Case Series

Apparent mineralocorticoid excess syndrome with nephrocalcinosis and renal complications: A case series of two siblings

P Aravindhmozhi[1], Sheik Sulthan Alavudeen[2], Jayalakshmi Seshadri[3], R Rajakumar[4], Charankumar Swamikkannu[1], Seenivasan Mookaiah[5]

From [1]Senior Resident, [2]Assistant Professor, [3]Professor, Institute of Nephrology, Madras Medical College, [4]Senior Resident, Department of Radiology, Barnard Institute of Radiology, Madras Medical College, [5]Associate Professor, Institute of Nephrology, Madras Medical College, Chennai, Tamil Nadu, India

ABSTRACT

Apparent mineralocorticoid excess (AME) syndrome is a rare autosomal recessive cause of secondary hypertension, especially in children and young adults. Its heterogeneous presentation often delays diagnosis. We report a case series of two siblings, born of a 2nd-degree consanguineous marriage, both with AME syndrome complicated by nephrocalcinosis. The elder sibling developed renal osteodystrophy, progressive renal dysfunction, and cardiovascular complications, whereas the younger sibling remained stable with early diagnosis and therapy. This case series highlights the prognostic impact of early diagnosis and treatment, as well as diagnostic challenges in differentiating AME from Liddle syndrome. Awareness is crucial in consanguineous populations where genetic risk is higher.

Key words: Apparent mineralocorticoid excess syndrome, Consanguinity, Hypertension, Hypokalemia, Liddle syndrome, Nephrocalcinosis

Apparent mineralocorticoid excess (AME) syndrome is a rare autosomal recessive disorder caused by a deficiency of 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) isozyme, which converts cortisol to its inactive metabolite cortisone [1]. As a result, excessive cortisol binds to mineralocorticoid receptors in the kidneys, causing features of mineralocorticoid excess, with low to undetectable aldosterone levels [1]. Globally, fewer than 100 cases have been reported, with limited reports from India.

Here, we report a case series of two siblings with AME syndrome, emphasizing the diagnostic and therapeutic challenges, as well as the prognostic differences arising from early versus delayed diagnosis.

CASE SERIES

Case 1

The first case is a 2nd born male child of a 2nd-degree consanguineous marriage, born at term with a birth weight of 2.6 kg and no significant perinatal issues. This consanguinity highlights the genetic risk in such families. His elder sister was in good health, and no relevant family history was noted. At 2 years of age, the child went to the nearby hospital with a urinary tract infection. On evaluation, he was incidentally found to have increased blood pressure and hypokalemia (2.4 mEq/L) with normal serum urea and creatinine values. He was started on oral nifedipine and potassium chloride syrup (Table 1). Given limited resources, further evaluation was not done at that time, and the child was maintained on oral antihypertensive medications and potassium supplementation for the next 2 years. In 2010, he was referred to a tertiary care center for further evaluation, where an ultrasound of the abdomen and non-contrast computed tomography (CT) showed bilateral medullary nephrocalcinosis (Fig. 1). He was evaluated further, and his serum urea and creatinine levels, serum cortisol level, serum 17 OH progesterone level, and serum aldosterone level were all within normal limits. Arterial blood gas analysis is suggestive of metabolic alkalosis. As a genetic study was not available, a presumptive diagnosis of Liddle syndrome was made, and the patient started on enalapril. An ENAC channel blocker, such as amiloride, was not available. At 15 years of age, he was diagnosed with bilateral grade 2 hypertensive retinopathy and renal osteodystrophy in the form of bilateral genu valgum. His antihypertensive medications were optimized, and for renal osteodystrophy, calcium and Vitamin D supplements were added. At 17 years of age, his serum

Access this article online	
Received - 10 August 2025 Initial Review - 28 August 2025 Accepted - 20 September 2025	Quick Response code
DOI: 10.32677/ijcr.v11i10.7804	

Correspondence to: P Aravindhmozhi, Institute of Nephrology, Madras Medical College, Chennai, Tamil Nadu, India. E-mail: mozhiaravindh@gmail.com

© 2025 Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC-ND 4.0).

