Case Report

Association of Bartter’s syndrome with vasculitis

Boriana Deliyska1, Valentin Lazarov1, Violina Minkova2, Dobrin Nikolov1 and Ivan Tishkov1

1Clinical Center of Nephrology and 2Department of Pathology, Medical University, Sofia, Bulgaria

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Introduction

Bartter’s syndrome is a rare disorder manifested by primary inherited renal tubular hypokalaemic metabolic alkalosis, marked elevation in plasma renin and aldosterone activity, pressor insensitivity to angiotensin II and normal or low values of plasma sodium, plasma chloride, low blood pressure and hyperplasia of the juxtaglomerular apparatus [1]. It is now evident that this syndrome does not represent a unique entity but encompasses a variety of disorders of renal electrolyte transport [2]. A case of Bartter’s syndrome with severe hypokalaemic alkalosis, hyperaldosteronism and hyperreninaemia with low blood pressure, associated with ANCA-negative vasculitis and minor glomerular changes is discussed. After therapy with steroids, plasmapheresis and cyclophosphamide, potassium supplements and Aldactone A the condition of the patient improved and became stable. No relapse of the immune activity of the vasculitis was detected during the period of observation.

Case

A 25-year-old woman was referred to our clinic 1 week after severe tetany associated with hypokalaemia. One year before that incident she had muscle weakness, fatigue, brief episodes of polyarthralgia, but systemic examinations were not carried out. No drug abuse connected with hypokalaemia was reported. The patient had consumed more than 2 l milk daily for many years. The blood pressure was 110/80 mmHg.

At presentation the following results were obtained: WBC was 10.3 × 109 (41% lymphocytes), haemoglobin 107 g/l, RBC 3.6 × 1012, serum creatinine 128 μmol/l, creatinine clearance 64 ml/min/1.73 m², uric acid 711 μmol, with normal serum total protein and serum albumin. The erythrocyte sedimentation rate was 31 mm in the 1st hour and 67 mm in the 2nd hour. Serum potassium was 2.8 mmol/l, sodium 133 mmol/l, chloride 79 mmol/l, calcium 2.3 mmol/l, phosphate 0.86 mmol/l, magnesium 0.9 mmol/l. A remarkable metabolic alkalosis was present: pH 7.58, HCO3⁻ 40.4 mmol/l, BE +18.4 mmol/l. The proteinuria was 0.8 g/day and the urine sediment was normal. The renal concentrating capacity was disturbed. Positive antinuclear antibodies were found: ssDNA 2+, adsDNA 3+, aSm 2+, circulating immune complexes 13.0 U (normal reference values <3 U). ANCA, aRNP and aSS-B were negative. Components of complement and cryoglobulins were normal. Marked elevations of the aldosterone and renin plasma levels were found. While abdominal ultrasonography showed hyperechogenic kidneys, the abdominal computerized tomography was normal. To clarify the nature of the disease kidney, skin–muscle biopsies were performed. In the kidney minor glomerular abnormalities with mild mesangial proliferation were observed. Part of the tubules showed thick basement membranes. Few interstitial infiltrates were detected. No changes in the vessels were found. Immunofluorescence was negative. In the skin biopsy, infiltrates in the deep part of the derma surrounding the arterioles, capillaries and venules were observed. In the hypoderma the vessels showed thickening walls with stenosis of the lumen and mononuclear infiltrates. The diagnosis from the skin biopsy gave evidence for a chronic vasculitis of the small vessels of the derma and hypoderma without immunofluorescence depositions.

Clinical evolution

The patient received pulse therapy with cyclophosphamide (10 mg/kg i.v.), followed by 1 mg/kg for 2 weeks, but later the drug had to be stopped because of an increase in the concentrations of liver enzymes. Prednisone (1 mg/kg) was applied for 6 months after which the dose was tapered and discontinued. At first

Correspondence and reprint requests to: Dr B. Deliyska, Clinical Center of Nephrology, Medical University, Damian Gruer Str. 8, Sofia 1303, Bulgaria.

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Bartter’s syndrome can be subdivided into at least three clinical phenotypes with different clinical entities: the hypercalciuric antenatal Bartter’s or hyperprostaglandin E syndrome; the classic Bartter’s syndrome and the hypocalciuric–hypomagnesaemic Gitelman variant [3,4]. Mutations in the genes encoding inwardly rectifying renal potassium channel (ROMK) and for Na-K-2Cl cotransporter (NKCC2) cause the antenatal variant. It is characterized by intratubular polyhydrations, premature delivery and life-threatening episodes of fever and dehydration and severe hypercalciuria with nephrocalcinosis and osteopenia [4]. Classic Bartter’s syndrome is due to defective chloride transport across the basolateral membrane in the distal nephron as a result of mutations in the chloride channel gene Cl CNKB [5,6]. Mutations in the genes, encoding the thiazide-sensitive sodium-chloride cotransporter underlie the pathogenesis of Gitelman syndrome [7–9]. There is some evidence that plasma factors affect the ion transport and may contribute to K+ wasting and hypokalaemia in patients with Bartter’s and Gitelman syndromes [10–12]. The Gitelman syndrome is a rare hereditary autosomal, recessive magnesium reabsorption defect in the distal tubule and is characterized by episodes of muscle weakness, abdominal pain and vomiting. Tetany may occur during a febrile illness. There is hypokalaemia, hypomagnesaemia and alkalosis with elevated urinary excretion of potassium and magnesium and diminished calcium and impaired renal conservation of potassium and magnesium [13,14]. Gitelman disease appears to be a homogenous post-loop of Henle disorder, while the Bartter’s syndrome is a heterogeneous disorder of Henle’s loop [15].

The initial findings in our patient had to differentiate Bartter’s syndrome from Gitelman syndrome and the differentiation between them is still not perfect. A milk-alkali syndrome was also suspected. We hypothesized that the patient suffered from mild Bartter’s syndrome at a young age, which became clinically manifest during the onset of the vasculitis. We speculated that the existing antibodies from the autoimmune disease aggravated the malfunction of the thick ascending limb and were responsible for the clinical manifestation of the pre-existing syndrome. We found some evidence for this explanation in the fact that remission of the vasculitis with immunosuppression was associated with a significant improvement in the clinical and laboratory findings of Bartter’s syndrome.

Few cases describing co-existations between Bartter’s syndrome and other kidney diseases are available. Higashi et al. [16] observed Sjögren’s syndrome associated with hypokalaemic myopathy due to Bartter’s syndrome; association with chronic renal failure due to chronic interstitial nephritis was reported by Maekava et al. [17]. Buluco published a case of Gitelman syndrome in association with focal glomerulosclerosis [18].

In conclusion we observed a patient in whom Bartter’s syndrome became manifest during activation of a vasculitis. Immunosuppressive treatment not only improved the vasculitis, but also the clinical course of Bartter’s syndrome.

References


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