The complementary explorations revealed the following:

The complete blood count and baseline coagulation parameters were normal. Urea 66 mg/dl, serum creatinine 2.3 mg/dl, creatinine clearance 35 ml/min., Na 145 mEq/l, K 4.8 mEq/l, Cl 109 mEq/l, PTH 92 pg/ml. The studies of hypercoagulability and autoimmunity proved negative. Twenty-four hour urine showed: pH 8, rest normal or negative, urine creatinine 38.1 mg/dl, proteins 0.5 g/d, urine Na 76 mEq/l, urine K 17.2 mEq/l, urine Cl 74 mEq/l. The urine sediment was normal. Abdominal ultrasound: a single left kidney measuring 12.6 cm in size, with loss of cortico-medullary differentiation. The echo-Doppler findings in the lower extremities were compatible with DVT, and computed tomographic angiography showed signs typical of bilateral PTE. Polysomnography revealed episodes of hypopnea and hypoventilation, without apnea. The observed pattern was not suggestive of obstructive sleep apnea syndrome (OSAS). The evolution of the blood gas parameters was as follows:

– Upon admission (arterial): pH 7.26, PCO_2 32.4, PO_2 68.4, HCO_3 14.4, base excess 11.2

– After anticoagulation (venous): pH 7.11, PCO_2 59.4, PO_2 22.4, HCO_3 21.9, base excess 6.1

– After start of treatment with BiPAP and bicarbonate: pH 7.27, PCO_2 44.8, PO_2 14.9, HCO_3 17.9, base excess 3.9

– Following the start of bi-level positive airway pressure ventilation (BiPAP), bicarbonate treatment and the withdrawal or topiramate: pH 7.33, PCO_2 35.8, HCO_3 19.3. The GAP anion was normal in all cases (between 11-14).

With anticoagulation, the PTE tended to resolve. A renal biopsy was discarded, and stage III CKF secondary to diminished nephron mass and probable chronic interstitial nephropathy was diagnosed. BiPAP corrected the respiratory component of acidosis associated to central hypopnea, although GAP anion-normal hyperchloremic metabolic acidosis persisted. On administering bicarbonate, the tendency towards acidosis persisted, though to a lesser degree, and the pH was corrected upon suspending topiramate.

Topiramate, in the same way as acetazolamide, is a potent inhibitor of carbonic anhydrase (CA) isoenzymes II and VI – this being the mechanism considered to involved in the development of metabolic acidosis when this drug is used. We recommend to the monitorization of serum bicarbonate during topiramate treatment, particularly in patients with respiratory problems or renal failure.

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S. Sujan[1], A. Torres de Rueda[1], L. Montero[2], R. Toledo[1], S. Ros[2] and G. Martín Reyes[2]

[1]Servicio de Nefrología. Hospital Carlos Haya. Málaga. [2]Servicio de Medicina Interna. Hospital Axarquia. Vélez-Málaga. Málaga.

Correspondence: *Álvaro Torres de Rueda. atorresnefro@yahoo.es. Hospital Carlos Haya. Avda. Carlos Haya, s/n. 29010 Málaga. España.*

Enema in a patient with renal failure: a cause of severe hyperphosphatemia

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To the editor: The use of phosphorus (P)-containing enemas is common practice as preparation for colonoscopy and for other applications (constipation, preoperative or pre-radiological intestinal cleansing), with generally unknown side effects. In patients with renal failure, such enemas can produce severe hyperphosphoremia,[1,2] as in the case described below.

