



Budesonide Induced Addison's Disease (Adrenal Insufficiency): A Case Report

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ABSTRACT

Addison's disease (AD) is a rare Endocrinal disorder, with several oral and systemic manifestations. A variety of pathological processes cause Addison's disease. The symptoms of this disease are hyperpigmentation which associated with the disease and intraoral pigmentation is perceived as the initial sign and develops earlier to dermatological pigmentation. In our study a 56 years old male patient presented with hyperpigmentation of skin, regions of tongue, Palms, feet, groin region, which is considered as hallmark of AD and patient was on Tab. Deriphylline, Inhaler Foracort (Budesonide + Formoterol), Syp. Salbutamol for his Past H/O Tuberculosis and K/C/O Chronic Obstructive Pulmonary Disease. By analyzing the Subjective and Objective evidences the patient was suspected to have BUDESONIDE INDUCED ADDISON'S DISEASE which was further confirmed by using WHO-UMC Causality Assessment Scale and Naranjo Scale Score.

Key WORDS: Budesonide, Addison's disease, Hyperpigmentation, Glucocorticoids, Serum-cortisol, Adrenal Insufficiency.

INTRODUCTION:

Addison's disease is a rare endocrinal disorder that affects 1 in 1,00,000 people it is seen in all age groups and affects male and female equally.^[1] In 1855, Thomas Addison described a clinical syndrome characterized by wasting and hyperpigmentation, and identified its cause as destruction of the adrenal gland. However, life-saving glucocorticoid-replacement therapy for the condition did not become available until 1949, when Kendall, Sarett, and Reichstein first synthesized cortisone. Furthermore, despite this breakthrough, there are still many advances and challenges with respect to the management of individuals with adrenal insufficiency.^[2] The symptoms of Addison's disease are due to low levels of cortisol and aldosterone, the release of cortisol involves hypothalamus which releases corticotrophin releasing hormone (CRH) and signals the anterior pituitary to release adrenocorticotrophic hormone (ACTH) and this in turn signals adrenal gland to release cortisol into body, when we start giving patient an external glucocorticoids i.e. Inhaled or oral, it sends negative feedback signals to adrenal gland such that these glands either reduce or stop secreting the chemicals eventually leading to adrenal suppression and depletion of cortisol, so we do not use oral steroids for long period so that we taper the dose over a period. We hereby present a 56 year old male who developed Addison's disease (adrenal insufficiency) as a result of budesonide which was prescribed for his COPD condition.

CASE REPORT:

A 56 year old male patient complaining of hyperpigmentation of skin (including palm, tongue and feet) since 1 month, breathlessness since 5 days, high grade fever since 5 days and 2 episodes of vomiting which was non-blood stained and contains food particles had been admitted to the hospital and had previous history of hospital admission with similar complaints 1 month back, with a past history of K/C/O PTB since 15 years and COPD since 10 years and was T. DERIPHYLLINE 100mg, SYP.SALBUTAMOL 10 ml, FORACORT INHALER (BUDESONIDE + FORTMOTEROL) since 1 month. On examination patient was febrile, BP was 90/60 mmHg, PR was 110 bpm, SPO2 was 98% reducing at room air and temperature was 41°C high grade fever and on systemic examination RS was B/L RHONCHI CREPTS (+), B/L air entry, CNS- conscious and oriented, CVS-S1 S2 heard no murmurs and he was known alcoholic since 20 years but left 10 years back and he was known smoker. On physical examination of patient it was found to have all hallmarks of Addison's disease and patient nails were examined which was found to be thin and brittle nails and nails developed longitudinal melanonychia and patient laboratory investigation reports showed the abnormal values of WBC-12880 cells/cumm, ESR-28 mm/hr, CRP-54.4 mg/L, sodium levels were 126mEq/L (hyponatremia), potassium levels were 5.8 mEq/L (hyperkalemia) and serum cortisol levels were 2.137 mcg/dl which are consider to be very low and indicates adrenal insufficiency due to steroid use and patient chest X-ray reports yields consolidations in apical and in upper lung zones, nodules and cavitations (+).



