Case Report

Unmasking Cushing's syndrome: An atypical case of pituitary microadenoma with cutaneous and pulmonary sequelae

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ABSTRACT

Cushing's syndrome (CS) is a rare endocrine disorder caused by long-term exposure to high levels of glucocorticoids. Although patients typically present with obesity, hypertension, diabetes, and characteristic cushingoid features, atypical presentations with severe pulmonary and cutaneous manifestations are uncommon and may delay diagnosis. We present a 28-year-old woman who came in with sudden breathlessness, non-healing bilateral lower limb ulcers, progressive weight gain, cushingoid features, and various systemic issues. Imaging and hormone tests confirmed a pituitary microadenoma causing Cushing disease. She successfully underwent endoscopic transnasal transsphenoidal resection with marked clinical improvement at follow-up. This case highlights the importance of a careful evaluation and a team approach for patients with uncommon CS. Early diagnosis and surgical intervention can greatly lower morbidity and enhance outcomes.

Key words: Cushing's syndrome, Pituitary microadenoma, Pulmonary edema, Pyoderma gangrenosum, Transsphenoidal surgery

Cushing's syndrome (CS) results from prolonged exposure to excess glucocorticoids. Most cases occur due to an adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma, often called Cushing's disease [1,2]. Incidence of CS is higher among women than among men, with new cases diagnosed at a ratio of 3–8 : 1 [3-6]. The peak incidence of Cushing disease is in women between 50 and 60 years old [7]. The clinical symptoms vary and can be subtle early on, leading to delays in diagnosis. Although weight gain, hypertension, diabetes mellitus, proximal muscle weakness, and characteristic Cushingoid appearance are well-recognized manifestations, atypical cases that involve cutaneous lesions and pulmonary complications can make it harder to recognize the syndrome on time.

We report a case of Cushing's disease in a young woman presenting with non-healing ulcers, acute pulmonary edema, and cutaneous neutrophilic dermatosis, ultimately diagnosed with a pituitary microadenoma. The rationale for reporting this case is that the simultaneous presentation with acute pulmonary edema, pyoderma gangrenosum, and multiple classical Cushingoid features secondary to a pituitary microadenoma is exceedingly rare. This report highlights the diagnostic challenges associated with the uncommon symptoms seen in Cushing's disease. Through this case, the importance of maintaining a high degree of suspicion, thorough endocrine and radiological evaluation, and timely management is highlighted.

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CASE REPORT

A woman in her 20s, known to have hypothyroidism on levothyroxine 25 mcg, presented with acute breathlessness and orthopnea of 1-day duration. Over the prior month, she developed progressive weight gain, facial puffiness, abdominal distension, and non-healing ulcers over both feet. Doppler ultrasonography of the lower extremities was normal.

On examination, her pulse rate was 104 beats/min, blood pressure was 124/80 mmHg, respiratory rate was 32 breaths/min, and oxygen saturation was 99% while receiving non-invasive ventilation with FiO_2 100%. Respiratory examination showed

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bilateral normal vesicular breath sounds with bilateral inspiratory crepitations. Examination of other systems was unremarkable. General examination revealed cushingoid facies (Fig. 1), hirsutism, dorsocervical fat pad, violaceous abdominal striae, acanthosis nigricans, thin skin, proximal muscle wasting, and ACTH-induced hyperpigmentation. Local examination showed a solitary ulcer measuring approximately 6 × 3 cm present over the dorsum of the right foot. The ulcer was irregular in shape with well-defined margins. The floor was covered with granulation tissue mixed with yellow slough. There was minimal serous exudate with no obvious purulent discharge. The surrounding skin showed hyperpigmentation, induration, and post-inflammatory changes. No exposed tendon or bone was visible. A solitary ulcer measuring approximately 3 × 3 cm was present over the medial malleolus of the left ankle. The ulcer was irregular in shape, and the floor consisted of pale granulation tissue with small areas of yellow slough. Mild serous discharge was present without frank pus. The surrounding skin demonstrated hyperpigmentation and chronic inflammatory changes. No exposed bone or tendon was noted (Fig. 2a).

She was initially managed as presumed acute respiratory distress syndrome (ARDS) with intravenous piperacillin–tazobactam (4.5 g IV twice daily) and dexamethasone (Dexona) 2 mg intravenously. She required admission to intensive care for increasing respiratory distress. There were bilateral pulmonary opacities on chest radiography, consistent with pulmonary edema. She improved with intravenous diuretics and ventilatory support and was extubated successfully after 48 h.



Figure 1: Cushingoid facies of the patient



Figure 2: (a) Solitary ulcer measuring approximately 6 × 3 cm present over the dorsum of the right foot; and (b) follow-up of the patient after 3 months

Initial biochemical assessment revealed a morning serum cortisol of 15.3 mcg/dL (normal: 8–23 mcg/dL) and an ACTH of 32 pg/mL (normal: 7–63 pg/mL), both of which were within the physiological range. In spite of these seemingly normal findings, the high clinical index of suspicion for hypercortisolism led to further investigation. Overnight dexamethasone suppression test (ONDST) revealed a post-dexamethasone cortisol of 2.25 mcg/dL, just below the diagnostic threshold (<2.5 mcg/dL), and was considered abnormal in the clinical setting. Pituitary magnetic resonance imaging (MRI) demonstrated a 4 mm right-sided microadenoma, which was further supported by Ga-68 Trivehexin positron emission tomography-computed tomography (PET-CT) with increased uptake (standardized uptake value 1.7) in the intrasellar lesion with mild pituitary stalk deviation.

