CASE REPORT

PRERENAL AZOTEMIA IN A DIABETIC PATIENT WITH HYPORENINEMIC HYPOALDOSTERONISM AND AUTONOMIC NEUROPATHY

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SUMMARY - Patients with hyporeninemic hypoaldosteronism show mild to moderate renal insufficiency, with a creatinine clearance of 20-75 ml/min, and asymptomatic hyperkalemia. A low degree of sodium wasting and mild hyperchloremic metabolic acidosis are also usually present. However, severe sodium wasting and volume depletion are not typically seen unless the patient is placed on severe sodium restriction or has some other cause of extrarenal sodium loss. In fact, acute renal failure has not been reported in such patients. We describe a diabetic patient with hyporeninemic hypoaldosteronism and autonomic neuropathy who developed recurrent episodes of acute renal failure due to prerenal azotemia during acute exacerbations of diarrhoea. In our case, despite significant hypovolemia, the renin-aldosterone axis was markedly suppressed, implying that sympathetic tone played a decisive role in renin regulation.

Key-words: hyporeninemic hypoaldosteronism, hyperkalemia, acute renal failure, prerenal azotemia, autonomic neuropathy, diarrhoea.

RÉSUMÉ - Azotémie prérénale chez un patient diabétique avec hypoaaldostéronisme hyporéninémiques et neuropathie autonome.

Les patients porteurs d’hypoaldostéronisme hyporéninémiques se présentent avec une insuffisance rénale modérée, une clairance de la créatinine de 20 à 75 ml/min et une hyperkaliémie asymptomatique. De plus, une certaine perte de sodium et une acidose métabolique hyperchlorémique modérée sont habituellement présentes. Toutefois, la perte sodée et l’hypovolémie ne sont pas habituelles sauf si le patient est mis en restriction sodée sévère ou présente une autre cause de perte sodée extra-rénale. Il n’a pas été rapporté d’insuffisance rénale aiguë chez de tels patients. Nous décrivons un patient diabétique avec hypoaldostéronisme hyporéninémique et neuropathie autonome qui a développé des épisodes récurrents d’insuffisance rénale aiguë due à une azotémie prérénale, lors d’épisodes de diarrhées sévères. Dans notre observation, malgré l’hypovolémie manifeste, renine et aldostérone étaient indosables illustrant le rôle clé du tonus sympathique dans la régulation de la sécrétion de rénine.

Mots-clés : hypoaldostéronisme hyporéninémique, hyperkaliémie, insuffisance rénale aiguë, azotémie prérénale, neuropathie autonome, diarrhée.
Hyporeninemic hypoaldosteronism commonly occurs in patients with diabetes mellitus [1, 2]. Even though most patients with this condition exhibit mild to moderate renal insufficiency with a creatinine clearance of 20 to 75 ml/min, acute renal failure has not been reported [1, 2]. The present study concerns a diabetic patient with hyporeninemic hypoadosteronism and diarrhoea due to diabetic enteropathy who developed recurrent episodes of prerenal azotemia caused by exacerbations of diarrhoea.

### CASE REPORT

A 72-year-old man was initially admitted to our department because of hyperkalemia (serum potassium 5.6 mmol/L) and a mild decrease in renal function. He had a long history of diabetes mellitus treated with intermediate-acting insulin followed by diabetic retinopathy and autonomic neuropathy, which presented with postural hypotension, impaired gastric emptying, and diarrhoea aggravated by food ingestion.