A 79-year old woman reported with abdominal pain and bloating, associated to constipation for the previous week. She had a history of arterial hypertension, diabetes mellitus, anemia, osteoporosis and cognitive deterioration. There were no data indicative of renal failure. Treatment consisted of metformin, insulin, indapamide, amlodipine, sertraline, omeprazole, tramadol, paracetamol, risedronate and ferrous sulfate. The physical examination revealed the following: good hydration with blood pressure 150/70 mmHg, severe abdominal bloating with pain in response to palpation, no defensive reaction or peritonism and metallic sounds. There were no other findings of interest. The abdominal X-rays revealed important colon dilatation without evidence of obstruction, while the CAT scan showed important dilatation from cecum to rectum, suggestive of acute colon pseudo-obstruction or Ogilvy's syndrome (fig. 1). The laboratory tests revealed the following: glucose 153 mg/dl, urea 186 mg/dl, creatinine 3.5 mg/dl, Na 140 mEq/l, K 5.7 mEq/l, and a urinary sediment with leukocyturia and bacteruria. Colonoscopy confirmed the above mentioned diagnosis, as a result of which decompression was carried out with the aspiration of 2000 ml of fecaloid fluid. During the first few days of admission the patient failed to improve; a rectal tube was thus placed for the instilment of four 250-ml Casen® enemas. A few hours later the patient suffered obnubilation and generalized tetany. Emergency laboratory testing revealed the following: urea 104 mg/dl, creatinine 2.7 mg/dl, Na 161 mEq/l, K 2.4 mEq/l, Ca 5.3 mg/dl, P 22 mg/dl and venous blood gases indicating pH 7.6, bicarbonate 12.8 mEq/l and pCO_2 13 mmHg. In view of these clinical and laboratory test data, dialysis was indicated but rejected by the