On the basis of above mentioned details physician diagnosed it as Addison's disease due to glucocorticoid use (budesonide) and was recommended to stop budesonide inhaler which was taken by the patient and patient was advised to use IPRATROPIUM and LEVOSALBUTAMOL nebulization three times a day and patient was shifted to male medical ward and started with INJ. CEFTRIAZONE 1gm TID, INJ. PANTOPRAZOLE 40 mg once a day INJ. FUROSEMIDE 20 mg, INJ. INSULIN 10 units in 25% dextrose (to treat hyperkalemia), T. MUCINAC 600mg TID, INJ. HYDROCORTISONE Stat (corticosteroid replacement therapy), T. AZITHROMYCIN 500 mg once a day and this treatment was continued for 6 days and on day 6 patient was advised to repeat laboratory investigations and all the laboratory investigations were in normal range and on day 7 patient was discharged and advised to take T. MUCINAC 600 mg TID, SYP. AMBROXOL 10ml TID, T. PARACETAMOL 500mg SOS, T. HYDROCORTISONE 25mg BD for 15 days and IPRATROPIUM +LEVOSALBUTAMOL nebulization to be continued.

This case was analyzed by using NARANJO SCALE and WHO-UMC causality assessment scale, according to NARANJO scale algorithm was 6 which is categorized as probable reaction and WHO causality assessment scale patient fall under CERTAIN on the basis of these scales it was concluded as BUDESONIDE INDUCED ADDISON'S DISEASE .

DISCUSSION:

Addison's Disease is a rare Endocrinal disorder, that affects 1 in 1,00,000 People seen in all the age groups and also affects Males and Females equally. This disease is named after Thomas Addison, who first described patients affected by this disorder. Addison's Disease can present as life threatening crisis because it is frequently unrecognized in its early stage.^[1] The normal mechanism involved in this is releasing of Corticotrophin-Releasing Hormone (CRH) by Hypothalamus, in turn activates Anterior Pituitary gland to release Adrenocorticotrophic Hormone (ACTH) activates Adrenal gland to release Glucocorticoids. Glucocorticoids are naturally produced by Adrenal gland, when we start giving an external glucocorticoids I.e. Steroid Inhalers or Oral Steroids, it sends negative feedback signals to Adrenal gland not to produce these hormones, so it starts decreasing the amount of chemicals it's producing and it leads to Adrenal Suppression as a result of administration of Glucocorticoids externally, So we do not use the steroids for long period of time so that we taper the dose over a period. Budesonide acts as a glucocorticoid receptor agonist, exerting anti-inflammatory and immunosuppressive effects. It inhibits the release of pro-inflammatory cytokines and reduces the migration of inflammatory cells. Budesonide also suppresses the hypothalamic-pituitary-adrenal (HPA) axis, leading to decreased production of endogenous cortisol. Prolonged use or high doses of budesonide can suppress the HPA axis, leading to adrenal insufficiency. Suppression of the HPA axis occurs due to the negative feedback loop, where exogenous glucocorticoids inhibit the release of adrenocorticotrophic hormone (ACTH) from the pituitary gland. Lack of ACTH stimulation results in reduced synthesis and secretion of cortisol by the adrenal glands. Reduced cortisol production in the adrenal glands leads to a deficiency of this hormone. Cortisol is crucial for maintaining glucose homeostasis, regulating immune response, and responding to stress. Lack of cortisol can result in various symptoms such as fatigue, weight loss, low blood pressure, and electrolyte imbalances. In addition to cortisol, the adrenal glands also produce aldosterone, a mineral corticoid hormone. Budesonide-induced Addison's disease can lead to aldosterone deficiency, contributing to electrolyte imbalances, particularly sodium and potassium. Sodium retention and potassium loss can result in low blood pressure, dehydration, and disturbances in electrolyte levels. Budesonide-induced Addison's Disease may have an autoimmune component, potentially triggered by the drug's immunosuppressive effects. The exact mechanisms by which budesonide induces autoimmunity in the adrenal glands are not fully understood and require further research. However, life saving glucocorticoids – replacement therapy for the condition did not become available for until 1949, when Kendall Sarett and Reichstein first synthesized cortisone, despite this breakthrough over 150 years, there are still many advances and challenges with repeat to the management of individuals with Adrenal insufficiency. There are two types of Adrenal Insufficiency Primary and Secondary. Therapeutic glucocorticoids administration is thought to be the most common cause of secondary Adrenal insufficiency, since chronic administration of exogenous glucocorticoids induces atrophy of Pituitary Corticotrophin cells, however iatrogenic Adrenal insufficiency becomes potentially relevant only during or after glucocorticoids withdrawal. Because iatrogenic Adrenal insufficiency is transient in most cases.^[2]

