Apparent Mineralocorticoid Excess Syndrome (AME): A Case Report of Two Twins

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Abstract

Ulick syndrome, also called apparent mineralocorticoid excess is an autosomal recessive disorder that causes severe hypertension with polyurea, polydipsia , and other symptoms. We report a case report of two dichorionic diamniotic twins from a first-degree consanguineous couple who suffered from variable symptoms of Ulick syndrome.

Introduction

Ulick syndrome (US), also called apparent mineralocorticoid excess (AME), is a rare autosomal recessive disorder caused by a genetic mutation of HSD11B2. Chr. 16q22.1. The HSD11B2 enzyme typically converts active cortisol into its inactive form. The HSD11B2 mutation will cause a deficiency of the enzyme, which in turn will induce more cortisol activation of the mineralocorticoid receptor resulting in hypertension [1]. However, the US may have an additional unknown enzyme that correlates with HSD11B2 activity or possibly some cortisol metabolizing enzyme [2].

Patients with the typical US show severe hypertension with both polyurea and polydipsia, low birth weight, hypokalemia, and low aldosterone. It is noted that US simulates all findings of primary aldosteronism except for the contrast low plasma aldosterone concentration. However, the severity of the symptoms can differ depending on the degree of the gene mutation [3].

US treatment involves decreasing cortisol endogenous synthesis or blocking the mineralocorticoid (MC) receptor. Dexamethasone 1.5 to 2 mg/day is usually the drug of choice but may not relieve all symptoms and has unwanted long-term side effects. Spironolactone or eplerenone -mineralocorticoid receptor blockers- can also be used to treat the US and correct hypokalemia. Some cases have reported that transplantation of a kidney with normal HSD11B2 activity had cured the disease [4].

Case presentation

We report two dichorionic diamniotic twins from a first-degree consanguineous couple with no pathological familial medical. The pregnancy was carried out at term and without incident. The elder sister is 11 years old and in good health. At 17 months, twin A developed hemiplegia and blindness for 04 weeks.

Brain imaging showed ischemic stroke, and further etiological investigation could not identify the origin of this event. Yet, the evolution was good with restoring the motor function and vision, and the patient was

discharged. Between 17 months and 06 years, both twins were lost from sight. At the age of 06, the second twin B, was hospitalized for a severe urinary infection. Investigations showed bilateral nephrocalcinosis, severe hypokalemia, and elevated blood pressure. Clinical examination, lab tests, and imaging were carried out for the second sister (A), who had a history of stroke.

They also revealed hypokalemia, nephrocalcinosis, and the existence of hypertension. Creatinine clearance for both sisters was under the normal limit, indicating kidney failure.

The treatment of both patients was based on amiloride, hydrochlorothiazide, and potassium supplementation.

An echocardiogram and fundus examination were requested to assess the impact of hypertension, and they were normal in both patients. During the follow-up, twin B had recurrent urinary tract infections. Retrograde urethrocystography showed bilateral vesicoureteral reflux (VUR) grade 3. Renal scintigraphy was recommended, and the patient has been referred to the surgeon to discuss the necessity of surgical treatment. A genetic study on twin B was consistent with Ulick syndrome. **Figure 1** demonstrated the exact pathophysiology of AME, while **Figure 2** showed the type of AME's inheritance as a family pedigree.

Discussion

In this case report, we described two twins diagnosed with AMES. Clinical, biochemical, and genetic data confirmed a congenital deficiency in the HSD11β2 enzyme (twin B). Usually, this syndrome is encountered early in the first decade of age. It is characterized by a set of symptoms such as high blood pressure, reduced renin and aldosterone levels, increased urine output and thirstiness, faltering growth, hypokalemia with metabolic alkalosis, and often a high level of calcium deposition in the kidneys. Cerebrovascular stroke is usually observed before age ten in undiagnosed, lately treated children [5–7]. Regarding inheritance of AMES, it is an AR (autosomal recessive) and caused by specific mutations. Homozygous/ compounds heterozygous or deletion mutations in a specific gene on chromosome 16 leads to the complete absence or significant decrease in the activity of the 11-b-HSD2 enzyme that produces cortisone from cortisol. The unprocessed active cortisol binds to its receptor, mineralocorticoid (MC) receptors, inducing the after-mentioned clinical features [8,9]. Our cases highlight many, if not all, of the features of the condition. Thus, in addition to the classical findings, they demonstrated a parent's consanguinity, a strong suspicion of the affected twin, hypertensive retinopathy, and hypokalemic nephropathy.

These features have been reported in many other cases in the literature. Al-Harbi and Al-Shaikh reported three cases, two females and one male, with AMES, who presented with severe hypertension, low aldosterone, low renin levels, and hypokalemia. Genetic analysis confirmed the AMES diagnosis in these children. All cases had the typical clinical presentation of AMES, and their parents were first-degree cousins, considered consanguineous parents [10]. Yau et al. reported about a consanguineous Omani family with six AMES cases. Genetic analysis of affected family members confirmed a novel homozygous p.T267A mutation in HSD11B2. The diagnosis was confirmed with clinical signs and symptoms and biochemical investigations [11].

