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Bartter's syndrome and captopril scintigraphy: a case report

Paolo COLAMUSSI,* Stefano PANAREO,* Corrado CITTANTI,* Melchiore GIGANTI,* Angelina FILICE,* Tanja BARESIC,* Salim EL MAOUED,* Roberto RIZZATI** and Adriano PIFFANELLI*

**Section of Nuclear Medicine, and **Section of Radiology, University of Ferrara, Italy*

We report a case of a woman who came to our attention because of hypokalemia, hyperreninemia and hyperaldosteronemia but with normal blood pressure. Under suspicion of a normotensive renal artery stenosis captopril and baseline scintigraphies were performed. Captopril scintigraphy demonstrated a bilateral progressive retention of radiopharmaceutical without significant excretion. The baseline study revealed a complete normalization of the scintigraphyc picture. A Magnetic Resonance Angiography (Angio-MRI) performed to evaluate renal arteries gave completely normal results. On the basis of the clinical picture and imaging findings a diagnosis of Bartter's syndrome was formulated. Renal function in Bartter's syndrome patients is maintained by hyperactivation of the renin angiotensin system. Acute administration of captopril in these patients induces an increase of renal plasma flow whereas it has no effects on glomerular filtration rate thus inducing a decrease of the filtration fraction: post captopril renal scintigraphy of our patient depicted exactly this feature. Although the diagnosis of Bartter's syndrome is based on the clinical picture and biochemical abnormalities, scintigraphic tests could be useful in differentiating Bartter's syndrome from other causes of hypokalemia.

Key words: Bartter's disease, radioisotope renography, technetium-99m MAG3, captopril, magnetic resonance angiography

INTRODUCTION

BARTTER'S SYNDROME is an autosomal recessive tubulopathis disorder involving juxtaglomerular cell hyperplasia characterized by hypokalemia due to potassium renal leakage and normal blood pressure despite increased plasma renin activity and secondary hyperaldosteronism.[1,2] The primary cause of Bartter's syndrome remains unknown but the most likely candidate is reduced sodium chloride reabsorption in the thick ascending limb of Henle's loop due to mutations in the chloride channel gene CLCNKB.[3] Pathogenesis includes bilateral hyperplasia of the juxtaglomerular apparatus, which causes excess renin production. Several studies have documented increased renal excretion of prostaglandins.[4,5] Most of the associated clinical phenomena in this syndrome are the result of hypokalemia. In early life many patients present symptoms such as muscle weakness and polyuria, which may be attributed to potassium depletion. A significant group of patients are asymptomatic.[6] The diagnosis is one of exclusion, mainly of surreptitious vomiting and diuretic abuse.[7] Therapeutic approaches to Bartter's syndrome focus on multiple agents to reduce massive potassium loss. They include potassium supplementation, prostaglandin synthesis inhibitors (nonsteroidal anti-inflammatory agents), aldosterone antagonists, and converting enzyme inhibitors.[8]

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For reprint contact: Stefano Panareo, M.D., Section of Nuclear Medicine, University of Ferrara, C.so Giovecca 203, 44100, Ferrara, ITALY.

E-mail: panaste@libero.it

CASE REPORT

A 43-year-old woman was investigated because an incidental blood test showed hypokalemia (3.1 mEq/*l*). Subsequent analysis revealed hyperreninemia (320 ng/m*l*)