Patient may experience Fatigue, weakness, weight loss and gastrointestinal upset. Symptoms are gradual and worsen over a period of years, making early diagnosis difficult the symptoms related to degree of cortisol, mineralocortisol and adrenal androgen deficiency at time of presentation Addison's disease is usually diagnosed after a significant stress or illness .Unmasks cortisol levels, Hypokalaemia and volume depletion. Hyperpigmentation is the physical finding characteristic of Addison's Disease, arising from continual stimulation of the corticotrophs in anterior pituitary specially it results from gross reactivity between the ACTH produced by the corticotrophs and melanocortin I receptor on Keratinocytes. Hyperpigmentation is usually generalized over the entire body and can be found in palmer - buccal mucosa, vermilion border of the lips and around scars and nipples.^[3]

In our current case patient presented with hyperpigmentation of skin involving palm, tongue and feet, followed by developing High grade fever, 2 episodes of vomiting and breathlessness and patient was on Tab. Deriphylline, Inhaler Foracort (Budesonide + Formoterol), Syp. Salbutamol and in this case suspected causative drug is Budesonide. Budesonide was withdrawn immediately and patient was managed symptomatically with supportive care and following therapy was added Inj.Ceftriaxone 1gm, Inj. Pantoprazole 40mg, Inj. Furosemide 20 mg,

Neb. Ipratropium Bromide+ Levosalbutamol, Inj. Insulin 10 units in 25% Dextrose which increase k⁺ uptake by tissues and reduces hyperkalemia, Tab. Mucinac 600mg, Inj. Hydrocortisone 100 mg Stat and Tab. Azithromycin 500mg.

In this study Addison's disease (Adrenal Insufficiency) was analyzed by using WHO Causality Assessment Scale and Naranjo Scale. According to WHO-UMC scale the Patient falls under the certain category and Total score of the Naranjo scale algorithm was 6 which is categorized as Probable reaction. The offending drug was Dechallenged as rechallenge was risky for patient condition and can also be life threatening. Foracort was replaced with levosalbutamol and ipratropium bromide to manage patient's COPD along with prophylactic antibiotics and mucolytics etc.

CONCLUSION:

Here we report a rare case of Budesonide induced Addison's Disease (Adrenal Insufficiency) in a 56 years old male in order to avoid morbidity and mortality associated with Addison's crisis, we need to be highly cautious and vigilance while using glucocorticoids as they are documented to cause adrenal insufficiency and AD, at most care should be taken to detect earliest symptoms of AD so that suitable interventions is made with alternative drug to ease the patients. It's drug Components need to be reconsidered in view of safer use and alternative available.

Patient Perspective:

During admission the patient was worried about his health condition and clinical manifestations, later after start of the treatment, which was yielding good positive results, the patient started to overcome from his previous health issues and showed remarkable progress both physically and mentally. We humbly thank the medical teams for timely intervention and successful treatment.

Consent of The Patient

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Author Agreement Statement

This is an original work and we solemnly declare that manuscript has not been published before in any other journal's. We also confirm that all the mentioned author are aware of all the declaration and agree to them.

Declaration Of Competing Interest

No conflict of Interest.

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