WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 19, 1089-1095. Case Study ISSN 2277–7105

FROM OVERUSE TO UNDERPRODUCTION: A CASE REPORT ON SECONDARY ADRENAL INSUFFICIENCY DUE TO GLUCOCORTICOID ABUSE

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Article Received on
15 August 2024,

Revised on 04 Sept. 2024,
Accepted on 25 Sept. 2024

DOI: 10.20959/wjpr202419-34103

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ABSTRACT

Adrenal insufficiency is a rare, serious condition characterized by reduced production of glucocorticoids, mineralocorticoids, and androgens due to the destruction of the adrenal gland or lack of stimulation. This case report pronounces a case on a 50-year-old female patient who was admitted to the hospital with chief complaints of loose stools and vomiting for the past 6 months with a history of pain in the abdomen. The past history reveals chronic corticosteroid intake for joint pain (Tab. Prednisolone 5 mg BD), which was abruptly discontinued 6 months ago. On examination, BP was 90/60 mmHg. Based on subjective and objective evidence along with laboratory reports, such as serum cortisol levels, the diagnosis was confirmed as secondary adrenal insufficiency. Along with symptomatic management, the patient was treated with Tab. Hydrocortisone 10 mg, Tab. Shelcal 500 mg, Tab. Calcitrol 0.25 mg, Cap. Vitamin D_3 60,000 IU, and Tab. Thyronorm 25 mcg. The patient responded well to the treatment and was stabilized and discharged.

KEYWORDS: Adrenal insufficiency, glucocorticoid-induced, Prednisolone, Serum cortisol, hypothalamic-pituitary-adrenal (HPA) axis, Adrenocorticotropic hormone (ACTH).

INTRODUCTION

Glucocorticoids were discovered in the 1940s, which are potent anti-inflammatory and immunosuppressive agents that have successfully revolutionized the management of acute and chronic inflammatory diseases; however, these drugs are misused most frequently.[1]

According to a study conducted in Italy, up to 1/3 of pharmacists's clients ask for systemic corticosteroids without a valid prescription, which can result in a variety of side effects and adverse effects such as severe infections, hypothalamic-pituitary-adrenal axis suppression, and Cushing syndrome.[2]

CASE STUDY

A 50-year-old female patient was presented in the emergency department of general medicine at VIMS, Ballari, with the chief complaints of loose stools (4-5 episodes/day, watery, foul-smelling) and vomiting (1 episode 2-3 days) for the past 6 months, and H/O pain in the abdomen. Past history: H/o chronic corticosteroid intake for joint pain [Tab. Prednisolone 5 mg BD] and was abruptly stopped 6 months ago. Since then, the patient has had the above complaints and was admitted with the same complaints 1 month ago and was diagnosed with hypotension, hypocalcemia, hypokalemia, subclinical hypothyroidism, and AKI (recovered). H/O weight loss from 75 kg to 45 kg. General physical examination: The patient was conscious and oriented. On examination, vitals were as follows: BP:90/60 mmHg, PR:99 bpm, SpO_2:98%. On systemic examination, CVS: S_1, S_2 heard, RS: B/L NVBS (+), PA: soft and tender.

LABORATORY INVESTIGATIONS:

Table 1: Laboratory Investigations Done During The Hospital Stay.

SL. NO	PARAMETER	D1	D3	D4	D7	D9	D11	D13	D15	D22	REFERNCE RANGE
01	Hemoglobin	11.6								9.3	12-16 gm%
02	WBC	17630								18470	4000-11000cells/cumm
03	RBC	3.61								3.30	4.5-5.5mil/cumm
04	PCV	29.5								28.1	35-46%
05	AST	38.74									0-46 U/L
06	ALP	134.51									40-202 U/L
07	Albumin	3.03									3.5-5 gm/dl
08	Globulin	3.16									1.5-3.0 gm/dl
09	Blood urea	13.85		19		20			20	22	15-45 mg/dl
10	BUN	6									7-23 mg/dL
11	Serum creatinine	1.4		1.0		1.1			1.1	1.1	0.7-1.4 mg/dL
12	Sodium	138.6	143	140	81.29	137	136	136	137	140	136-145mEq/L
13	Potassium	2.29	2.0	3.9	7.27	2.2	2.2	2.6	3.0	3.9	3.48-5 mEq/L
14	Chloride	101.5	104	99	84.92	97	97	97	98	96	96-106 mEq/L
15	Ionic calcium	2.25			50.43						3.2-4.2 mg/dL
16	Serum calcium	6.8									9-11 mg%
17	Total calcium					6.3	8.0	8.3	8.0		8.6-10.2 mg/dL

18	CRP	60.93									0-6 mg/dl
19	ESR	34									0-15 mm/hr
20	APTT									19.0	30-40 seconds

OTHER INVESTIGATIONS

SERUM CORTISOL(Morning): 9.691, 10.08

ACTH: 13.8

Hence based on subjective and objective evidence, the provisional diagnosis was "Chronic Diarrhoea Under Evaluation, Dyselectrolemia, and Hypothyroidism."