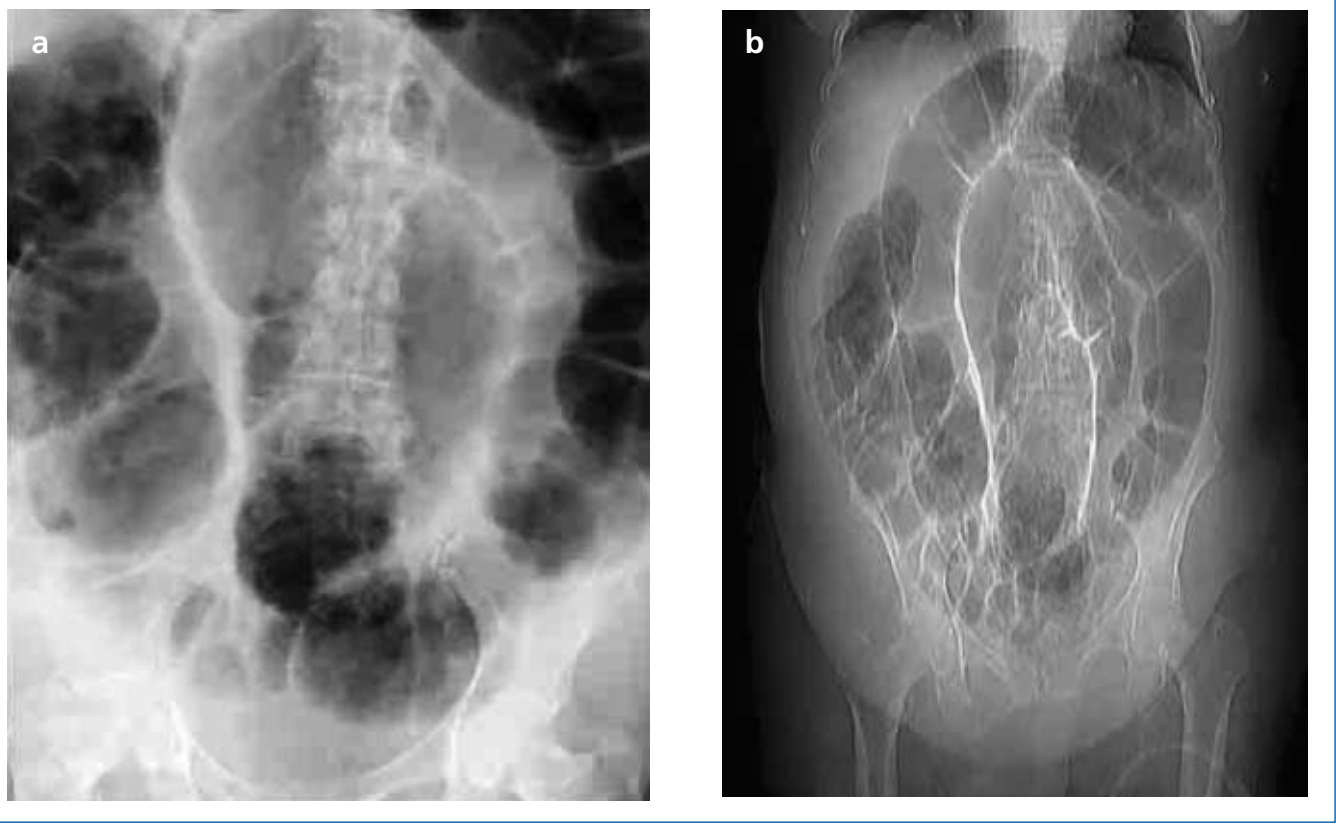

Figure 1. a) Abdominal X-rays showing colon dilatation; b) Abdominal CAT scan showing dilatation from cecum to rectum.

family. Treatment was therefore provided in the form of 5% glucose solution, calcium gluconate and KCl via the intravenous route. However, due to persistence of the tetany, with only partial improvement of the laboratory parameters, we convinced the family to accept a hemodialysis session lasting about 150 minutes, with a Ca-rich bath (3.5 mEq/l). Following this session the laboratory parameters normalized, as reflected in figure 2. The patient was subsequently discharged and programmed for follow-up by the Service of Geriatrics.

Phosphorus metabolism is greatly altered in patients with both acute and chronic renal failure, since the elimination of P is essentially in urine; as a result, the administration of P-containing compounds via any route is contraindicated in such situations. While this measure of caution is well known to physicians caring for such patients in any clinical unit, the side effects of enemas are less well known. In this context, many enemas contain important amounts of P, and as such may lead to potentially fatal hyperphosphoremia. In our patient, the existence of renal failure, with an evident pre-renal component (third space), is an example of the hazard involved when administering P-containing enemas, including apparently innocuous Casen® – which is very rich in P (8 g of disodium hydrogen phosphate and 16 g of sodium dihydrogen phosphate, per 100 ml).[3] Although the absorption of P fundamentally takes place in the duodenum and jejunum, in the presence of intestinal pathology (e.g., Ogilvy's syndrome), increased P retention occurs in the bowel lumen, with an increase in absorption. Ogilvy's syndrome is characterized by acute and intense colon dilatation (particularly on the

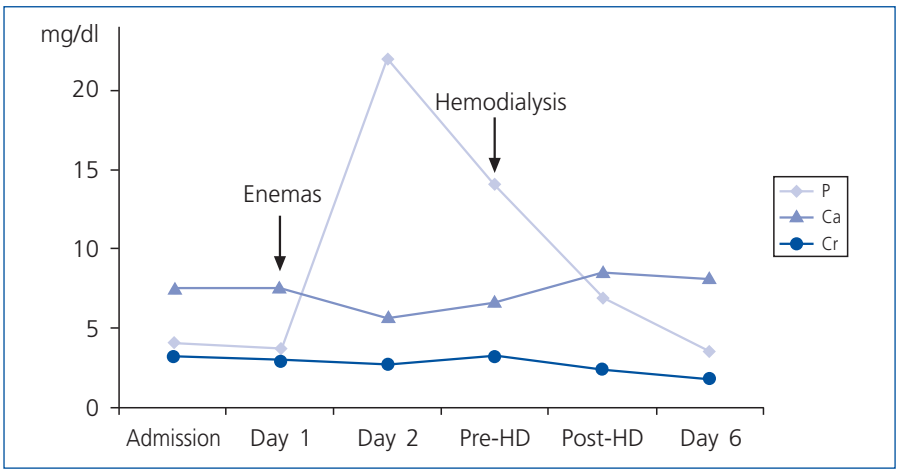

Figure 2. Evolution of the laboratory test parameters.

right side), without organic obstruction. This is a serious condition that can be complicated by perforation, peritonitis and death. The underlying cause is multifactorial (altered regulation of the intestinal sympathetic – parasympathetic system, among other factors), and treatment is fundamented on endoscopic decompression.[4] It has been reported that certain drugs such as the calcium antagonists used by our patient (amlodipine) aggravate intestinal dilatation.

