Rev. Colomb. Nefrol. 2016; 3(1): 49 -54. http//www.revistanefrologia.org

Case report

http//doi.org/10.22265/acnef.3.1.240

Cathartic agent nephropathy based on sodium phosphate in kidney patients transplanted. Report of case

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Abstract

Sodium phosphate nephropathy consists of damage to the kidneys caused by the use of laxatives containing sodium phosphate. Depending on the time of use of these drugs used for colonic preparation this disease can be acute or chronic. The acute condition can be cured with a suitable treatment, but the chronic condition can cause irreversible kidney damage.

This case is about a patient who receives our services in the unit in Fundación Cardio Infantil in Bogotá, Colombia, with an acute kidney injurywith renal transplant being monitored. Sodium phosphate was used to be prepared the kidney for a colonoscopy.

Key words: Chronic kidney disease, nephropathy by sodium phosphate, Diagnosis.(MeSHsource).

Nefropatía por agente catártico basado en fosfato de sodio en paciente renal trasplantado. Reporte de un caso

Resumen

La nefropatía por fosfato de sodio es una forma de lesión renal que ocurre posterior al uso de laxantes que contienen fosfato de sodio. Puede presentarse de manera aguda o crónica según el tiempo de utilización de dichos medicamentos utilizados para la preparación colónica. La forma aguda puede resolverse con un adecuado tratamiento, pero la forma crónica puede causar daño renal irreversible.

Este caso se trata de una paciente con trasplante renal, en seguimiento en la Fundación Cardioinfantil en Bogotá, Colombia, en quien se utilizó fosfato de sodio para una preparación de colonoscopia y se presentó a nuestro servicio con una lesión renal aguda.

Palabras clave: Enfermedad renal crónica, nefropatía por fosfato de sodio, diagnóstico (fuente DeCS).

Received: 24 February 2016 Accepted: 1 May 2016

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General description

40 years female patient, who was attended for a kidney transplant consult and monitoring, with acute flushedrise. To study her acute kidney injury during renal transplant, she was hospitalized.

During hospitalization, she reported diarrhea(more than 3 times per day) for nearly 5 months of progression without emesis or abdominal pain. Through a colonoscopy this symptomatic state was studied for two weeks. The bowel preparation was performed with phosphate enema. The rest of the review by the system was negative.

Based on pathological antecedents, the patient had arterial hypertension, because of urinary tract infection to repetition, deep vein thrombosis 10 years prior, pulmonary thrombo embolism, 10 years prior, and systemic lupus erythematous that produced chronic kidney disease that required renal replacement therapy, initially treatment with hemo-dialysis and 5 years before, and renal transplantation. The immune suppression consisted of tacrolimus XL 4 mg/day, mycophenolatemofetil of 720 mg/d, omeprazole 20 mg/day, Deflazacort 6 mg/day, Enalapril 20 mg/day.

There were no alterations in their physical examination, patientvital signs eranTA: 139/76,FC: 72/m, Fr: 16/m. The paraclinical are summarized in Table 1:

Outpatient Colonoscopy: study within normal limits.

Urine - analysis: density: 1010,Ph: 5.5, proteins: negative; sediment=leukocytes: 3.96, erythrocytes:1.78, bacteria:+.

Anti DNA: negative Snap-in: Normal.

Table 1

Azoados variation

	Serum creatinine (mg/dL)	Blood urea nitrogen (mg/dL)
Basal Values	1,2	22
At the time of the present disease	1,8	43

Levels of tacrolimus: 5.39.

Echo Doppler of transplanted kidney: normal.

Stool=Ph: 8, hidden blood: negative, not observed parasites. ZN modified stool: negative for Cryptosporidium, cyclospora and microsporidium.

HIV: negative.

It was decided to perform renal biopsy, which showed existence of tubular acute damage with changes of regeneration, presence of calcium phosphate crystals and distribution in bands. Tubular damaged is caused by the presence of interstitial nephritis moderate with tubular mild. Without evidence of polyoma virus nephropathy or nephropathy immune complexes.