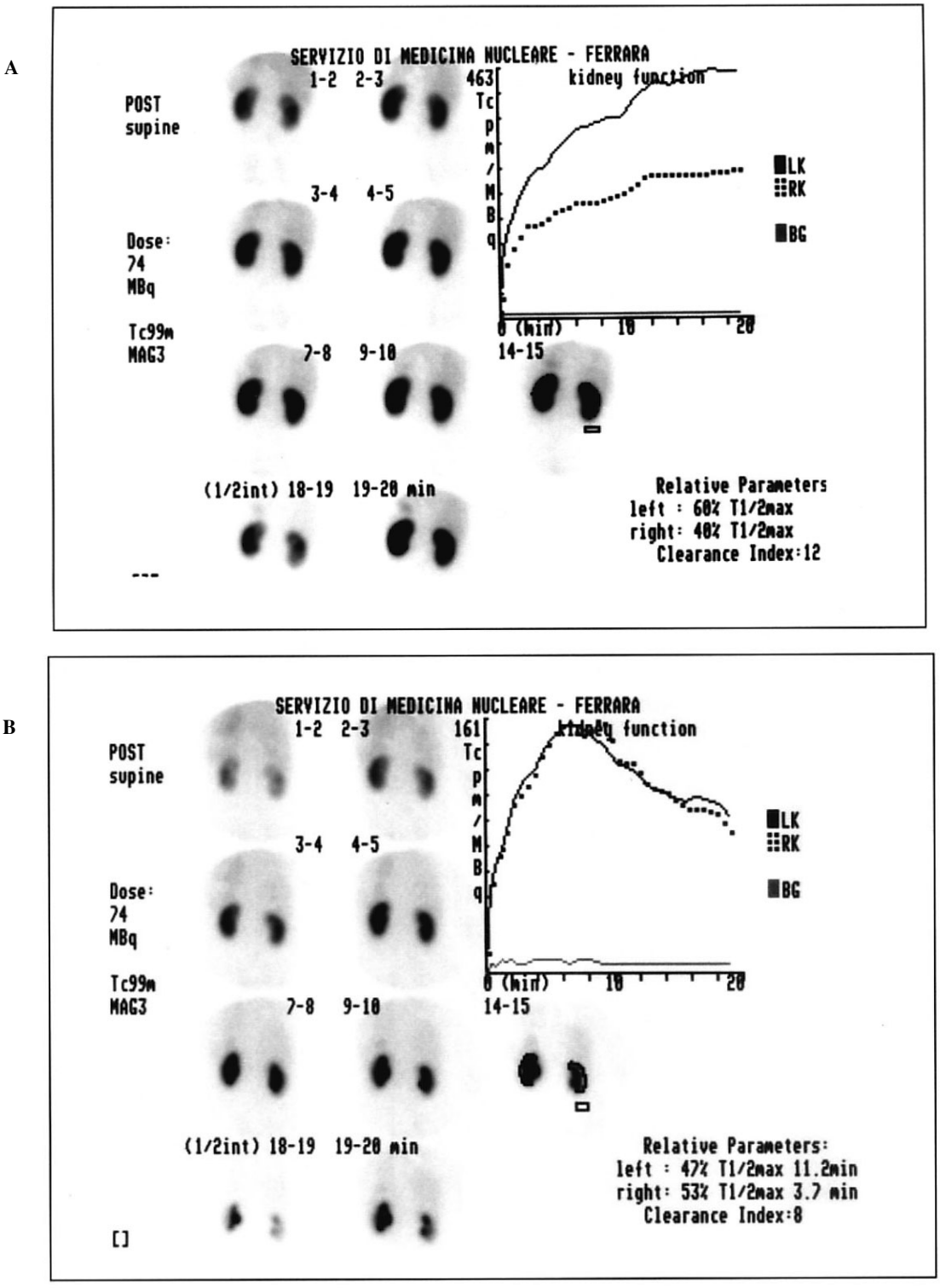

Fig. 1 Renal scintigraphy with (A) and without (B) captopril administration. LK: left kidney; RK: right kidney; BK: background region

and hyperaldosteronemia (500 pg/m*l*).

The patient was asymptomatic and the blood pressure levels were constantly good. A renal ultrasound evaluation showed left pelvic and calyceal dilation without stone images.

Under suspicion of a normotensive renal artery stenosis captopril and baseline scintigraphies were performed. After good hydration, captopril (50 mg) was given and 1

