A Case Report and Review on Cushing's Syndrome

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ABSTRACT

Cushing's syndrome is a rare endocrine disorder that comprises a large group of signs and symptoms resulting from chronic exposure to excess cortisol, a hormone that adrenal gland produces and corticosteroids. Most cases of Cushing's syndrome are due to increased adrenocorticotropic hormone production from a pituitary adenoma, which is referred to as Cushing's disease. Most of the signs and symptoms are nons-pecific and common in the general population, making a diagnosis often challenging. However, several dermatological manifestations, such as fragile skin, easy bruising and reddish purple striae, are more discriminatory. Because uncontrolled Cushing's syndrome of any etiology is associated with substantial morbidity, including increased cardiovascular disease and mortality, it is important to make an early diagnosis. Unfortunately, median delays of 2 years to diagnosis have been reported. We report a case of a female paediatric patient who is a known case of idiopathic thrombocytopenic purpura who had multiple dermatological findings, including facial plethora, easy bruising, hirsutism and acne, the latter 2 signs reflecting androgen excess.

Key words: Cushing's syndrome, Cortisol, Corticosteroids, Adrenocorticotropic hormone.

INTRODUCTION

Cushing's syndrome is characterized by signs and symptoms that result from prolonged exposure to excessive plasma corticosteroids. While the most common cause is iatrogenic from medically prescribed corticosteroids, endogenous Cushing's syndrome is a relatively rare disease. A US-based study estimated the incidence of endogenous Cushing's syndrome at 8 per million people.[1] Pituitary-secreting tumors, first described by Harvey Cushing in 1912 and now referred to as Cushing's disease, account for approximately 70% of cases, while ectopic adrenocorticotropic hormone (ACTH)-secreting tumors and adrenal tumors account for 10 and 20% of cases, respectively.[2] Although the diagnosis of Cushing's syndrome can be straightforward, when several clinical findings are present, it is often challenging to make the diagnosis. None of the symptoms or signs are pathognomonic of the syndrome and many symptoms (such as obesity, hypertension, glucose intolerance, weight gain, fatigue, weakness, menstrual abnormalities and depression) are found in the general population. In contrast, the dermatological manifestations of Cushing's syndrome that include skin atrophy, alopecia, easy bruisability and striae are less commonly observed in other individuals.[3] We report an unusual case of a woman who presented with a chief complaint of hair loss and who was found to have Cushing's disease.

Case Report

A female patient of 9 years old was admitted to Paediatric ward with complaints of petechiae and bleeding since 10 days and also abdominal distention, bloating, muscle weakness, facial swelling, easy bruising, hirsuitism and obesity. Although she had been experiencing progressive weight gain for about 6 months.

Patient had angioedema and was on treatment. She was taking Tab. Danazole 200mg 1-0-0. Diagnosed with Pulmonary TB at 9 months of age and completed 1-year antitubercular treatment. Repeated episodes of cough and cold from 2 years of age, once in 15 days, presently frequency decreased to once in 2 months. Adenotonsillectomy done

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in 2015 i/v/o recurrent tonsillitis.

1st episode of petechiae, bleeding gum in August 2018, was admitted in KMC hospital Manipal and treated with IVIG and platelets and advised Wysolone for 3 weeks; parents discontinued Wysolone after 1 week; 2nd episode on October 2018 treated outside with Wysolone 5 days; 3rd episode on January 26 2019 treated with Wysolone 10mg 1-1-1.

Serum ferritin, iron, thyroid-stimulating hormone, antinuclear antibody, albumin and total protein were all within normal limits. Subsequent tests were ordered: 24-h urine cortisol: 238 μg (range 3.5–45 μg/24 h) and ACTH: 69 pg/mL (range 9–52 pg/mL). The results were consistent with a diagnosis of Cushing's disease.

DISCUSSION

Dermatologists may encounter skin findings that reflect an underlying endocrine disorder. While many of the signs and symptoms of Cushing's syndrome are nonspecific, those features that best distinguish Cushing's syndrome are proximal muscle weakness, facial plethora, easy bruising and purple (violaceous) striae.[3]

The often-prominent skin findings reflect the hypercatabolic effects of hypercortisolism inhibition of epidermal cell division and collagen synthesis, resulting in thinning of the stratum corneum and loss of subcutaneous fat.[4] Skin atrophy may be prominent and the loss of subcutaneous connective tissue results in easy bruising after minimal injury. The atrophy and disruption of collagenous subcutaneous fibers lead to the development of broad, purple striae because the increasingly thin skin does not hide the color of venous blood in the underlying dermis. Another skin finding is hyperpigmentation due to excess ACTH, which is most commonly seen in ectopic ACTH syndrome, less commonly in Cushing's disease (i.e., pituitary-secreting ACTH tumor) and never in adrenal Cushing's syndrome; is the hyperpigmentation a result of ACTH binding to melanocyte - stimulating hormone receptors.

In contrast to the aforementioned skin changes, female baldness or female hair loss has been variably reported and is rarely the chief complaint of a patient presenting with Cushing's syndrome.[2] In a review of Cushing's syndrome that included 7 case series of 33–100 patients, 4 case series did not report female baldness, whereas it was reported in 3 of the case series with an incidence ranging from 13 to 51%.[5] In a recent matched case-control study using a commercial health-care insurance claims data-base that included 1,875 patients with Cushing's syndrome, female balding was found to be 5 times more common than in the matched controls; the combination of weakness/fatigue and female baldness was 10 times more common.[6]

In a review of Cushing's syndrome, Findling and Raff[7] noted that the diagnosis of Cushing's syndrome "is the most challenging problem in clinical endocrinology." Patients with Cushing's syndrome and persistent hypercortisolism have a 4–5 times excess mortality compared to the general population, highlighting the urgency of diagnosis.[8] They found that general practitioners were consulted 76% of the time, endocrinologists 25%, gynecologists 24%, psychiatrists/psychologists 12%, rheumatologists 11% and dermatologists 8% of the time.

As noted above, the majority of clinical signs and symptoms of Cushing's syndrome are relatively nonspecific, whereas dermatological manifestations, such as fragile skin, easy bruising and purple striae, are more discriminatory.[3] Broder *et al.*[6] noted hirsutism to be 61 times more common in Cushing's syndrome than in the general population. In contrast, FPHL is commonly seen in the general population, although with a 5 times greater frequency in patients with Cushing's syndrome.

CONCLUSION

Cushing's disease is a rarity that can be difficult to diagnose due to the significant number of varied pathologies indicated by its signs and symptoms. This is an interesting case of Cushing's disease as the level of cortisol measured in the patient was high and shown with symptoms of Cushing's syndrome.

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CONFLICT OF INTEREST

There is no conflict of interest between the authors.

ABBREVIATIONS

US: United States; **IVIG:** Intravenous immunoglobulin; **TB:** Tuberculosis; **ACTH:** Adrenocorticotropic hormone.

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