Azara et al. reported a consanguineous family from Iran with three affected cases. Two females and one male were diagnosed at 14, 11, and 4, respectively. At the time of presentation, low-renin hypertension, retinopathy, hypertrophy of the left ventricle, and mutation in R337C, within exon five of the 11ßHSD2's gene, were found in this family with AMES [12]. The mainstay of treatment of our patients were potassium supplementations, thiazide (hydrochlorothiazide) and potassium sparing-diuretic (amiloride). We used thiazide diuretics to treat the nephrocalcinosis and associated hypercalciuria, while urine potassium loss could occur due to this drug; therefore, potassium supplementations were used. Amiloride was used as an alternative diuretic for thiazide if it was needed. Calcium channel blockers, dexamethasone, and other candidate treatments have been described in many cases with variable successes [13].

Conclusion

The AMES presents in childhood, typically with high blood pressure, hypokalemia, and low renin and aldosterone levels. The hallmark of the syndrome is increased cortisol-to-cortisone metabolites in the urine.

Spironolactone, which blocks receptors of cortisol and aldosterone, was adopted. Adjunctive treatments are supplementation with potassium and a diet with low sodium. Cortisol formation can be suppressed through ACTH feedback inhibition using dexamethasone, but a consistent antihypertensive effect is not guaranteed and has significant long-term adverse events. To prevent or improve end-organ damage (EOD) morbidity, diagnosis then treatment should be early.

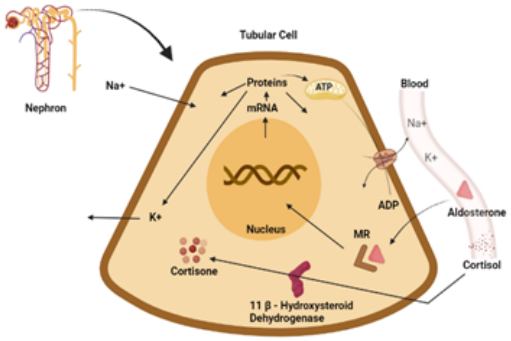

Figure 1. Syndrome of apparent mineralocorticoid excess (AMES). The exact pathophysiology is shown here in detail.

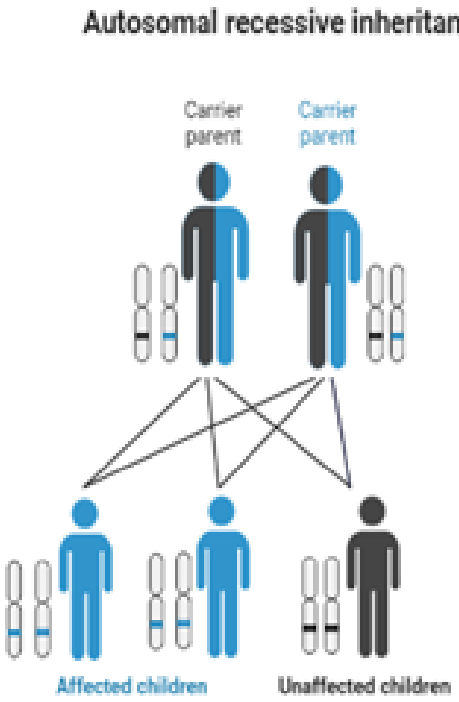

Figure 2. Family pedigree.

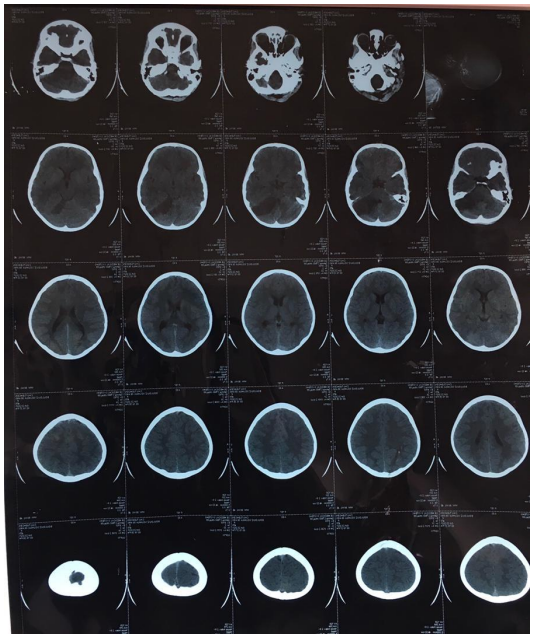

Figure 3. Magnetic resonance imaging of the brain that confirm an established stroke.

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Figure Legends:

Figure 1. Syndrome of apparent mineralocorticoid excess (AMES). Exact pathophysiology is shown here in details.

Figure 2. Family pedigree.

Figure 3. Magnetic resonance imaging of the brain that confirm an established stroke.

Declarations:

***Consent for publication**

Written informed consent was obtained from the patients' parents for the publication of this case report and any accompanying images. A copy of the written consent will be available for review by the Editor of this journal if required.

***Availability of data and material**

All data generated or analyzed are included in this article

***Competing interests**

No conflict of interest exits in the submission of this manuscript.

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***Authors' contributions**

All authors have read and approved the manuscript

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