In our case we observed all the described complications following the intestinal infusion of P-rich enemas – including hypernatremia, possibly due to increased Na absorption, fluid sequestration in the bowel lumen, and volume depletion causing hypertonic dehydration with functional renal failure. Hyperphosphoremia is associated with hypocalcemia, tetanic contractions and extraskeletal calcium phosphate deposits. Hemodialysis is the treatment of choice.[5] In our patient, a single session sufficed to improve the condition, though the medical treatment provided must have contributed to such improvement. Lastly, it should be pointed out that there are other types of enemas that do not contain P and which can be administered to patients with renal failure, such as X-Prep® or Puntualex® (sennosides A and B).

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M. Bennouna, S. Anaya, M.ª D. Sánchez de la Nieta and F. Rivera

Sección de Nefrología. Hospital General de Ciudad Real.

Correspondence: *Francisco Rivera Hernández. friverahdez@senefro.org. Hospital General de Ciudad Real. 13005 Ciudad Real. España.*

Compound heterozygosis for intrón 9 + 1 g > T and Leu 850pro mutations in the SLC12A3 gene in Gitelman's syndrome

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To the editor: Gitelman's syndrome is the most frequent hereditary tubular disease in Europe (1% of heterozygous individuals),[1] and is characterized by hypopotassemia, metabolic alkalosis, hypomagnesemia and hypocalciuria.[2] A recessive autosomal hereditary pattern is observed, related to mutations of the SLC12A3 gene, which encodes for the Na/Cl co-transporter in the renal distal tubule, causing sodium reabsorption failure and secondary hyperaldosteronism. Over 100 different mutations have been reported.

CLINICAL CASE

A 35-year-old male presented with a history of generalized weakness in the course of an episode of acute diarrhea. Plasma potassium concentration was 1.1 mEq/l. Upon readmission to a tertiary hospital due to the relapse of severe and symptomatic hypopotassemia, the laboratory tests revealed the presence of full Gitelman's syndrome (table I). A study of the family detected a similar biochemical condition only in the male sibling of the patient; both individuals had suffered scant previous repercussions in the form of carpopedal spasms in childhood, in relation to fever episodes, and occasionally also in adult life. Treatment was provided in the form of potassium and magnesium supplements, spironolactone, amiloride and finally eplerenone, at very high doses for normalization of the plasma levels – with the persistence of important potassium elimination in urine. The genetic study showed both siblings to carry the int. 9 + 1G > T mutation, present in the father, and the Leu850Pro mutation in exon 22, present in the mother. The two children of the patient carried only the Leu850Pro mutation.

DISCUSSION

The association of these two mutations is reported for the first time. The variant int. 9 + 1G > T has been found in the largest published series with a common mutation: 12 gypsy families with no relation to each other.[3] In this group, the affected individuals were homozygous, while the parents and descendents were healthy heterozygous carriers. This points to the possible reinforcing effect of the second mutation (Leu850Pro) upon the first, since ours are the first patients described with clinical involvement in which the variant int. 9 + 1G > T is present in heterozygosis. All patients with clinical manifestations in which a single mutation is detected should be regarded as compound heterozygotes in which the second mutation has not been detected, due to incomplete sequencing of the gene. The presence of compound heterozygosis suggests that the transporter alteration requires at least two variations in order to

Table I. Representative blood and urine test parameters of the original patient, upon tertiary hospital admission. The normal values, corresponding to body weight, appear in parentheses. The transtubular potassium gradient was 36

Plasma Mg	1.11 mg/dl	(1.4-2.7)
Plasma K	2.3 mEq/l	(3.5-5.1)
Urine K	81 mEq/l	
Urine Ca	116 mg/24 h	(350-360 mg/24 h)
Plasma renin activity	29.7	(0.2-2.3)
Plasma aldosterone	1,256.64 pg/ml	(40-300)