Table 1: Laboratory investigations of case 1

Parameters	At presentation	Current status	Normal values	Units
Age	2	19	-	years
Hemoglobin	10.9	12.1	13–16	g/dL
Total leukocyte count	6380	8200	4,000–11,000	cells/mm^3
Platelets	261,000	289,000	150,000–400,000	cells/mm^3
Urea	19	48	15–40	mg/dL
Creatinine	0.6	2.5	0.5–1.3	mg/dL
Sodium	128	134	136–146	mEq/L
Potassium	2.4	3.6	3.5–5.0	mEq/L
Calcium	8.1	8.4	8.6–10.0	mg/dL
Phosphorus	2.1	2.8	2.5–4.5	mg/dL
Urine albumin	Nil	Nil	Absent	
Urine protein–creatinine ratio	0.4	0.6	<0.2	g/g
Height	78 (<3rd percentile)	161	-	cm
Weight	9 (<3rd percentile)	42	-	kg
Body mass index	14.8	16.2	18.5–24.9	kg/m^2

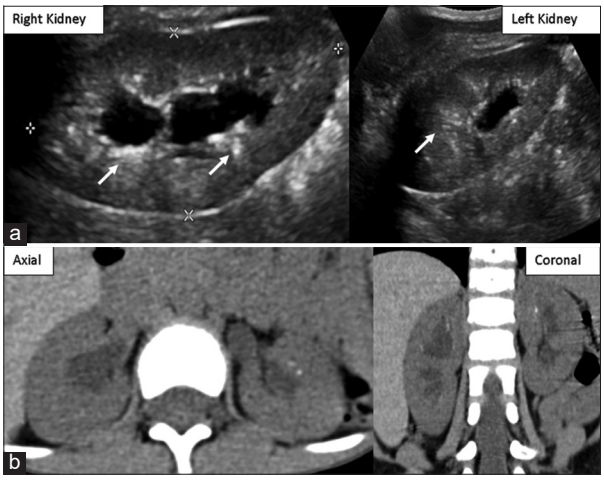

Figure 1: (a) Renal ultrasound showing medullary nephrocalcinosis (white arrows) (Case 1), (b) Non-contrast computed tomography scan (axial and coronal sections) showing bilateral medullary nephrocalcinosis (case 1)

creatinine increased to 2.0 mg/dL, and corticomedullary differentiation was lost in the kidneys. The patient was referred to our center, and genetic analysis was done. Clinical exome revealed a homozygous variant in exon 3 of the *HSD11B2* gene. High-dose spironolactone was added along with other medications. A 2D echocardiogram revealed severe aortic regurgitation with pulmonary hypertension. The patient is currently being managed with enalapril, furosemide, spironolactone, nifedipine, and oral potassium supplementation. His blood pressure is well controlled, and his serum creatinine remains stable around 2.5 mg/dL.

Case 2

In 2018, at 4 years of age, the child presented to a nearby hospital with weakness of both upper and lower limbs. Evaluation revealed severe hypokalemia (2.0 mEq/L) and elevated blood pressure (156/90 mmHg) (Table 2). His abdominal ultrasound and non-contrast CT showed features of bilateral medullary nephrocalcinosis (Figs. 2 and 3). He was managed with intravenous potassium supplementation. As his elder brother had been suspected of having Liddle syndrome, this child was also diagnosed with probable Liddle syndrome and treated with nifedipine, enalapril, and potassium chloride syrup. At 9 years of age, he presented with bilateral genu valgum and a distal fibula fracture and was diagnosed with renal osteodystrophy. He was managed conservatively, and oral calcium and Vitamin D supplements were initiated. Genetic analysis was done, which revealed a homozygous variant in exon 3 of the *HSD11B2* gene, confirming the diagnosis of AME. High-dose spironolactone was added to his treatment regimen. The child is currently on nifedipine, enalapril, spironolactone, and oral potassium supplementation with a stable creatinine of 0.7 mg/dL.

DISCUSSION

AME was first reported by Werder *et al*. in 1974 in a 3-year-old girl who had low birth weight, delayed growth, hypertension, polyuria, and polydipsia [2]. AME is a rare autosomal recessive disorder due to multiple pathogenic variants in the *HSD11B2* gene on chromosome 16q22.1, leading to severe deficiency of 11β-HSD2 enzyme [3,4]. Since the identification of the first HSD11B2 mutation, more than 51 deleterious mutations have been identified as causative mutations of AME [2]. Most pathogenic mutations occur in exons 3–5, which are critical for maintaining stable 11β-HSD2 activity. Cortisol levels are regulated by two isoforms of 11β-HSD:11β-HSD1 and 11β-HSD2. 11β-HSD2 converts active steroid cortisol to inactive metabolite cortisone, but 11β-HSD1 has the opposite action [2]. As a result of 11β-HSD2 deficiency, cortisol cannot be converted to inactive cortisone.

