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Diagnostic Challenges in Atypical Familial Glucocorticoid Deficiency: A Case Report

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Abstract

INTRODUCTION
Familial glucocorticoid deficiency (FGD) is a rare cause of primary adrenal insufficiency characterized by ACTH resistance and isolated cortisol deficiency with preserved mineralocorticoid function, typically presenting in childhood with hypoglycemia, hyperpigmentation, and markedly elevated ACTH with undetectable cortisol. We report an atypical adult presentation with partial adrenal reserve, highlighting diagnostic challenges when genetic confirmation is unavailable.

CASE DESCRIPTION
A 29-year-old asymptomatic man with history of childhood growth hormone deficiency and low bone mass treated till adulthood presented for endocrine evaluation. Laboratory testing revealed elevated ACTH (78–102 pg/mL; reference 6–50) with low cortisol (4.5–5.8 µg/dL; reference 7–25). There was no electrolyte abnormality. Cosyntropin stimulation demonstrated borderline adrenal reserve with peak cortisol of 18.5 µg/dL. Plasma renin was mildly elevated at 7.63ng/ml/hr with non-suppressed aldosterone 5ng/dl, and DHEAS was normal. Negative Anti-21-hydroxylase antibodies ruled out autoimmune adrenalitis. Normal Very long-chain fatty acid testing excluded X-linked adrenoleukodystrophy. Pituitary axis was otherwise intact.

The differential diagnosis favored genetic causes of ACTH resistance, including FGD variants involving MC2R, MRAP, NNT, or TXNRD2. However, genetic testing was unavailable due to insurance limitations.

Given preserved partial adrenal function and absence of symptoms, daily glucocorticoid replacement was deferred. The patient received comprehensive education on stress-dose steroids and emergency hydrocortisone with close clinical monitoring.

CONCLUSION
This case illustrates the diagnostic complexity of atypical FGD presentations in adults. When genetic testing is unavailable, systematic exclusion of common etiologies combined with careful clinical phenotyping guides management. Patients with borderline adrenal reserve require individualized treatment decisions