Hypocalcaemia, hyperphosphataemia and elevated parathyroid hormone, a difficult differential diagnosis?

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To the Editor:

Pseudohypoparathyroidism[1] (PHP) is a heterogeneous condition characterised by hypocalcaemia and secondary hyperparathyroidism, whose aetiology lies in the resistance to the biological action of circulating parathyroid hormone (PTH). It is generally diagnosed during childhood. When the diagnosis is made in adulthood, it may be difficult to distinguish it from secondary hyperparathyroidism,[2] especially in patients with renal failure.

CASE STUDY

We report the case of an 18-year-old male with a history of functionally bicuspid aortic valve, who came to the Emergency Department due to colicky hypogastric pain lasting 72 hours, which did not subside when treated with non-steroidal anti-inflammatory drugs (NSAIDs) every 8 hours. The patient had previously experienced similar episodes. On admission, he had blood pressure of 120/80mmHg and I/IV early diastolic murmur, with the rest of the examination being normal. The laboratory test displayed urea 71mg/dl, creatinine 3.69mg/dl, Mg 2.1mg/dl, Ca 5.2mg/dl, P 7.6mg/dl, total protein 6.27g/dl, albumin 3.6g/dl, intact PTH 216pg/ml, 25-hydroxyvitamin D 7.3ng/ml, normal thyroid hormones, venous blood gases: pH 7.37, pO_2 50mmHg, pCO_2 37mmHg, bicarbonate 21mmol/l, renal function in urine: EF Na 0.71%, glucose 9mg/dl, urea 946mg/dl, Cr 86.37mg/dl, Na 27mmol/l, K 21.2mmol/l, Ca 7.8mg/day and P 850.2mg/day; systematic and normal urinary sediment, with negative haematuria and proteinuria; blood count: haemoglobin 15.1g/dl, leukocytes 11,000/ul, platelets 167,000/ul. Laboratory tests were reviewed and they revealed previous hypocalcaemia and hyperphosphataemia, with normal renal function, which had not been detected for at least three years (Figure 1). The biochemical study of his parents' calcaemia, phosphataemia and PTH were normal. The patient's clinical progression was good after we withdrew the NSAIDs, to which the aetiology of acute renal failure was attributed, oral and intravenous hydration, oral calcium and vitamin D, with kidney function being normal on discharge. Abdominal symptoms subsided after hypocalcaemia was corrected, without recurrences of similar episodes.

DISCUSSION

The term PHP encompasses a heterogeneous group of uncommon metabolic disorders whose common denominator is variable resistance to PTH action.[1-3] Two types of PHP can be distinguished in accordance with the response of urinary cAMP after the intravenous injection of PTH: type I PHP, in which cAMP does not increase following the administration of PTH, and type II PHP, in which cAMP increases.[4] Type I PHP is divided into three subtypes: Ia, Ib and Ic. Patients with subtypes Ia and Ic have an autosomal dominant inheritance pattern and generally present the Albright osteodystrophy phenotype[4] (short height, obesity, learning difficulties, subcutaneous calcifications and typical skeletal defects) and multi-hormone resistance. Subtype Ib is characterised by isolated resistance to PTH, it may have a normal phenotype or the Albright osteodystrophy phenotype and the defect is usually sporadic, but it is occasionally has autosomal dominant inheritance. In type II PHP, no molecular defect has been identified, but it lacks the Albright phenotype and multi-hormone resistance and it is not usually familial.[5]

We performed a differential diagnosis between chronic kidney disease, vitamin D deficiency and PHP. The reversibility of renal failure and persistent hypocalcaemia, hyperphosphataemia and elevated PTH ruled out chronic kidney disease as aetiology, and the absence of hypophosphataemia ruled out vitamin D deficiency. We concluded that this patient had type Ib or II PHP, given the absence of the AHO phenotype and multi-hormone resistance. However, we cannot determine clearly whether our patient corresponded to type Ib or type II PHP.

In summary, we reported the case of a patient with renal failure, hypocalcaemia, hyperphosphataemia and elevated PTH of long progression. The nephrologists' knowledge of the calcium-phosphorus metabolism pathophysiology allowed us to make an early diagnosis and carry out

