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Letters to the Editor

Valvular calcifications in CKD: Mineral and bone disease or previous cardiovascular risk?☆

¿Calcificaciones valvulares en ERC: enfermedad mineral ósea o riesgo cardiovascular previo?

To the Editor,

We read with great interest the article by Carmen Sánchez-Perales et al., recently published in Nefrología.[1] In this study, the authors analysed the presence of valvular calcification in patients starting dialysis and its relationship to cardiovascular events and cardiovascular death. We would like to offer some comments on the study.

Valvular calcification may occur in the presence or absence of renal disease. In individuals without renal disease, calcification is usually a result of a pro-inflammatory state caused by other comorbidities such as diabetes, dyslipidaemia, and hypertension. In individuals with chronic kidney disease (CKD), often it cannot be established with certainty whether calcification is due to changes in bone mineral metabolism, inflammation caused by comorbidities, or both.[2]

In the "methods" section of the study, the authors stated that they measured serum levels of phosphorus, calcium, and parathyroid hormone (PTH). However, calcium and PTH were not included in the univariate analysis. We think that the statistical analysis of these two variables would be relevant, because the studies performed by Streja et al.[3] and Floege et al.,[4] found that patients with serum values of intact PTH, calcium, and phosphate outside the ranges recommended by the Kidney Disease Outcomes Quality Initiative (KDOQI™)[5] (iPTH, 150–300 pg/mL; calcium, 2.10–2.37 mmol/L; and phosphate, 1.13–1.78 mmol/L) had a higher mortality risk than patients with values within these ranges.

In the multivariate analysis by Sánchez-Perales et al., the authors state that the model was adjusted for factors with statistical significance in the univariate analysis and for other factors that were potentially involved in the valvular calcification process. However, it was not clear why variables associated with valvular calcification in patients with CKD (PTH, calcium, and phosphate) were not included.

Finally, whilst the study demonstrates that the presence of valvular calcification is a predictor of mortality, the analysis performed does not establish whether calcification is secondary to atherogenic comorbidities or to an imbalance of bone mineral metabolism. Future studies could further explore this association.

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Lots of steroids and vitamins, tons of complications. Hypercalcemia and nephrocalcinosis as important complications of performance-enhancing drugs

Montones de esteroides y vitaminas, toneladas de complicaciones. Hipercalcemia y nefrocalcinosis como complicaciones importantes de los fármacos para mejorar el rendimiento

Dear Editor,

Chronic hypercalcemia can be an important complication of anabolic steroid and vitamin supplement abuse. We report the case of a 30-year-old bodybuilder that for more than 4 years used injectable anabolic-androgenic steroids (AAS) and one veterinary polyvitamin formulation with vitamin A (2,100,000 IU), D (ergocalciferol: 60,000 IU), and E (55 IU) on a monthly basis. He also reported self-injecting mineral oil intramuscularly for esthetic purposes for more than 2 years. He presented to the emergency room with an acute, severe epigastric pain, associated with nausea and vomiting. Laboratory evaluation (Table 1) demonstrated an elevated amylase 2500 IU/L (50–160 IU/L); lipase of 612 IU/L (0–75 IU/L); a corrected serum calcium of 12.5 mg/dL (8.5–10.5 mg/dL); PTH of 73.2 pg/mL (15–68.3 pg/mL) and 25(OH)D of 65.1 ng/mL (30–100 ng/mL). Serum creatinine was 1.2 mg/dL (0.6–1.2 mg/dL). Abdominal ultrasound showed a diffusely edematous pancreas, bilateral ureterolithiasis and nephrocalcinosis. A high-resolution CT of the chest and abdomen was performed and revealed absence of granulomas and lymphadenopathies. He had a tormented clinical course, with acute kidney injury (attributed to volume depletion and renal vasoconstriction in the setting of hypercalcemia) without the need of hemodialysis; protracted vomiting that lead to a laparoscopic duodenum–jejunum anastomosis with improvement of complains and multiple infectious complications. Serum calcium and PTH returned to normal levels (9 mg/dL and 35 pg/mL, respectively) after vitamin D discontinuation, vigorous venous hydration with 0.9% saline infusion and therapy with furosemide and corticosteroids. After more than 60 days of hospitalization he was discharged home having made a full recovery.

With the desire to improve performance, some athletes or amateurs use performance-enhancing drugs. The widespread use of these substances without medical prescription or clinical follow-up can lead to serious health problems as described on several reports.[1–3] We believe that the main clinical features seen in this patient are due to chronic hypercalcemia due to multiple substance abuse and paraffinomas. The association between focal segmental glomerulosclerosis and anabolic steroids abuse may be explained by increase in lean body mass and potential direct nephrotoxic effects of anabolic steroids.[1] Furthermore, this drug modulates steroid hydroxylase activity predisposing to hypercalcemia.[4] The association of vitamin A toxicity and hypercalcemia is rare but well recognized. It is attributed to a direct effect on bone (activation of bone reabsorption with increased osteoclast activity),[5] on the parathyroid, or in both.[6] According to Chertow et al., vitamin A stimulate PTH secretion in bovine parathyroid tissue and in men.[6,7] The minimum dose of vitamin A required to produce hypercalcemia cannot be stated with certainty; toxicity has been described from doses ranging from 50,000 to 500,000 IU/day.[5] Although we did not measure the value of vitamin A in blood, the patient injected more than 2,100,000 IU/month (which correspond 70.000 IU of vitamin A/day) for more than 4 years, which is compatible with toxicity. Hypercalcemia is a well-known but uncommon complication of vitamin D intake.[8] Usually results from doses that exceed 10,000 IU/day, and is generally associated with serum levels of 25-hydroxyvitamin D that are well above 150 ng/mL.[8] In this case, 60,000 IU of ergocalciferol were inject monthly and serum vitamin D was in the upper limit of normal. The tolerable upper level of daily vitamin D intake recently set by the Institute of Medicine is 4000 IU.[8] Vitamin A and D can act synergistically to cause hypercalcemia. Contrary