B) BRIEF CASE REPORTS

Acute renal failure due to haemoglobinuria secondary to P antigen

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To the Editor,

The P antigen is a high-incidence antigen present in erythrocytes, platelets, lymphocytes, fibroblasts, the placenta and uroepithelial cells. More than 99.9% of the population has this antigen. Individuals with P phenotype are characterised by a lack of Pk, P and P1 erythrocyte antigens and by forming anti-Tja antibodies (anti-PP1PK), without previous immunization. Knowledge of this type of antibodies is important because they are involved in severe post-transfusion reactions.[1]

CASE REPORT

The patient was a 68-year-old female, whose only history of significance was iron deficiency anaemia, examined by Gastroenterology since May 2013, with no history of nephrology problems. Following progressive anaemia (haemoglobin: 6.5g/dl), the patient was referred to the hospital centre for a red blood cell transfusion. We observed a post-transfusion reaction and progressive deterioration of renal function, reaching a maximum creatinine level of 7.67mg/dl, urea 171mg/dl and oligoanuria. The patient was admitted to the Nephrology Department, where a complete study was carried out. We observed values of haemoglobin up to 4.2mg/dl, LDH 997UI/l, indirect bilirubin 1.1mg/dl, reticulocytes 2.9%, haptoglobin 36.40mg/dl and anisopoikilocytosis with polychromasia in the blood smear. Haematuria and pyuria were detected in the urine test strip. The data suggested autoimmune intravascular haemolytic anaemia due to blood incompatibility.

The Haematology Department was consulted, which reported the presence of irregular antibodies of anti-Tja specificity at a titre of 1:16. These results are compatible with the absence of a high-incidence antigen in the general population, the P antigen. During the hospital admission, renal function improved. The patient required various sessions of haemodialysis, support treatment with intense fluid therapy and alkalinisation, and treatment of anaemia with erythropoietin and intravenous iron, and four units of packed erythrocyte transfusion. Currently the patient has a creatinine level of 0.3mg/dl and haemoglobin level of 10.6g/dl.

DISCUSSION

This case covers two conditions rare in normal clinical practice: the absence of the P antigen and acute renal failure (ARF) due to haemoglobinuria. Despite the diagnostic suspicion being intravascular haemolytic anaemia secondary to blood incompatibility, doubts arose due to the urine testing negative for haemosiderin and haemoglobin, as well as in the Coombs test.

The absence of the P, Pk and P1 antigens, structurally related, occurred as a result of the loss of activity of 4-alpha-galactosyltransferase, a type II membrane protein with 353 amino acids. In addition to being associated with post-transfusion reactions, it can also cause abortions through haemolytic disease of the fetus and newborn and, according to some theories, different infectious diseases (infectious erythema or haemolytic-uraemic syndrome).[2,3]

ARF can be triggered by rhabdomyolysis and haemolysis, due to myoglobin and haemoglobin respectively, proteins that contain the "haemo" pigment which damages the kidney, causing tubular obstruction, acute tubular necrosis and vasoconstriction. Haemoglobin has a greater molecular weight (65 000Da) than myoglobin (17 000Da) and, in contrast, binds to proteins such as haptoglobin, making its filtration and excretion more difficult. Both cases presented dark-coloured urine, testing positive for blood in the urine test strip, and increase in plasma LDH levels. In myoglobinuria, the level of creatine-kinase enzyme increased and in the case of haemolysis, we detected anaemia, a decrease in haptoglobin and an increase of indirect bilirubin with the appearance of dysmorphic red blood cells in peripheral blood.[4,5]

Treating a rare blood-type is a complicated task because of the difficulty in finding blood of the same phenotype. Consequently, the options were to carry out cryopreservation of autologous red blood cells or to find compatible individuals within the patient's family. In our case, blood from another hospital was reserved and blood from a family member was used.

Conflicts of interest

Lecture fees: Yes, but not related with the content of the published study.

Council Membership: The author (F.J. Gainza) is a member of the editorial committee of the magazine Nefrología and a reviewer of other international magazines.

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Gitelman syndrome with hyponatraemia, a rare presentation

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Dear Editor,

Hypokalemia is one of the most common electrolyte abnormalities which etiology can be unclear and the incorrect diagnosis can result in the wrong treatment.

Gitelman syndrome (GS) is an autosomal recessive disorder of the thiazide-sensitive sodium chloride cotransporter, expressed at the distal convoluted tubule (DCT). The mutation is found in the *SLC12A3* gene, but there are also others. Its prevalence is estimated to range 25 cases per 1 million.[1] Acquired GS is rarer and usually associated with autoimmune diseases or after renal transplantation.[2]

GS phenotype is characterized by hypokalemic alkalosis, hypomagnesemia, hypocalciuria, and secondary aldosteronism without hypertension. Hyponatraemia is not a recognised feature of GS.[3]

CASE REPORT

A 34 year old caucasian woman with no prior medical presented with severe hypokalemia; hypomagnesemia and mild hyponatremia. Her past medical and family history were unremarkable. She was on no medication and denied any symptoms, unless for occasionally muscle cramps. Water intake ≥3L/day. She was normotensive, no edemas and normal urine output. The review of systems was otherwise negative.

Table 1 summarizes laboratory investigation.

Patient was managed with oral magnesium and spironolactone 50mg/day. Her condition improved significantly and her last routine lab control showed serum potassium 3.78mmol/L, magnesium 0.79mmol/L and sodium 136.0mmol/L, without any other changes.

DISCUSSION

Potassium excretion is mostly derived from secretion in the distal nephron, driven by an electrochemical gradient increased by aldosterone-induced sodium reabsorption; and by an electroneutral K^+ Cl^- secretory mechanism.[4]

Hypokalemia may result from decreased intake, increased translocation into the cells, or, most often, increased losses in the urine, gastrointestinal tract, or sweat.

Although these causes were sought by history taking and clinical examination, we needed to exclude surreptitious vomiting or drugs abuse because high urinary potassium, metabolic alkalosis and alkaline urine can also be present in these two disorders. Differential diagnosis with vomiting was made through urinary chloride which is low in hypovolemia due to hyperaldosteronism, opposing to patient normal values poiting to a renal disorder. Diuretic abuse was excluded through a negative urinary screen.

Because the patient was normotensive, we stood with Gitelman or Bartter's.

Magnesium excretion rate is regulated by distal reabsorption that depends on epithelial TRPM6 channels, which gene suffers a downregulation mutation in GS, inducing urinary magnesium wasting leading to hypomagnesemia,[5] opposing to Bartter syndrome.

Calcium is absorbed in proximal nephron driven by an electronegative transcellular gradient induced by chloride–sodium transport; and in DCT driven by parathyroid hormone and Vitamin D. Hypocalciuria pathogenesis still remains debated but an important role is played by metabolic alkalosis.[6]

At the end, our patient fulfilled the diagnostic criteria for GS, although few unusual aspects. First, the inappropriately high urine pH and pCO2 (directly proportional to bicarbonate (HCO_3^-) concentration) could be explain through high chloride delivery that enhances HCO_3^- secretion in type A intercalated cells (to maintain electroneutrality). Adding to this, hypokalemia suppresses aldosterone secretion, which reduces sodium reabsorption (no hypovolemia) increasing back-diffusion of hydrogen, allowing the urine to become more alkaline than plasma.[6] Aldosterone activity degree could be accessed through tubular fluid potassium concentration at distal cortical collecting tubule, estimated from transtubular potassium gradient but this would only be usefull in hyperkalemia