This excess cortisol can bind to the mineralocorticoid receptor with equal affinity to aldosterone, leading to sodium and water reabsorption, hypertension, and other

Table 2: Laboratory investigations of case 2

Parameters	At presentation	Current status	Normal values	Units
Age	4	11	-	years
Hemoglobin	11.7	12.3	13–16	g/dL
Total leukocyte count	8950	5400	4000–11000	cells/mm^3
Platelets	213000	313000	150000–400000	cells/mm^3
Urea	15	22	15–40	mg/dL
Creatinine	0.6	0.7	0.5–1.3	mg/dL
Sodium	131	136	136–146	mEq/L
Potassium	2.0	3.2	3.5–5.0	mEq/L
Calcium	7.7	9.2	8.6–10.0	mg/dL
Phosphorus	2.4	3.2	2.5–4.5	mg/dL
Urine albumin	Nil	Nil	Absent	
Urine protein–creatinine ratio		0.8	<0.2	g/g
Height	94 (<3rd percentile)	126	-	cm
Weight	12.5 (<3rd percentile)	27	-	kg
Body mass index	13.8	17	18.5–24.9	kg/m^2

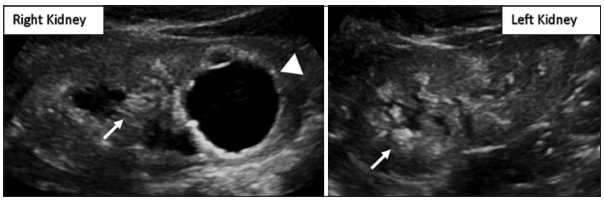

Figure 2: Renal ultrasound showing medullary nephrocalcinosis (white arrows) and cysts in the right kidney (arrowhead) (Case 2)

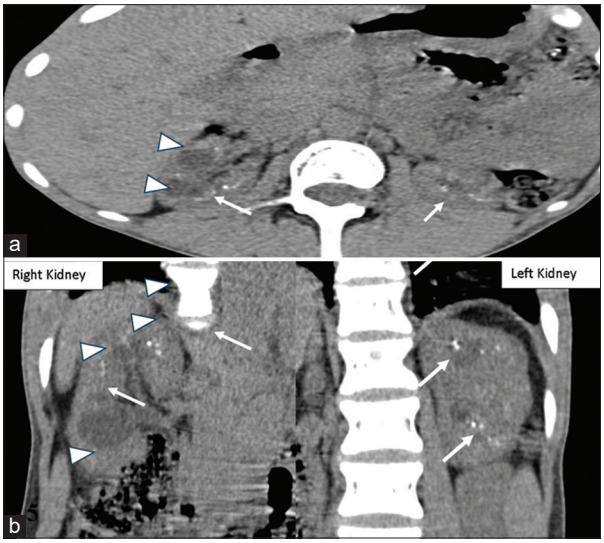

Figure 3: (a) Non-contrast computed tomography (CT) scan (axial section) showing bilateral medullary nephrocalcinosis (white arrows) with cysts in the right kidney (arrowhead), (b) Non-contrast CT Scan (coronal section) showing bilateral medullary nephrocalcinosis (white arrows) with cysts in the right kidney (arrowhead) (Case 2)

manifestations [3]. Affected patients can present with increased blood pressure, low renin and aldosterone levels, increased urine output, increased thirst, faltering growth, hypokalemia with metabolic alkalosis, and high levels of calcium deposition in the kidneys [4]. Uncommon features of AME include nephrocalcinosis, renal cysts, and cerebrovascular complications, which may be due to long-standing hypertension [1,4]. Despite suppressed levels of renin and aldosterone, AME patients will show features of mineralocorticoid excess and hypertension [5].

AME can be classified into classic AME and non-classic AME. Classic AME usually presents in infancy or early childhood with severe features, whereas non-classic AME has a milder phenotype, with atypical or delayed presentation into adolescence or adulthood [3]. As the clinical presentation is heterogeneous, it is challenging to accurately diagnose the disease early [3]. In our patients, both siblings had nephrocalcinosis. Other causes of nephrocalcinosis, such as hypercalcemia, hypercalciuria, renal tubular acidosis, and hyperoxaluria, have been excluded [6]. Nephrocalcinosis and renal cyst in our patients can be associated with long-standing hypokalemia of AME syndrome [7] or it can be ascribed to the role of 11β-HSD 2 in calcium regulation [5].