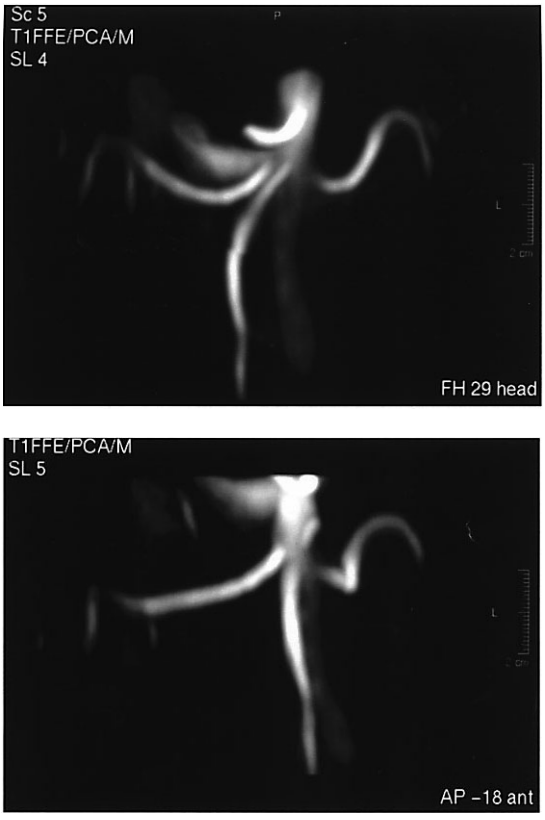

Fig. 2 Angio-MRI study of abdominal vessels.

hour later the patient was injected with 111 MBq of Tc-99m mercapto-acetyl-triglycinic acid (MAG3). Dynamic renal scintigraphic images were obtained at a rate of 1 frame/10 sec for 20 minutes with the camera head under the cot. Before captopril administration, blood pressure levels were within the normal range (115/75 mmHg); 30 minutes after captopril administration an asymptomatic reduction of blood pressure (105/65 mmHg) was observed with normalization within 2 hours. Captopril scintigraphy processing showed a bilateral progressive retention of radiopharmaceutical without excretion (Fig. 1A). A basal renal scintigraphy, acquired the next week with the same procedure except for captopril administration, showed a restoration of renal curves (Fig. 1B). To exclude renal artery stenosis an Angio-MRI was performed. A dynamic 3D FFE T1-weighted sequence was obtained after the infusion of 0.2 mmol/kg of gadolinium-DTPA at a rate of 2 m*l*/sec. Image evaluation did not show any abnormalities of the renal vessels (Fig. 2).

Following analysis of these results, the patient's clinical picture was re-evaluated, and other investigations carried out. Arterial blood gas analysis showed signs of metabolic alkalosis (pH 7.48, PaO_2 of 80 mmHg, $PaCO_2$ of 45 mmHg, and HCO_3 of 34 mmol/*l*) and the determination of the magnesium serum concentration indicated mild hypomagnesemia (1.2 mEq/*l*).

These findings led to the diagnosis of Bartter's syndrome. The patient was treated with potassium chloride, magnesium, alimentary sodium, and regularly monitored with blood tests. After 6 months normalization of kalemia and magnesemia (respectively 4.3 mEq/*l*, and 1.8 mEq/*l*) and an almost complete recovery of renin and aldosterone plasma values (respectively 80 ng/m*l* and 160 pg/m*l*) were observed.

DISCUSSION

Bartter's syndrome is an intriguing clinical picture that includes hypokalemia, hyperactivation of the renin-angiotensin II-aldosterone axis, but hyporesponsiveness to the pressor action of angiotensin II that causes a persistent normo-hypotension in spite of biochemical and hormonal abnormalities typical of hypertension. These features are probably linked to some alterations in the intracellular sequence events leading to vascular smooth muscle activation.[1–4] Partial occlusion of the renal artery by atherosclerotic narrowing or by fibromuscolar dysplasia is associated with normo-hypotension in about 2% of cases.[9,10] In the case reported, initial imaging evaluation and laboratory tests could be associated with a normotensive renal artery stenosis. This is the reason why captopril scintigraphy and Angio-MRI were performed. In light of the clinical picture and imaging results a diagnosis of Bartter's syndrome was postulated. Previous studies performed to evaluate the effects of captopril in Bartter's syndrome patients demonstrated that the drug induces an increase of renal plasma flow whereas it has no effects on glomerular filtration rate thus inducing a decrease of the filtration fraction[11,12]: post captopril renal scintigraphy of our patient showed exactly this feature. Although the diagnosis of Bartter's syndrome is based on the clinical picture and biochemical abnormalities, scintigraphic tests could be useful in differentiating Bartter's syndrome from other causes of hypokalemia such as diuretic intoxication and laxative abuse.

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