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 occasional 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 transepithelial 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 [HCO₃⁻] concentration) could be explain through high chloride delivery that enhances HCO₃⁻ 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.
and renal failure, hyponatraemia associated to normal volemia, inappropriately high urine osmolality and urinary sodium concentration suggested the presence of a syndrome of inappropriate secretion of antidiuretic hormone (SIADH). The stimulus for this secretion is unclear. Although chronic hypokalemia could be characterized by some resistance of tube collector cells to ADH, GS has a urinary diluting capacity disturbed creating a SIADH like effect. Opposing to Bartters, GS has a preserved concentrating ability, because medullary thick ascending limb is intact. Since there is no hypovolemia, urinary sodium excretion is high to maintain electroneutrality as HCO$_3^-$ is being excreted. Adding to this, in severe hypokalemia, via unknown mechanism, distal chloride excretion is increased causing a paralell sodium waste.

There are only a few cases of GS with hyponatraemia reported and in two of them a combination of high water intake with an impaired urinary dilution capacity caused by GS was described as a possible explanation for SIADH-like biochemical features.\textsuperscript{8,9} Adding to water, our patient must had a high intake of salt which raised the sodium delivery to the collecting duct and could explain both sodium and HCO$_3^-$ excretion increase, with water free of electrolytes retention. To the best of our knowledge it was what happened to our patient. A genetical study would confirm the diagnosis and clarify about additional anomalies but we didn’t perform it because of economic issues. However, we still don’t have many doubts about the diagnosis because there is a large phenotype variability without relationship between the clinical severity and type of mutations. Furthermore, heterozygotes have a higher rate of sodium excretion than wild-type individuals, probably due to higher salt intake.\textsuperscript{10}

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**Conflicts of interest**

The authors declare that they have no conflicts of interest related to the contents of this article.
Multigene involvement in congenital nephrotic syndrome

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To the Editor,

Congenital nephrotic syndrome (CNS) is a serious, rare disease which in most cases has autosomal recessive monogenic inheritance. Several genes are implicated, the most frequent of which are NPHS1, NPHS2, WT1 and LAMB2.1,2 It manifests clinically with massive proteinuria, general oedema, hypoaalbuninaemia and hypertriglyceridaemia appearing in the first three months of life.3 Here, we present the first case of a CNS patient with multigenic alteration of three of the four most common genes.

CASE REPORT

Our patient was a one-month-old male from Morocco, who came to the Emergency department after presenting symptoms such as vomiting, rejection of food and abdominal distension which had lasted 4 days. The pregnancy was controlled, with no relevant obstetric or perinatal history. The baby was born for the WT1 gene. When CNS was suspected, the patient began to undergo intensive diuretic and antiproteinuric therapy, antithrombotic prophylaxis, adjuvant treatment with alfacalcidol, iron, calcium carbonate and levothyroxin, as well as enteral nutrition with hyperprotein, hypercaloric formula. He required treatment with serum albumin and erythropoietin. Moderate pulmonary valve stenosis and atrial septal defect were diagnosed in the cardiology study. The genetic study revealed mutations of the frameshift type for the NPHS1 gene, of the intronic variant type for the NPHS2 gene and of the missense type for the WT1 gene.

At three months of age he was readmitted due to convulsive status epilepticus secondary to severe hypocalcaemia. The high quantities of intravenous calcium which needed treatment via peripheral venous access caused a third-degree burn which required a cutaneous graft to be placed.

Intensive care was required on two occasions, at 4 and 6 months of age, for sepsis secondary to Staphylococcus hominis and Enterococcus faecalis respectively, which were resolved with empirical antibiotic treatment and then according to the results of the antibiogram.

Finally, the patient died at 8 months of age due to bilateral pneumonia linked to pneumothorax with decompensation of the underlying pathology which caused refractory hypoxaemia.

DISCUSSION

CNS may be suspected in the prenatal period due to high levels of alphaphetoprotein, maintaining normal figures for cholinesterase from the 15th week of gestation in amniotic fluid and maternal blood.2,4 At birth the link between premature birth and a large placenta can provide guidance, factors which were not present in our patient.

The most frequent cause of this condition is the NPHS1 gene mutation,