In this particular case,consisten tchanges in acute cellular rejection are identified by the presence of insufficient quantities of tubular-intestinal inflammatory infiltrates, associated with the presence of tubular-highlights and the presence of two types of crystals:1)Calcium, whose presence indicates two types of tubular damages. The first of them, calcium oxalates, characterized by the presence of yellowish crystals, Hematoxylin coloration appearance and Eosin, which protrude when exposed to the polarized light; and 2) crystals derived from renal tubular damage. Its presence was indicated but resolved because of the status of tubular scarring due to catharsis by enema of sodium phosphate.

The presence of nephropathy by crystals of phosphate was handled by administering postprandial aluminum, calcium carbonate postprandial and a short course of steroids was conducted. With this treatment, the patient showed the improvement of kidney function to base values.

Comments

For colon cleaning and preparation several agents were used. One of the most frequently used is a sodium phosphate based enema which was introduced therapeutically for first time by Vannery collaborators in 1990[1].

Sodium phosphate enemas function as osmotic laxative preparations, i.e. by its high osmolarity to “for-

Figura 1

A. Imagen correspondiente a panorámica de la biopsia renal. Nótese la presencia de corteza renal con algunos grupos inflamatorios (Hematoxilina y Eosina a 4X)
B. Imagen correspondiente a panorámica de la biopsia renal, otras áreas con características similares a las vistas en A. (Hematoxilina y Eosina a 4X)

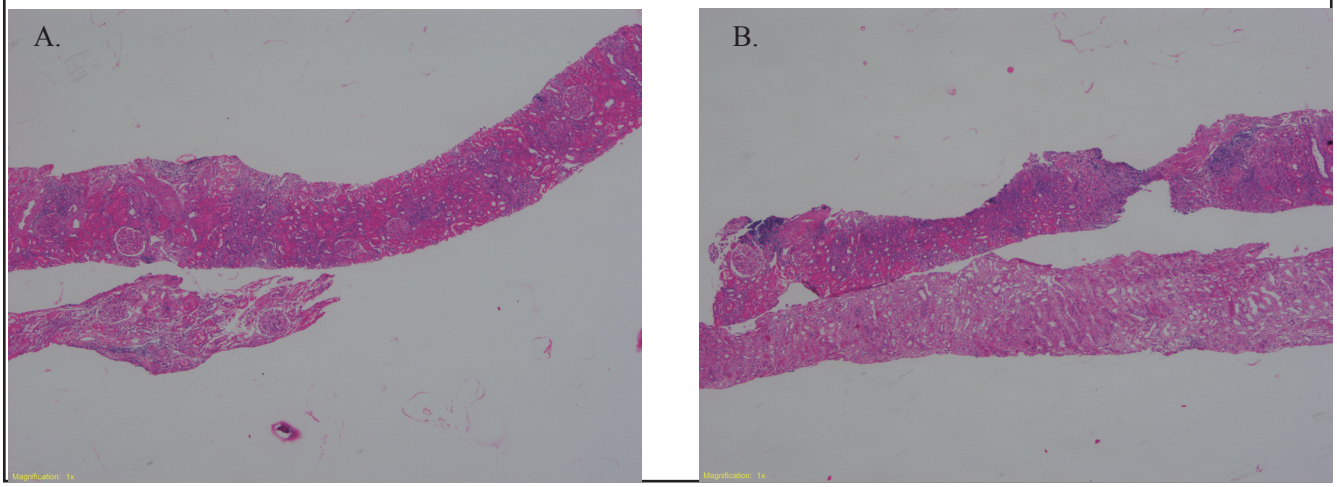


Figura 2

Imágenes de una porción de la biopsia sin (C, E) y con exposición a luz polarizada (D, F). Nótese la presencia de los cristales birrefringentes indicativos de la presencia de cristales de oxalatos (Hematoxilina y Eosina 10X)

