Liddle's-Like Syndrome in the Elderly

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An 88-year-old woman was undergoing inpatient rehabilitation following hip fracture surgery. Her background history included Alzheimer's dementia, untreated hypertension, and hypercholesterolemia. There was no family history of early onset or familial hypertension.

During her hospital stay, she was hypertensive (systolic blood pressure ranging from 160 to 185 mm Hg) with unexplained hypokalemia (2.5–3.2 mmol/L) and concomitant metabolic alkalosis. Further tests revealed hyporeninemic hypoaldosteronism. Normal urinary cortisol levels and metabolites excluded the diagnosis of hypercortisolism and apparent mineralocorticoid excess. Liddle's syndrome was considered a probable diagnosis and amiloride was administered with improvement in her serum potassium level and blood pressure. Subsequent genetic testing of ENaC sequences (Liddle's gene) returned negative results.

DISCUSSION

Liddle's syndrome is classically associated with early-onset hypertension with hypokalemic metabolic alkalosis and hyporeninemic hypoaldosteronism. Primary sodium retention resulting from enhanced activity of epithelial sodium channels in the cortical collecting duct of the nephrons leads to hypertension and associated hypokalemic metabolic alkalosis.

In a recent publication by Tapolyai and colleagues, high prevalence of Liddle's syndrome phenotype was described in an elderly population. Their study effectively highlighted limited recognition of hypertension associated with hyporeninemic hypoaldosteronism in this age group; however, data regarding genetic testing for Liddle's syndrome were not provided. A negative gene test in our patient was interesting as it opened up further possibilities such as presence of a previously undescribed genetic defect or a variant of Liddle's syndrome with possibly different inherited or acquired mutation, which may present in older adults, as does the variant of hypertrophic cardiomyopathy.

The second possibility is age- or medication-related dysfunction of epithelial sodium channels leading to a Liddle's-like biochemical profile.

Screening the adult population with hypertension for this Liddle's-like syndrome could be challenging due to multiple reasons, including polypharmacy, presence of isolated systolic hypertension, dietary habits, presence of renal disease, variability of presence of hypertension and hypokalaemia; however, like many other disorders, we may be looking at only the tip of the iceberg and many older adults thought to have systolic hypertension might actually have this particular type of disorder. This raises the need for criteria to look for the presence of hyporeninemic hypertension in this population.

Testing for serum renin and aldosterone, however, should be done following normalizing serum potassium and after withholding relevant medications that might interfere with the results.

Our proposed criteria to investigate for hyporeninemic hypoaldosteronism in hypertensive adults is presented in the Table.

TABLE. Proposed Criteria to Investigate Hyporeninemic Hypoaldosteronism

1.	Serum sodium >140 mmol/L on at least two occasions
2.	Serum potassium ≤3.5 mmol/L on two occasions
3.	Serum bicarbonate ≥28 mmol/L on two occasions
4.	At least two of the above findings that could not be explained by other means

Monitoring and reviewing other family members may also be important.

Lastly, the defect that causes this Liddle's-like profile could be similar to the epithelial Na channel mutants that cause Liddle's syndrome; however, the mechanism involved and its initiation could be different from Liddle's syndrome, which may warrant further research.