TREATMENT GIVEN

Table 2: treatment given during the hospital stay.

SL. NO	MEDICATION	DOSE	ROUTE	FREQ	No of days given
01	INJ.CIPROFLOXACIN	100ml	IV	1-0-1	2 days
02	INJ.METRONIDAZOLE	100ml	IV	1-1-1	2 days
03	INJ.CALCIUM GLUCONATE ((10% 10ml in 100ml NS))		IV	1-1-1	11 days
04	INJ.POTASSIUM CHLORIDE (2amp in 1 pint NS)		IV	1-0-1	11 days
05	TAB.THYRONORM	25mcg	PO	1-0-0	11 days
06	TAB.CALCIUM	500mg	PO	1-1-1	11 days
07	SYP.POTCHLOR	15ml	PO	1-1-1	11 days
08	TAB.RACECADOTRIL	100mg	PO	1-1-1	5 days
09	TAB.SPOROLAC		PO	1-1-1	5 days
10	INJ.PANTOPRAZOLE	40mg	PO	1-0-0	11 days
11	INJ.ONDANSETRON	4mg	PO	1-1-1	11 days
12	TAB.RIFAXIMIN	400mg	PO	1-0-1	9 days
13	INJ.METOCLOPRAMIDE (1amp in 100ml NS)		IV		8 days
14	INJ.NORADRENALINE (2 amp in 1 pint NS)		IV		7 days
15	INJ.MAGNESIUM SULPHATE (2g in 1 pint NS)		Over 12	hours	5 days

The case was discussed with the endocrinologist, who advised to undergo the following tests: ABG analysis, urinary electrolytes, and an ACTH stimulation test (INJ.SYNTROPAC 250 mcg) were injected through IM in the gluteal region, and after 60 min, the serum cortisol levels were checked, as well as ACTH levels and magnesium levels. After the above investigations were done, the patient was asked to review with the reports and was diagnosed with "secondary adrenal insufficiency." The management of this condition was done using the following medications.

Table 3: Treatment for adrenal insufficiency.

SL.NO	MEDICATION	DOSE	FREQUENCY
01	TAB.HYDROCORTISONE	10mg	½ -½ - ½ (8 am-12 pm-6 pm)
02	TAB.SHELCAL	500mg	2-1-1
03	TAB.CALCITROL	0.25mg	1-0-1
04	CAP. VITAMIN D_3	60,000IU	Once in a week for 6 weeks
05	TAB. THYRONORM	25mcg	1-0-0

The patient responded well to the above treatment, and the symptoms reduced gradually; hence, she was discharged with the above medications and was asked to review after 15 days. The patient was also advised to undergo colonoscopy i/v/o chronic diarrhea.

DISCUSSION

The adrenal glands, also known as suprarenal glands, are a pair of small, triangular-shaped glands situated on top of each kidney. They play an important role in producing hormones that regulate metabolism, the immune system, blood pressure, and the body's response to stress. These hormones are synthesized from two distinct parts of the adrenal glands: the cortex and the medulla. The adrenal cortex synthesizes mineralocorticoids, glucocorticoids, and androgens. The adrenal medulla is important for maintaining sympathetic tone by secretion of catecholamines.[3] The adrenal cortex comprises 3 layers: Zona glomerulosa is the outer layer responsible for synthesizing mineralocorticoids, the most important of which is aldosterone, the salt- and water-regulating hormone. Zona fasciculata is the middle layer, and hormones manufactured in the adrenal cortex are glucocorticoids (e.g., cortisol) and sex steroids (e.g., testosterone). Zona reticularis is the inner layer of the adrenal cortex. It has similar functional characteristics of synthesis and secretion of glucocorticoids and androgens.[4]

ADRENAL INSUFFICIENCY (AI): This is a rare, serious condition characterized by reduced production of glucocorticoids, mineralocorticoids, and androgens due to the destruction of the adrenal gland or lack of stimulation.[5]

TYPES

Primary adrenal insufficiency: due to destruction of the adrenal cortex.