Early diagnosis and early initiation of treatment are important in AME because poor blood pressure control and hypokalemia can cause end-organ damage such as hypertensive retinopathy, early stroke, and progressive renal dysfunction [2]. One of our patients had hypertensive retinopathy, renal failure, aortic regurgitation, and pulmonary hypertension. Recent Indian pediatric reports have also described AME presenting with severe, early-onset hypertension, emphasizing the need for heightened clinical suspicion in children with unexplained endocrine hypertension [8]. Consanguinity has repeatedly been implicated in AME, with a recent case report describing genetically confirmed cases among siblings of related parents, highlighting the need for genetic counseling in such populations [9].

Our patient was initially diagnosed as probable Liddle syndrome because both AME and Liddle syndrome share similar clinical features. Liddle and AME can be differentiated from each other by urinary steroid profile and genetic testing [1]. A markedly elevated urinary ratio of tetrahydrocortisol and allo-tetrahydrocortisol to tetrahydrocortisone is diagnostic of AME, whereas this ratio remains normal in Liddle syndrome. A urine steroid

test was not done for our patients because of the lack of access to reliable tests.

Treatment of AME syndrome includes mineralocorticoid antagonists such as spironolactone or eplerenone, amiloride, potassium-sparing diuretics, salt restriction, blood pressure control, and potassium supplementation [2,3]. Although amiloride remains a targeted therapeutic option in AME by inhibiting epithelial channels, its real-world use is rare because of limited availability and cost constraints [10].

CONCLUSION

In our case series, early initiation of therapy in the younger sibling resulted in preserved renal function and normal growth parameters, whereas the elder sibling had progressive renal dysfunction and cardiovascular complications due to delayed diagnosis. This highlights the importance of timely diagnosis and appropriate mineralocorticoid receptor blockade in altering disease trajectory.

REFERENCES

1. Moudgil A, Rodich G, Jordan SC, Kamil ES. Nephrocalcinosis and renal cysts associated with apparent mineralocorticoid excess syndrome. Pediatr Nephrol 2000;15:60-2.
2. Lu YT, Zhang D, Zhang QY, Zhou ZM, Yang KQ, Zhou XL, *et al*. Apparent mineralocorticoid excess: Comprehensive overview of molecular genetics. J Transl Med 2022;20:500.
3. Carvajal CA, Tapia-Castillo A, Vecchiola A, Baudrand R, Fardella CE. Classic and nonclassic apparent mineralocorticoid excess syndrome. J Clin Endocrinol Metab 2020;105:dgz315.
4. Kaddour A, Almoshantaf MB, Aljabali A, Tchouar AH, Benmelouka AY. Apparent Mineralocorticoid Excess Syndrome (AME): A Case Report of Two Twins. Available from: https://www.authorea.com/users/513604/articles/589724-apparent-mineralocorticoid-excess-syndrome-ame-a-case-report-of-two-twins [Last accessed on 2025 Jul 03].
5. Yadav M, Sinha A, Hari P, Bagga A. Impaired distal tubular acidification, renal cysts and nephrocalcinosis in monogenic hypertension. Indian J Pediatr 2021;88:579-81.
6. Shavit L, Jaeger P, Unwin RJ. What is nephrocalcinosis? Kidney Int 2015;88:35-43.
7. Vijayakumar V, Kumar N, Kumar D, Abhinay A, Singh A, Prasad R. A rare case of apparent mineralocorticoid excess presenting as endocrine hypertension. Indian J Nephrol 2025;35:427-8.
8. Verma S, Dabadghao P, Moirangthem A. Apparent mineralocorticoid excess - a rare cause of endocrine hypertension. Indian Pediatr Case Rep 2022;2:36-9.
9. Alsaadoun SA, Alrasheedi AT, Gazar SH, Alsallum GA. Apparent mineralocorticoid excess syndrome: Case report. Int Med Case Rep J 2025;18:671-6.
10. Park SJ, Shin JI. Diagnosis and treatment of monogenic hypertension in children. Yonsei Med J 2023;64:77-86.

Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Aravindhmozhi P, Alavudeen SS, Seshadri J, Rajakumar R, Swamikkannu C, Mookaiah S. Apparent mineralocorticoid excess syndrome with nephrocalcinosis and renal complications: A case series of two siblings. Indian J Case Reports. 2025; 11(10):486-489.