PENDRED SYNDROME CAN BE COMPLICATED BY SEVERE ALKALOSIS

Kandasamy N, Fugazzola L, Evans M, Chatterjee VK, Karet F. **Life-threatening metabolic alkalosis in Pendred syndrome.** Eur J Endocrinol 2011;165:167-70. Epub May 6, 2011.

SUMMARY

BACKGROUND

Pendred syndrome, the most common form of syndromic deafness, is well known to thyroidologists because some patients with this syndrome present with a diffuse or multinodular goiter with or without moderate hypothyroidism. The main characteristic of Pendred syndrome is congenital or acquired sensorineural deafness. The molecular basis of the disease is a biallelic defect of pendrin, a multifunctional anion exchanger encoded by the SLC26A4/PDS gene (1,2). This protein is localized at the apical border of the follicular cell and appears to be involved in iodide transport into the lumen. In the inner ear, pendrin transports bicarbonate into the endolymph and absorbs chloride. It has also been identified in the kidney, where it secretes bicarbonate and reabsorbs chloride. Under physiologic conditions, however, there is no detectable renal phenotype. So far, alkalosis has been reported to have developed in only one pediatric patient with Pendred syndrome. The case under discussion represents the second observation.

CASE REPORT

This 46-year-old female patient had childhood-onset sensorineural hearing loss. Mild hypothyroidism was diagnosed in adulthood and treated for 1 year before the current event. The patient, a severe alcoholic, was discovered on the floor in a confused state with rigid limbs. In the hospital, severe potassium, chloride, and magnesium deficiencies (K, 1.4 mmol/L; Cl, 86 mmol/L; Mg, 0.19 mmol/L) and bicarbonate and base excess (bicarbonate, 45 mmol/L; base excess, +20.4) were recorded. She was treated with fluid and electrolyte replacement. Recovery was complicated by a respiratory arrest and an episode of atrial fibrillation. A review of her medical history revealed that she had had a similar episode of hypokalemia 1 year earlier. The diagnosis of Pendred syndrome was established by magnetic resonance imaging of the inner ear, which showed a characteristic enlargement of the endolymphatic system, and by mutational analysis of the SLC26A4 gene.

CONCLUSIONS

Under normal conditions, problems with electrolyte and acid–base imbalance are not seen in patients with Pendred syndrome because with a Western acid-rich diet, the kidneys rarely need pendrin for bicarbonate excretion and chloride reabsorption. Yet experimental studies indicate a much larger role for renal pendrin, also affecting blood pressure and extracellular volume. Inhibition of the function of pendrin may become limiting in selected instances and result in metabolic alkalosis. As illustrated by this patient, the limited capacity for bicarbonate excretion may become deleterious in cases of vomiting and alcohol abuse; other causes include eating an exclusively vegetarian diet or having diarrhea.

COMMENTARY

Being aware of acute alkalosis as a rare but life-threatening complication in patients with Pendred syndrome is important, since many of us take care of patients with this syndrome. In addition, the role of pendrin in the renal bicarbonate–chloride balance may be far more important than expected based on this case report. Pendrin is likely to play a crucial role in the control of blood pressure; the antihypertensive action of thiazides may in part be due to targeting renal pendrin (3).

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