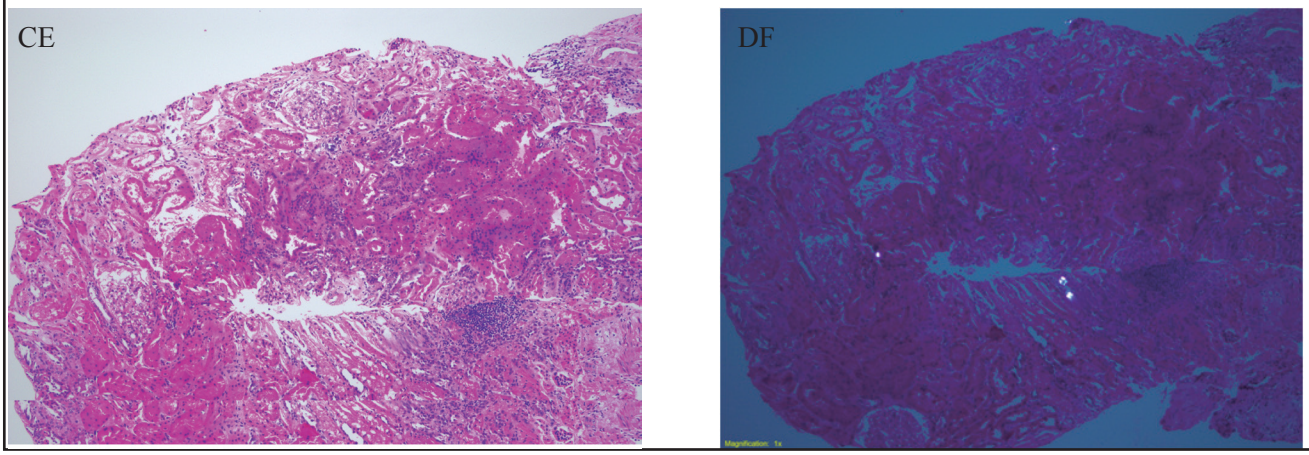
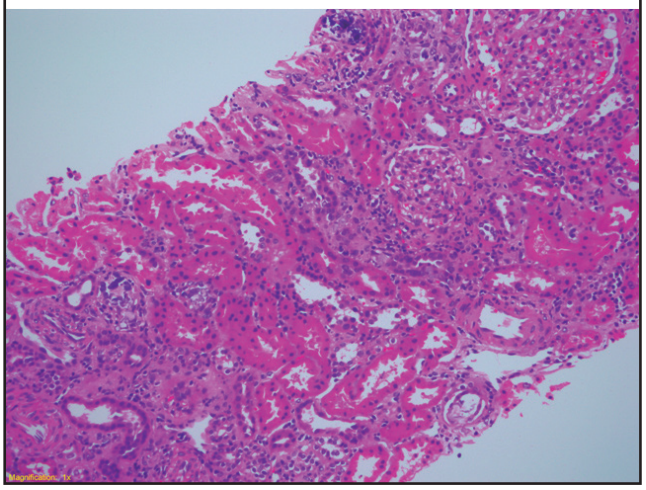


Figura 3

Presencia de cristales de fosfatos de calcio en las luces tubulares, evidentes como concreciones basófilas (flechas) irregulares, las cuales no polarizan al exponerlas a la luz polarizada. También se aprecian bandas de fibrosis intersticial asociadas a atrofia tubular.



ce" water excretion in the intestinal lumen, giving as a result an increase of the peristalsis and bowel movement[2]. The usual dose of sodium phosphate is two doses between 8 and 12 hourintervals[3]. Forty-five milliliters of sodium phosphate contain[5] grams of sodium and 17 grams of phosphate (equivalent to 11.5 g of elemental phosphorus). That dosage can cause a loss of up to 1.6 lde intestinal fluid. This loss of volume, together with the oral ingestion, dictated by pre-colonoscopy protocols, can produce alterations of the electrolytes and increases the risk of kidney damage in patients receiving these agents (4).

For first time in 2003, an unusual form of nephro calcinosis cortical due to "acute nephropathy by phosphate" was described. Since then, several reports have been associated with renal insult, both acute and chronic[2,3].Since its discovery, 37 cases (between 2003 and 2010) approximately, have been documented. A majority of the cases were derived from centers of study in the USA, others from Norway, Netherlands, Belgium, United Kingdom, Lebanon, Korea, New Zealand and five fromIsrael. This reference reflects that sodium phosphate[5] is on the widespread.

Dr. Ehrenpreis and collaborators' retrospective study, was based on the data of adverse events from the Food and Drug Administration(FDA),from2004 to 2009. The data showed that in women with an average weight lower than normal (68.57 ± 1.78 kg) [6], the tablet of sodium phosphate consumption is associated with renal lesions.

