Hypertension Secondary to 17 Alpha-Hydroxylase Deficiency in a Young Male: A Case Report

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Abstract

This case report describes a 19-year-old male who initially presented with altered sensorium. The patient, without a relevant medical or family history, was first treated for hypokalaemia, which resolved with potassium supplementation. Subsequent cardiology evaluation revealed persistent hypertension with blood pressures peaking at 170/110 mm Hg. Further investigations confirmed 17 alpha-hydroxylase deficiency, a rare cause of secondary hypertension associated with mineralocorticoid deficiency. This case underscores the importance of considering rare endocrinological disorders in young patients presenting with hypertension and electrolyte imbalances. Management strategies, diagnostic challenges, and outcomes are discussed, emphasizing the need for a thorough endocrinological assessment in similar presentations.

Keywords: Hypertension, 17-alpha-Hydroxylase Deficiency, Hypokalaemia, Altered Sensorium.

INTRODUCTION

17 alpha-hydroxylase deficiency is a rare genetic disorder impacting steroid biosynthesis, leading to decreased production of cortisol and sex steroids, while enhancing mineralocorticoid precursor production, which can manifest as hypertension and hypokalemia.[1] This autosomal recessive condition predominantly affects the adrenal glands and gonads,.

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contributing to complex clinical scenarios typically presenting in adolescence or early adulthood.[2]

Epidemiologically, this condition is exceedingly rare with few reported cases globally, contributing to challenges in recognition and diagnosis due to its non-specific presentation and similarity to other forms of secondary hypertension. Pathophysiologically, the deficiency in 17 alpha-hydroxylase blocks the synthesis of cortisol from progesterone, causing an accumulation of mineralocorticoid precursors that mimic aldosterone's action, leading to sodium retention, hypertension, and hypokalemia.[3]

Clinically, patients often present with vague symptoms such as fatigue, headaches, or in severe cases, altered mental status due to acute electrolyte imbalances, as demonstrated in the current case. Diagnosis typically involves biochemical assays revealing low cortisol levels accompanied by high levels of mineralocorticoid precursors and genetic testing confirming CYP17A1 gene mutations. [4]

The identification of hypertension due to this specific enzymatic deficiency is significant as it dictates specific management strategies that include glucocorticoid replacement, addressing not only the hormonal imbalance but also ameliorating the hypertension and preventing further metabolic complications.[5]

CASE REPORT

A 19-year-old male with no significant past medical or family history was referred to a tertiary care center following the incidental discovery of hypokalaemia (2.6 mmol/L) during evaluation for an episode of altered sensorium. Initial management with potassium supplementation corrected the electrolyte imbalance; however, persistent hypertension prompted further evaluation.

On presentation to the cardiology department, physical examination was unremarkable except for elevated blood pressure readings consistently around 180/110 mm Hg. Laboratory investigations included normal renal function tests, a hormonal profile indicating low cortisol and elevated ACTH levels, and genetic testing that identified mutations in the CYP17A1 gene, confirming a diagnosis of 17 alpha-hydroxylase deficiency (Table 1).

Laboratory Test	Patient's Values	Normal Values	Interpretation
Serum Potassium (K^+)	2.6 mmol/L	3.5 - 5.0 mmol/L	Hypokalaemia; significantly below normal
Serum Sodium (Na^+)	142 mmol/L	135 - 145 mmol/L	Normal, often unaffected in this condition
Serum Cortisol (8 AM)	2 µg/dL	10-20 µg/dL	Significantly lower than normal, indicating adrenal insufficiency
Adrenocorticotropic Hormone (ACTH)	125 pg./mL	10-60 pg/mL	Significantly elevated, suggestive of primary adrenal insufficiency
Plasma Renin Activity	0.2 ng/mL/hr	0.65-5.0 ng/mL/hr	Decreased, typical for this disorder due to suppressed renin levels from mineralocorticoid excess effects
Aldosterone	4 ng/dL	3-16 ng/dL	Low normal; not typical for primary hyperaldosteronism but expected due to specific enzyme deficiency
Genetic Testing (CYP17A1)	Mutation detected	No mutation	Confirmatory for 17 alpha-hydroxylase deficiency

Table 1 :- Outcome of Laboratory investigation in the case.

