

Bartter's, Gitelman's, and Liddle's

Key Points:

1. These syndromes are rare, so it's important to rule out more common causes (ie diuretics, prescribed or surreptitious).
2. Consider these syndromes when pt has hypokalemic metabolic alkalosis and is chloride resistant (high urinary chloride)..
3. Bartter's is like "lasix", Gitelman's is like "thiazide", and Liddle's is like "hyper-aldo".
4. Treatment is lifelong and often includes NSAIDs, potassium-sparing diuretic, and electrolyte replacement.

Bartter's Syndrome

Pathophysiology: Described in 1962 by Bartter. Autosomal recessive disorder. Genetic defect involving the transporter's in the thick ascending limb of the glomerulus. Defects in Na-K-2Cl cotransporter, K or Cl channels result in lack of concentrating ability.

Clinical presentation: Early in life. Often with sensorineural deafness (has to do with potassium-secreting dark cells of inner ear), triangular facies with drooping mouth and large eyes and pinnae, and renal failure. Pts c/o **polyuria and polydipsia**.

Lab data: Chloride resistant metabolic alkalosis and hypokalemia (due to increased distal flow causing hyperaldo state and wasting of potassium and hydrogen). **Normal serum magnesium**. Hypercalciuric so at risk for **kidney stones**.

Differential diagnosis: Consider surreptitious diuretic use (can check urine assays for diuretics). Urine chloride concentration can be high or low (if volume depletion). Surreptitious vomiting usually has low urinary chloride and some patients have characteristic scarring on hands and dental erosions.

Treatment: Lifelong. Try to minimize aldosterone and prostaglandin production with NSAIDs and potassium-sparing diuretic (spironolactone or amiloride). Consider ACE inhibitor. Often need potassium and magnesium supplementation.

Gitelman's Syndrome

Pathophysiology: Described in 1966 in three patients by Gitelman. Autosomal recessive disorder with 99% penetrance. One study showed that heterozygosity in Italians and Swedish was 1% and mutant allele frequency is 1/200. Genetic defect in Na-Cl cotransporter in the distal tubule.

Clinical presentation: Late childhood or early adulthood. Often present with **muscle cramping and spasms**, significant fatigue. Can see lower than average blood pressure due to salt wasting. Polyuria and nocturia in 50-80%.

Lab data: Chloride-resistant metabolic alkalosis and hypokalemia. **Hypomagnesemia and hypocalciuria** (this disorder, like thiazides, tends to stimulate calcium absorption). Note that serum calcium tends to be normal due to lower PTH levels. Increased plasma renin and aldosterone/ K⁺ ratio.

Differential Diagnosis: same as for Bartter's.

Treatment: Lifelong. Not all patients need to be treated if they are asymptomatic. Treatment is same as in Bartter's, although NSAIDs may be of less help since in this disorder there is less secondary prostaglandin production.

Liddle's Syndrome

Pathophysiology: **Autosomal dominant** disorder. Genetic defect in the collecting tubule sodium channel, resulting in increased sodium reabsorption and lack of inhibition by higher levels of intracellular sodium.

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Clinical presentation: Often diagnosed at young age, but can present in adulthood due to phenotypic variation. Classic triad of **hypertension**, metabolic alkalosis, and usually hypokalemia. Consider if family history of hypertension at young age and some family members having hypokalemia.

Lab data: Metabolic alkalosis, hypokalemia (although some are low normal), low urinary aldosterone secretion.

Differential diagnosis: congenital adrenal hyperplasia, familial cortisol resistance, apparent mineralocorticoid excess (ie licorice ingestion), aldosterone-secreting tumor.

Treatment: Lifelong. Potassium-sparing diuretic which closes the sodium channel (**amiloride or triamterene**). Spironolactone does not work because aldosterone is not causing the sodium channel to be open.

References:

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Kurtz, I. Molecular pathogenesis of Bartter's and Gitelman's syndromes. Kidney International. Vol 54, 1998. Nephrology textbook.