The laboratory data on admission were haematocrit 35% (0.35), serum urea 45 mg/dl (16 mmol/L), creatinine 1.6 mg/dl (141.4 µmol/L), glucose 154 mg/dl (8.5 mmol/L), HbA1c 8.4%, total protein 6.9 g/dl (69 g/L), sodium 138 mmol/L, potassium 5.6 mmol/L, chloride 109 mmol/L, bicarbonate 18 mmol/L, anion gap 11 mmol/L, arterial pH 7.32, and PCO2 32 mmHg (4.25 kPa). Creatinine clearance was 60 ml/min. The patient spontaneously lowered his urine pH to 5.1 on repeated occasions. Twenty-four-hour urine protein was 0.9 g, while urine sediment contained 8-10 red cells, 5-6 white cells and a few granular casts per high-power field. The transtubular potassium gradient (TTKG) was 2.6, significantly increasing to 5.2 after fludrocoritsone administration. Plasma renin activity (PRA) was 0.09 ng/ml/h, and serum aldosterone level was 15 pg/ml. A diagnosis of hyporeninemic hypoadosteronism due to evident diabetic neuropathy was reached, and a low potassium diet was advised.

However, one month later, the patient experienced a deterioration of watery diarrhoea of 3 days’ duration and was readmitted to our department. On physical examination, there were signs indicative of profound volume depletion, such as diminished skin turgor and postural hypotension (blood pressure was 130/90 mmHg in sitting position and 105/75 mmHg in upright position). The results of laboratory investigations are shown in the accompanying table. Prerenal azotemia was evident, with increases in haematocrit, serum total proteins and the urea/creatinine ratio. Careful rehydration was followed by significant improvement in the parameters of renal function [serum urea 28 mg/dl (10 mmol/L), serum creatinine 1.6 mg/dl (141.4 µmol/L)]. The patient recalled that similar, though lesser, deterioration of renal function had occurred twice in the past after exacerbations of diarrhoea [serum creatinine 1.9 mg/dl (168 µmol/L) and 2.3 mg/dl (203.3 µmol/L), respectively].

### DISCUSSION

Our patient who presented with autonomic neuropathy and hyporeninemic hypoadosteronism developed recurrent episodes of prerenal azotemia during exacerbations of diarrhoea. It is well-known that pa-
patients with hyporeninemic hypoaldosteronism typically present with asymptomatic hyperkalemia. However, in addition to hyperkalemia a small degree of sodium wasting as well as mild hyperchloremic metabolic acidosis are present, since aldosterone normally promotes sodium reabsorption and hydrogen and potassium secretion [1, 3]. Severe sodium wasting and volume depletion are not typically seen unless the patient is placed on severe sodium restriction or has some other cause of extrarenal sodium loss [1]. Other factors such as norepinephrine and mild reduction in blood pressure can combine to maintain relatively normal sodium balance in this setting, despite reduced levels of aldosterone [4]. What is generally lost, however, is the ability to conserve sodium maximally, as evidenced by increased urine sodium and FENa+ despite volume depletion. In our case, this impaired ability to conserve sodium was followed by a deterioration of renal function owing to prerenal azotemia. Our patient had mild renal insufficiency possibly due to diabetic nephropathy, which could also have played a role in the rapid deterioration of renal function. In such cases, sodium wasting is aggravated by osmotic diuresis in the remaining functioning nephrons as well as by the inability to shut off natriuretic forces acutely [5-7]. Autonomic neuropathy leading to decreased sympathetic activity has also been suggested to explain hyporeninemia in diabetic subjects with hypoaldosteronism. In fact, Tuck et al. [8] found decreased plasma renin response to isoproterenol in five hyperkalemic diabetic patients with hyporeninemic hypoaldosteronism and evidence of autonomic and/or peripheral neuropathy. Moreover, Fernandez-Cruz et al. [9] reported a correlation between stimulated PRA and the velocity of esophageal peristalsis in 16 patients with mild renal disease. In our case, despite significant hypovolemia, the renin-aldosterone axis was markedly suppressed, implying that sympathetic tone played a decisive role in renin regulation. It is noteworthy that hyperkalemia occurred in spite of increased gastrointestinal potassium losses due to diarrhoea, which suggests that decreased urinary potassium excretion in patients with hyporeninemic hypoaldosteronism is of decisive significance in potassium homeostasis [1, 2]. Finally, it should be noted that diarrhoea-induced deterioration of hyperchloremic metabolic acidosis can occur as a result of hypoaldosteronism and subsequent hyperkalemia [1, 10].

REFERENCES

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