A biopsy of the long-standing ulcer on the foot revealed histological findings typical of pyoderma gangrenosum. Pulmonary function tests revealed a restrictive pattern that was indicative of interstitial lung disease. In combination, these tests assisted in the diagnosis of Cushing's disease with atypical pulmonary and cutaneous manifestations.

The patient's acute respiratory distress with bilateral pulmonary infiltrates at presentation led us to suspect ARDS due to infection. The lack of fever, sterile cultures, and quick improvement with diuretics, however, favored cardiogenic pulmonary edema, which in hindsight was caused by fluid retention secondary to cortisol. The fact that, there were several foot ulcers to begin with caused concern for infective cellulitis or vasculitic ulcers. Doppler studies ruled out peripheral arterial disease and venous thrombosis. Failure to improve on antibiotics, added to by histopathology, supported the diagnosis of pyoderma gangrenosum, a neutrophilic dermatosis sometimes related to endocrinopathies like Cushing's syndrome.

Biochemically, normal morning cortisol and ACTH levels initially spoke against hypercortisolism. Despite this discordance between the dramatic clinical presentation and laboratory findings, dynamic testing was required. ONDST proved to be inadequate, thus confirming cortisol excess. Considerations for differential diagnosis were Cushing's disease (pituitary ACTH production) versus ectopic ACTH secretion (such as from a neuroendocrine tumor). The presence of a pituitary microadenoma on MRI, with supportive uptake on Ga-68 PET-CT, favored the diagnosis of pituitary-dependent Cushing's syndrome.

She underwent endoscopic transnasal transsphenoidal resection of the pituitary microadenoma under general anesthesia with intraoperative neuronavigation. Local

fusidic acid was applied to foot ulcers with planned post-operative systemic immunosuppression.

Her post-operative course was uneventful without cerebrospinal fluid leak or diabetes insipidus. Respiratory function stabilized without additional ventilatory support. On review after 3 months, the patient showed substantial improvement in cutaneous ulcers and a gradual decline in weight, reflecting early reversal of hypercortisolism (Fig. 2b).

DISCUSSION

Previous case reports have similarly highlighted the diagnostic challenges associated with Cushing syndrome due to its variable clinical presentations. One such case report showed a woman with ACTH-independent Cushing syndrome caused by bilateral adrenocortical adenomas who presented with classical manifestations. Following biochemical confirmation and radiological identification of bilateral adrenal masses, the patient underwent bilateral adrenalectomy with significant clinical improvement. Their report showed the importance of correlating clinical features with appropriate investigations to establish the diagnosis of Cushing syndrome. In contrast, our patient had ACTH-dependent Cushing disease secondary to a pituitary microadenoma that presented with unusual cutaneous and pulmonary manifestations, making the diagnosis more challenging [8].

Similarly, another previous case report has shown a woman with Cushing disease whose diagnosis was delayed because her symptoms initially mimicked polycystic ovarian syndrome. Although she exhibited amenorrhea, hirsutism, acne, redistribution of body fat, and muscle weakness, initial pituitary MRI was negative, and repeat high-resolution imaging eventually identified a pituitary microadenoma. She achieved remission following transsphenoidal surgery [9]. Similar to their study, our patient required a high index of clinical suspicion and in depth endocrine evaluation before definitive diagnosis. However, unlike the previously reported case, our patient presented with life-threatening pulmonary complications and biopsy-confirmed pyoderma gangrenosum, highlighting atypical manifestations of Cushing disease.

This case showcases the diagnostic challenges posed by unusual presentations of Cushing's disease. The patient faced a serious pulmonary issue at the start, which is rarely the first sign of CS [10]. High cortisol levels can lead to fluid retention, immune problems, and fragile blood vessels, which may explain her respiratory failure and skin ulcers.

Pyoderma gangrenosum has been reported in CS, linked to problems with neutrophil regulation [11]. Her pancytopenia might be due to bone marrow suppression from high cortisol levels or sepsis-related issues. The combination of imaging and biochemical suppression testing was crucial for identifying the pituitary microadenoma. Quick neurosurgical intervention using a minimally invasive technique enabled early recovery and reduced complications. This case emphasizes the importance of team-based care involving endocrinology, dermatology, pulmonology, and neurosurgery when handling complex endocrine conditions.

CONCLUSION

This case shows the need for increased clinical awareness of Cushing's disease in patients with unexplained multiple system issues. Early evaluation by endocrinologists, thorough imaging, and teamwork are essential for good outcomes. Quick surgical action in this young patient not only resolved life-threatening complications but also improved her long-term prospects.

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