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Case Report

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Gentamicin-Induced Acquired Bartter-Like Syndrome: A Case Report and Review of the Literature

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Abstract

Aminoglycosides are a group of antibiotics commonly used in the treatment of serious gram-negative bacterial infections. We report a case of acquired Bartter-like syndrome (ABLS) observed following gentamicin treatment for acute infective exacerbation of chronic lung disease. A 38-year-old male was admitted with sudden-onset, rapid symmetrical flaccid weakness in the proximal lower-extremity muscles. His history was remarkable for an acute infective exacerbation of chronic pulmonary disease 11 days before, treated with intravenous amoxicillin/clavulanic acid and gentamicin. The patient paralyzed due to hypokalemia. He was diagnosed with aminoglycosides-induced ABLS. He was managed with potassium and calcium supplements given intravenously for 1 week, followed by 3 weeks of oral administration for both. ABLS induced by gentamicin has rarely been documented in the literature. Early diagnosis and adequate treatment can ensure a good prognosis.

Keywords: Gentamicin, aminoglycosides, acquired Bartter-like syndrome

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INTRODUCTION

Bartter syndrome (BS) is a hereditary disorder characterized by hypokalemia, metabolic alkalosis, hypochloremia, and hypertrophy of the juxtaglomerular complex associated with hyperreninemic hyperaldosteronism and normal blood pressure (1). In addition, BS is associated with hypercalciuria and mild hypomagnesemia. The cause of BS is the primary defect in sodium chloride reabsorption in the medullary thick ascending limb of the loop of Henle (2). It was first reported by Bartter et al. (3).

Aminoglycosides are among the potent bactericidal antibiotics used to treat serious gram-negative infections (4). Gentamicin-induced renal tubular dysfunction may present as an acquired Bartter-like Syndrome (ABLS). In the literature, ABLS due to aminoglycoside therapy has been reported in several cases (2, 5-8). We report a male who was given gentamicin for 10 days to treat the acute infective exacerbation of chronic lung disease and who then presented with ABLS.

CASE PRESENTATION

A 38-year-old male was admitted to the Emergency Department with sudden-onset, symmetrical flaccid weakness in the proximal lower-extremity muscles. His vital signs were the blood pressure 117/74 mmHg, heart rate 78 beats/min, and body temperature 36.8°C. He did not complain of nausea, vomiting, and diarrhea. He had motor weakness with power 2/5 in the lower limbs. His cranial nerves and sensory system findings were within normal limits. Deep tendon reflexes were diminished. There was no history of immunosuppressive disease or drug use. Also, the patient had not used furosemide and thiazide diuretics. His history was remarkable for

Table 1. Laboratory Data at the Time of Presentation and at 1-Week Follow-Up

Parameter	Beginning of Antibiotic Treatment	At Time of Presentation	Day 1	Day3	Day 5	Day 7	Normal Range
Creatinine (mg/dL)	0.9	1	1	-	0.9	1	0.6-1.2
Sodium (mEq/L)	136	122	124	127	130	136	135-145
Potassium (mEq/L)	4.1	1.9	2.2	2.6	3.1	3.8	3.6-5.1
Chloride (mEq/L)	104	74	78	85	89	97	95-105
Calcium (mg/dL)	9.3	7.1	7.3	7.7	8.2	8.8	8.5-10.2
Bicarbonate (mmol/L)	-	42	39	35	31	26	24-32
Magnesium (mg/dL)	-	1.6	-	1.9		1.8	1.7-2.2
Blood gas analysis	pH: 7.53 (7.38-7.42); PCO2: 44 mmHg (36-42); PO2: 94 mmHg; bicarbonate: 42 mmol/L; SPO2: 96.3%						
Urine analysis	pH: 6.0, spot potassium 64 mEq/L, spot sodium 117 mEq/L, spot chloride 92 mEq/L						
Other laboratory tests	Renin: 14.0 ng/mL (Upper limit<6.0ng/mL) Aldosterone: 56.7 ng/dL (Upper limit<31ng/dL) Parathyroid hormone: 66 pg/mL (18.5-88 pg/mL) 25-Hydroxycholecalciferol: 38 ng/mL (30-70 ng/mL) Cortisol: 17.8 mcg/dL (3-18 mcg/dL) Thyroid-stimulating hormone: 2.3 IU/mL (0.4-4)						

an acute infective exacerbation of chronic pulmonary disease 11 days before, treated with intravenous amoxicillin/clavulanic acid, 1 g, twice daily, and gentamicin, 80 mg daily. He was on that antibiotic regimen for 10 days.

Biochemical test results were as follows: glucose at 106 mg/dL, creatinine 1 mg/dL, sodium 122 mmol/L, potassium 1.9 mmol/L, chloride 74 mmol/L, and calcium 7.1 mg/dL. The blood gas analysis revealed a pH of 7.53 and bicarbonate at 42 mmol/L (24-32). The 24-hour urinary potassium excretion was 244 mEq/day (40-120 mEq/dL), magnesium 72 mg/day (65-125 mg/dL), sodium 323 mmol/day (80-180 mmol/d), chloride 386 mmol/dL (110-230 mmol/dL), calcium 478 mg/d (100-300 mg/dL), protein 171 mg/dL, and albuminuria 19 mg/dL. Plasma renin and aldosterone levels were elevated. 25-Hydroxycholecalciferol and parathyroid hormone levels were normal. The results of other laboratory tests are listed in Table 1. The patient's urinary ultrasonography revealed normal kidneys. Cranial computed tomography findings were normal.