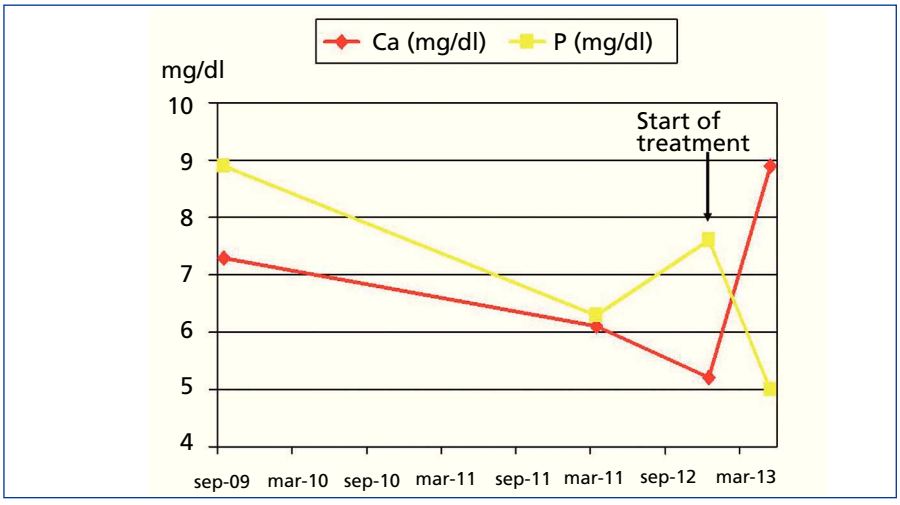

Figure 1. Progression of calcium and phosphorus (mg/dl) prior to diagnosis and from the start of treatment.

early treatment of an uncommon condition for nephrologists and, as its late diagnosis reveals, one that is also uncommon for the other medical specialties. It is necessary to emphasise the importance of early PHP treatment in order to normalise serum calcium and prevent the bone loss that can occur in the long term if a chronically high level of PTH is maintained. The objective of treatment was to normalise serum calcium levels and curb PTH hypersecretion, and as such, vitamin D derivatives and calcium supplements were used.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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Spontaneous fistulae in the arms: a case study

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To the Editor:

Arteriovenous fistulae (AVF) can be defined as "abnormal" connections between the venous and arterial systems that bypass the normal anatomic capillary bed. An AVF may be located in any area of the body and be congenital or acquired after some event (e.g. trauma). Lower limb fistulae are far more common acquired AVF, since the groin is a very common location for both arterial and venous vascular access.[1-3]

Predisposing factors include high blood pressure, overweight, anticoagulation or antifibrinolytic therapy, old age, the left side and female sex, as well as a history of punctures in the limbs.[1,2] Labropoulos et al. reported the occurrence of AVF after episodes of deep vein thrombosis (DVT), particularly in large deep and proximal veins such as the femoral and popliteal veins. After the occlusion of an artery or vein, changes take place with the purpose of redirecting blood flow. In the case of arteries, the new circulation should have the purpose of providing oxygen and nutrition to organs and tissues; this arterial development is known as "collateralisation". For veins, the adjustment is aimed at draining blood, and the term used to describe the new vein formation process is "neovascularisation". While ischaemia is the stimulus for collateral formation, the mechanism responsible for venous neoformation is unclear. In any case, the fact that AVF particularly appear in proximal veins prompts us to ask whether low-resistance flow loss might be the stimulus for neovascularisation more than the thrombosis itself.[4-6]

Clinical assessment: in most cases of acquired AVF, there are no symptoms and if there are, they may appear within days or months and include thrill in the inguinal area, dyspnoea or new or worsening ischaemia in the limbs. Physical examination of the limb may reveal murmur, thrill, haematoma or pulsatile mass. Oedema, DVT, nerve compression or worsening of previous varicosities may also occur.

Diagnosis: Doppler is the preferred method of diagnosis, with angiography being used as a therapeutic tool for endovascular treatment.

Treatment: in small asymptomatic AVF, there is usually spontaneous thrombosis, and they do not require treatment, but treatment is indicated in cases in which symptoms appear. Currently, the techniques of choice are ultrasound-guided compression[7,8] and percutaneous techniques, with surgery being reserved for selected cases, such as steal syndrome with claudication or significant distal ischaemia of the limb, oedema or venous insufficiency due to venous hypertension, heart failure due to AVF volume, AVF caused by stab wounds or fire and iatrogenic AVF that do not close spontaneously.

We report the case of a 58-year-old male with chronic kidney disease of unknown aetiology, on renal replacement therapy since December 2010. He was initially treated with peritoneal dialysis (PD) but was transferred to haemodialysis (HD) in December 2011. This patient had a spontaneous AVF in his left arm, which was eventually used as vascular access, with satisfactory results. The patient came to our clinic in 2007-2008, presenting with advanced renal failure (creatinine 3.5, estimated glomerular filtration rate 20ml/min; immunological study, tumour markers and serologies without findings and chronic ultrasound data). His medical history showed that he had high blood pressure, was a smoker and had an iliac blade fracture in 1998, after a fall, which required surgery. The physical examination was normal, except for the presence of an exophytic lesion on his upper lip, and he was diagnosed with moderately differentiated squamous-cell carcinoma of the supraglottic larynx and was treated with surgery and coadjuvant