
	Cl	105	96-106 mEq/L
	CT scan of the abdomen	No abnormalities	--
	X-Ray of the pelvic region	Decreased bone density (**Figure 4)**	--

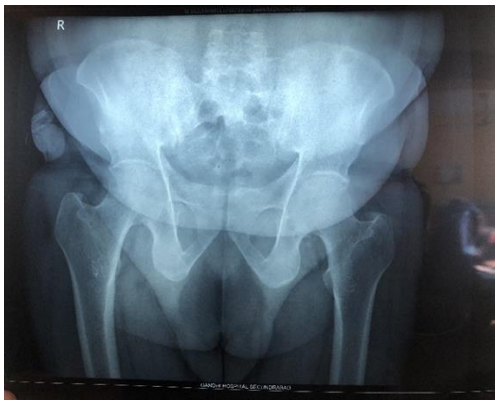

Figure 4. X-ray report of the patient's hip region showing a loss in bone density indicating osteoporosis.

RESULTS AND DISCUSSION

Generally, 1% of the general population are long-term users of high doses of corticosteroids for the treatment of various diseases which may lead to the development of iatrogenic Cushing syndrome [4]. In this case, the patient had clinical features such as moon face, buffalo hump, and fat deposition in the neck region, central obesity, thinning of limbs as positive clinical features of iatrogenic Cushing syndrome. The estimation of serum cortisol has confirmed the diagnosis. The patient also had underlying co-morbid conditions such as hypertension and hyperglycemia. In the normal subject, the plasma cortisol levels are at their highest in the morning and lowest at midnight [7]. The same was performed in this case by obtaining the saliva sample at morning 6.30 am. The circadian rhythm is lost in patients with Cushing syndrome as the plasma cortisol level was 42 nmol/L in this patient. A careful clinical examination and related laboratory test help to diagnose iatrogenic Cushing syndrome, a similar approach was adopted in this case to establish the diagnosis. Glucocorticoids affect the bone which leads to the inhibition of bone formation and enhancing bone resorption. The loss of bone mass due to Cushing syndrome can be recovered after the normalization of cortisol levels [8]. The X-ray findings of the patient's pelvic region showed decreased bone density indicating osteoporosis. Furthermore, the ectopic causes of Cushing syndrome in this patient were ruled out by taking a computed tomography scan (CT scan) of the adrenal region which was normal. It was therefore concluded that it is a case of iatrogenic Cushing syndrome only.

To deal with this condition, steroid doses must be tapered gradually to bring back the adrenal function to normal as it gets suppressed due to chronic steroids [9, 10]. Therefore, it requires several months to recover. The co-morbid condition leads to worsening of overall health condition in patients with iatrogenic Cushing syndrome. Therefore, strict control of the co-morbid condition must be a priority in such cases as normalization of co-morbidities may not occur quickly after the Cortisol levels are reduced [11]. Consequently, steroids must be tapered slowly as sudden stoppage may lead to an adrenal crisis. Similar management strategies were adopted in this case by slowly tapering the dose weekly along with the addition of Furosemide and Metformin to the treatment regimen to control the underlying co-morbid conditions [12].

CONCLUSION

Chronic steroid usage may lead to the development of iatrogenic Cushing syndrome which is characterized by central obesity with redistribution of fat to truncal areas, dorsocervical and supraclavicular fat pads (buffalo hump), and classic moon face. A similar condition was identified in this case and was also diagnosed as ICS. The case was well managed with appropriate guidelines followed by medication. Identification and diagnosis of this kind of clinical condition are not always clear and consistent. Hence, awareness of diverse forms of presentation of this disorder should be encouraged. Clinical pharmacists have to be aware of these rare syndromes and support the clinicians in whatever ability is required. Far outreach to all healthcare professionals in the form of such case studies can also be an additional tool to create awareness.

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