Based on the clinical findings with hypokalemia, kaliuresis, hypocalcemia, hypercalciuria, and metabolic alkalosis, the patient was diagnosed with ABLS. Potassium and calcium supplements were initially given with intravenous potassium chloride and calcium gluconate. His electrolytes normalized after 7 days (Table 1). Four weeks following discharge from the hospital, his renal function was stable with serum creatinine of 0.9 mg/dL, potassium 4.1 mmol/L, sodium 137 mmol/L, calcium 8.9 mg/dl, and bicarbonate of 25 mmol/L. Written informed consent was obtained from the patient who participated in this study.

DISCUSSION

Aminoglycosides may cause non-oliguric acute kidney injury, which occurs within first 7-10 days of therapy (5). Nephrotoxicity is mostly mild and often reversible. Aminoglycoside-induced renal tubular dysfunction could result in diffuse tubular damage or may present as Fanconi-like syndrome, ABLS, or distal renal tubular acidosis (5, 6). ABLS can manifest itself at any age, but BS most frequently affects newborns, infants, and children. Our patient was a young man.

The pathophysiology of gentamicin-induced ABLS is unclear but may involve a transporter defect situated in the thick ascending loop of the renal tubule similar to the hereditary variant of BS. There are five types of BS according to genotype. ABLS phenotypically resembles autosomal dominant Type 5 BS (9). The basic pathology of this type is the Ca-sensing receptors mutation in the thick arm of the Henle loop (6, 9). Mitochondrial dysfunction and impaired ATP production induced by the use of aminoglycosides are thought to cause tubular dysfunction (2, 9). Aminoglycosides cause the loss of sodium, potassium, chloride, and calcium from the thick arm level of the Henle loop (2, 6). Hyperreninemic hyperaldosteronism is also caused by water and salt loss. We believe that in this particular patient, ABLS was due to gentamicin toxicity. Because amoxicillin+clavulanic acid have not been shown to cause any particular renal tubular adverse effects, transient changes observed in our patient may be secondary to gentamicin use. As other potential causes of presented clinical picture, there was no history of other causes of acid-base disturbances and/or electrolyte imbalance, acute or chronic kidney disease, and diuretic or laxative use.

Table 2. Demographic and Clinical Features of Development of Acquired Bartter-Like Syndrome Following Aminoglycoside Treatment in Adult Patients

REFERENCES	AGE	GENDER	AMINOGLYCOSIDE	TREATMENT DURATION	RECOVERY
2	26	M	Gentamicin	7 days	13 days
5	39	M	Amikacin	8 days	15 days
6	66	M	Gentamicin	15 days	Not recovered
7	57	F	Gentamicin	7 days	6 weeks
7	51	F	Gentamicin	15 days	4 weeks
7	82	F	Gentamicin	7 days	4 weeks
7	35	F	Gentamicin	10 days	2 weeks
8	26	F	Gentamicin	4 hours	80 days
9	23	F	Capreomycin	2 months	2 days
11	25	M	Capreomycin	15 months	Exitus
12	21	F	Tobramycin	12 days	25 days
13	40	F	Streptomycin	14 days	2 weeks
14	45	F	Gentamicin	10 days	>6 weeks
15	34	F	Gentamicin	6 months (weekly gentamicin)	>1 year

F: Female; M: Male

ABLS can be induced by some antibiotics (amphotericin B, capreomycin, amikacin); antineoplastic drugs (cisplatin); diuretics (furosemide); or other drugs (prostaglandins and heavy metals) (9-11). Kidney biopsy is not required for the diagnosis of ABLS because laboratory findings and clinical picture are rather characteristic. Differential diagnosis was made with Gitelman's syndrome with hypocalcemia and hypercalciuria, with normal serum magnesium levels. The incidence of ABLS after aminoglycosides use was frequently due to gentamicin although ABLS has also been reported in adult patients following the use of amikacin (5), tobramycin (12), streptomycin (13), and capreomycin (9, 11). Our patient was on gentamycin treatment for 10 days, and the dose was 7.6 mg/kg/day. In the literature, ABLS developed after 1-2 weeks of treatment, except for capreomycin (2, 5, 6, 14). It was reported that after a few weeks (2-6 weeks) of gentamicin or amikacin treatment, the tubular functions are expected to be restored, but the improvement of the tubular function following capreomycin may take longer (Table 2) (9, 11). According to Workeneh et al. (15), tubular dysfunction may last for more than a year, despite the termination of gentamicin therapy. Demographic and clinical findings of ABLS following aminoglycoside treatment in adult patients are summarized in Table 2.

BS is a serious and occasionally seen and there is no established treatment except supportive treatment with adequate hydration and correction of electrolyte imbalances. Indomethacin, potassium-sparing diuretics, and/or aldosterone receptor antagonists have also been recommended (10). Therefore, an early detection of potential tubular dysfunction is necessary. Frequently, as in our patient, the renal tubular functional recovery may take several weeks after the cessation of aminoglycosides (5). One of the ABLS characteristic features is the transient character of electrolyte/acid-base imbalance and a rapid response to fluid electrolyte treatment, as it has been observed in our patient, who had an early recovery in about 1 week, following the initiation of intravenous/oral electrolyte replacement (K+, Ca2+) and spironolactone (50 mg/day).

CONCLUSION

We have reported a case of a 38-year-old man who developed ABLS following gentamicin use. Renal functions should be monitored in patients using aminoglycosides, not only with glomerular filtration rate markers, but also with a reference to renal tubular functions.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

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