In Brazil, one in every thousand doses sold of sodium phosphate develops acute nephropathy by phosphate. The relationship between the sodium ingestion and the calcium and phosphate reservoir are related with renal lesion with an interstitial and concomitant renal function loss.

Additionally, the sodium phosphate enema preparation causes increases in serum phosphorus, even among patients with normal renal function. Phosphorus levels with normal renal function ranged between 3.7 to 7.3 mg/dL, after administering sodium phosphate[7]. Another study found levels of phosphorus above 8 mg/dl in 28% of patients treated with sodium phosphate[8].

On the other hand, some studies report a significant trend toward better results in renal outcomes after the use of sodium phosphate, compared with other laxatives[9-11]. A study in an Asian population did not demonstrate alterations in renal function during 12 to 24 months of monitoring, after using sodium phosphate for colonic preparation[5].

The acute phosphate nephropathy (APN,by its acronym in English) occurs after the use of these colon agents preparation, and it has two forms of presentation: acute kidney injury (AKI) and the chronic renal disease (CRD)[3].

AR presentation might occur in hours or days; it is accompanied by Hypocalcemia and normally it is of short duration. It can be treated with chelating agents of phosphorus conservative therapy that often lead to a total renal recovery 12. The acute Hypocalcemia is almost characteristic of this entity and is secondary to calcium and phosphorus precipitation, which could be further exacerbated if the patient presents an acute respiratory alkalosis, which could lead to the tetany manifestation [1].

The chronic form of APN may occur weeks after the initial exposure, which hinders its identification,

being almost always diagnosis based on a judicious and interrogation in renal biopsy, since its symptoms are unspecific and easily explainable by the deterioration of renal function. Renal biopsy in patients with CKD due to APN, usually show nephrocalcinosis. Nephrocalcinosis is a tubular-interstitial disease, with prominent tubular calcification with tubular atrophy and interstitial fibrosis. There is tubular injury, secondary to the deposit of crystals of calcium and phosphorus and the increase of the phosphate concentration intertubular and hyperphosphatemia. Most of the calcium phosphate precipitations are found in distal and main fold tubules.

An increase in the re-absorption of sodium and water in the proximal tubule (which is impervious to the phosphorus) and the re-absorption of water without phosphorus re-absorption in the loop of Henle is led by the volume depletion that accompanies the use of these osmotic laxatives agents, exacerbating this process, which results in a higher relative concentration of calcium and phosphorus in the distal tubule[13]. The deposit of calcium phosphate crystals in the distal renal tubule can only be confirmed by a biopsy, because the inter-renal tank, in hyperphosphatemia acute, is not usually detectable in the radiological images[2,4,14,15].

The presentation of APN is potential, at the time a patient with renal dysfunction is exposed to high doses of phosphate.

In addition to the potential risk of APN, the preparations of sodium phosphate enema include transient hypocalcemia and hypopotassemia in more than 50% ofthe elderly,[16] even with normal renal function. The hyperkalemia and hypokalemia that occur after its use, it might affect the cardiac rhythm, prolonging the QT interval and producing ventricular arrhythmias, as well as macroscopic and histological changes in the mucosa, so use must be avoided in those with inflammatory bowel disease[17].

The risk factors for nephropathy by sodium phosphate are: ERC, females greater than 55 years, and medications to decrease the intravascular volume and renal perfusion (e.g. antagonistic diuretics, angiotensin receptor -converting enzyme inhibitors, non-steroidal anti-inflammatory drugs, etc.), the frequency of the medication dose (every 6 hours vs. every 12 hours increases the levels of phosphorus) and its use should be avoided in intestinal obstruction and active colitis[18].

The way to prevent the disease[19]:

1. Avoid use in high-risk patients.
2. Use the minimum effective dose, the total amount of phosphate which is excreted in the urine after the second dose is from three to four times greater than that eliminated after the first dose; this suggests that the second dose is particularly dangerous, so that a reduction or replacement with another agent (p.e.polyethylene glycol) is indicated.
3. Increasing the interval between doses; an interval of 24 h reduces the incidence of hyperphosphatemia, which is considered clinically important, without loss of effectiveness in comparison with a range of 9-12 h.
4. Avoid dehydration; abundant liquid should be administered orally or intravenously.
5. Perform biochemical tests before the colonoscopy and measure the renal function and electrolytes; mainly in patients with high risk or unstable.

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