Management involved the initiation of glucocorticoid therapy to reduce ACTH levels and correct the hormonal imbalance, leading to normalization of blood pressure and potassium levels. The patient's follow-up over six months showed stable control of blood pressure and no further episodes of hypokalaemia.

DISCUSSION

The diagnosis of 17 alpha-hydroxylase deficiency in this young patient highlights a rare but important etiology of secondary hypertension and hypokalaemia. The pathogenesis of this condition is deeply rooted in the enzymatic block at the 17 alpha-hydroxylase steps of steroid biosynthesis, which is catalysed by the enzyme CYP17A1. This enzymatic blockage leads to reduced synthesis of glucocorticoids and sex steroids, while simultaneously increasing the production of mineralocorticoid precursors. These precursors exert similar effects to aldosterone, resulting in sodium retention, volume expansion, and subsequent hypertension, as well as potassium loss, leading to hypokalaemia.[6]

The clinical significance of recognizing such a rare cause of secondary hypertension is paramount, as it guides specific treatment strategies that differ markedly from those used for primary hypertension. Traditional antihypertensive therapies may not be effective or could potentially worsen the patient's underlying metabolic disturbances. In this case, the administration of glucocorticoids provided a dual benefit. Firstly, it reduced the production of ACTH, curtailing the stimulus for further precursor production. Secondly, it corrected the deficiency of cortisol, thereby alleviating the metabolic disarray that contributed to the patient's hypertension and electrolyte imbalances.[7]

Moreover, this case underscores the importance of considering genetic causes in patients who present with unusual features for common conditions like hypertension, especially when occurring in younger individuals without typical risk factors. Genetic testing confirmed the presence of mutations in the CYP17A1 gene, establishing a definitive diagnosis and highlighting the role of genetic assays in modern diagnostic processes. This is particularly relevant in conditions with low prevalence, as misdiagnosis can lead to inappropriate management, which may not only be ineffectual but could potentially exacerbate the underlying condition.[8]

Furthermore, this case emphasizes the importance of a multidisciplinary approach in managing rare diseases. The collaboration between endocrinologists, cardiologists, and geneticists was crucial in diagnosing and managing the patient effectively. This integrated approach not only facilitated a comprehensive assessment and understanding of the patient's condition but also aided in tailoring a personalized treatment plan that addressed the specific needs arising from the enzymatic deficiency.

In terms of challenges, diagnosing 17 alpha-hydroxylase deficiency can be complex due to its rarity and the non-specific nature of its presentation. The initial symptoms can be quite vague and easily attributed to more common diseases, leading to potential delays in the correct diagnosis. The biochemical profile of low cortisol and elevated ACTH is suggestive of primary adrenal insufficiency but without detailed biochemical and genetic analyses, the specific enzymatic block would not be evident. Early recognition of the pattern of electrolyte abnormalities, in conjunction with hypertension, is critical in prompting further detailed endocrinological evaluation and genetic studies.[9]

The prognosis for patients with 17 alpha-hydroxylase deficiency largely depends on the timely initiation and appropriateness of treatment. With appropriate hormonal replacement therapy, as demonstrated in this case, patients can have significant improvement in their symptoms and long-term outcomes. This reinforces the need for awareness and consideration of rare genetic disorders in the differential diagnosis of common clinical presentations like hypertension, particularly in young patients.[10]

CONCLUSION

This case illustrates the complex interplay between rare genetic disorders and common clinical symptoms like hypertension and hypokalaemia. It emphasizes the necessity for clinicians to consider rare endocrinopathies in differential diagnoses, particularly in young patients with persistent hypertension and associated metabolic abnormalities. Early recognition and appropriate management can significantly improve outcomes and prevent long-term complications.

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