Secondary adrenal insufficiency: due to hypothalamic or pituitary disorders or prolonged administration of exogenous glucocorticoids.[3]

The clinical presentations include weakness, weight loss, gastrointestinal symptoms, craving for salt, headaches, memory impairment, depression, and postural dizziness. Early symptoms

of acute adrenal insufficiency also include myalgia, malaise, and anorexia. As the situation progresses, vomiting, fever, hypotension, and shock will develop.

Secondary adrenal insufficiency: This results from diminished secretion of ACTH. ACTH deficiency may be in two ways, i.e., Selective ACTH deficiency due to prolonged administration of high doses of glucocorticoids. This leads to suppression of ACTH release from the pituitary gland and selective deficiency.

Panhypopituitarism due to hypothalamus-pituitary diseases is associated with a deficiency of multiple trophic hormones.

Exogenous glucocorticoids such as prednisolone, prednisone, hydrocortisone, and dexamethasone are used in the management of various inflammatory conditions, but prolonged use of these drugs leads to suppression of the hypothalamic-pituitary-adrenal (HPA) axis, which results in adrenal insufficiency.[6] Excessive glucocorticoids from either endogenous or from an exogenous source bind to receptors present in the hypothalamus and pituitary and trigger negative feedback on adrenocorticotrophic hormone release. The chronic suppression of ACTH leads to atrophy of the zona fasciculata, leading to impaired cortisol secretion.[7]

In patients with HPA axis suppression, the recovery is assessed in many ways, such as measurement of morning cortisol levels, synthetic ATCH stimulation test, metyrapone test, and the inulin tolerance test. The inulin tolerance test is the gold standard for assessing the HPA axis, but it is not widely used due to the risk of hypoglycemia and many contraindications. The metyrapone stimulation test is sensitive, but the use of this test is quite challenging due to its unavailability and risk of adrenal crisis. The ACTH stimulation test includes a high-dose and low-dose ACTH stimulation test. The high-dose (250 mcg) ACTH stimulation test uses supra-physiologic doses of ACTH that are sufficient to stimulate the atrophied adrenal glands, leading to false negative results; hence, the low-dose (1 mcg) ACTH stimulation test has high sensitivity, but the lack of standard protocols for preparation of ACTH leads to controversies about the accuracy. The 250 mg ACTH stimulation test examines the direct response of the adrenal gland to supraphysiologic ACTH stimulation. The serum cortisol levels are checked after 60 min post-stimulation; if there is no response, it indicates secondary adrenal insufficiency, and a rise from baseline to 18 mcg/dl at 60 min post-stimulation suggests that the adrenal suppression is minimal.[8] So, in the above-

discussed case, the patient was given 250 mcg of ACTH, and the serum cortisol level was checked 60 min later and showed an increase from 9.6 mcg/dl to 10.08 mcg, and hence it indicates that the patient has secondary adrenal insufficiency. The management of this condition is done by using hydrocortisone in 2 or 3 divided doses with a typical daily dose of 15-20 mg.[9]

COMPLICATION OF ADRENAL INSUFFICIENCY

- Adrenal crisis is a serious complication that can also lead to death if untreated.
- Life-threatening low blood pressure, low blood glucose, low serum electrolytes (sodium, potassium).

The inadequate stimulation of the adrenal glands due to insufficiency or inadequate secretion of the ACTH hormone leads to secondary adrenal insufficiency. The abrupt withdrawal of exogenous glucocorticoids results in adrenal insufficiency by suppressing the hypothalamic pituitary adrenal (HPA) axis. Hence there are more chances of developing adrenal insufficiency if they are not monitored closely, and the dose of the glucocorticoids should be tapered gradually to prevent the occurrence of adrenal insufficiency.

CONCLUSION

Patients who take exogenous glucocorticoids are at a risk of developing adrenal insufficiency. Educating the patients in detail about the risks associated with the use of glucocorticoids can help in the prevention of the occurrence of such harmful effects. Hence, we conclude that the role of clinical pharmacists plays a major role in the rational use of drugs and in preventing the development of such adverse effects as they engage in educating the patient regarding the disease, drugs, and the associated side effects. This helps the patient to understand and be cautious about the use of medications; these drugs therefore should not be dispensed without a proper prescription prescribed by a registered health care practitioner.

ABBREVIATION

Hypothalamic-pituitary-adrenal (HPA) axis, Adrenocorticotropic hormone (ACTH), Adrenal Insufficiency (AI).

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