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Celiac disease as differential diagnosis of normocalcemic hyperparathyroidism

Doença celíaca como diagnóstico diferencial do hiperparatireoidismo normocalcêmico

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ABSTRACT

There is no recommendation to investigate celiac disease (CD) in patients with elevated parathyroid hormone (PTH) and normal blood calcium if they are asymptomatic, especially if they do not have hypovitaminosis D. CD was diagnosed in a 30-year-old asymptomatic man without vitamin D deficiency, who had total calcium 9.2 mg/dl, 25-hydroxyvitamin D 36 ng/dl, PTH 112 pg/ml, total IgA 42 mg/dl, anti-tissue transglutaminase (tTG) IgA 22 U/ml. Duodenal biopsy by endoscopy confirmed CD. The patient started a gluten-free diet that was maintained. After six months, the patient had total calcium 9.5 mg/dl, 25-hydroxyvitamin D 42 ng/dl, and PTH 48 pg/ml. In most patients with elevated PTH and normal blood calcium, clinical history, assessment of renal function, vitamin D and phosphorus measurement, and calciuria define the cause of secondary hyperparathyroidism. However, in the few cases in which this initial investigation is negative, even asymptomatic individuals should be tested for CD antibodies before the diagnosis of normocalcemic primary hyperparathyroidism is made.

Key words: primary hyperparathyroidism; secondary hyperparathyroidism; celiac disease.

RESUMO

Não há recomendação para investigar doença celíaca (DC) em pacientes com paratormônio (PTH) elevado e cálcio sérico normal se eles são assintomáticos, principalmente se não têm hipovitaminose D. Relatamos um caso de DC diagnosticada em um homem de 30 anos, assintomático, sem deficiência de vitamina D. Os exames apresentaram cálcio total 9,2 mg/dl, 25-hidroxivitamina D 36 ng/dl, PTH 112 pg/ml, imunoglobulina da classe A (IgA) total 42 mg/dl e antienzima transglutaminase tecidual (tTG) IgA 22 U/ml. Biópsia duodenal por endoscopia confirmou o diagnóstico de DC. O paciente iniciou dieta sem glúten. Após seis meses, apresentou cálcio total 9,5 mg/dl, 25-hidroxivitamina D 42 ng/dl e PTH 48 pg/ml. Na maioria dos pacientes com PTH elevado e cálcio sérico normal, a história clínica, a avaliação da função renal e as dosagens de vitamina D, fósforo e calciúria definem a causa do hiperparatireoidismo secundário. Porém, nos poucos casos em que essa investigação inicial é negativa, até os indivíduos assintomáticos deveriam ser testados para anticorpos para DC antes de o diagnóstico de hiperparatireoidismo primário normocalcêmico ser firmado.

Unitermos: *hiperparatireoidismo primário; hiperparatireoidismo secundário; doença celíaca.*

RESUMEN

No hay recomendaciones para investigar enfermedad celíaca (EC) en pacientes con niveles elevados de hormona paratiroidea y calcio sérico normal si ellos son asintomáticos, principalmente si no tienen hipovitaminosis D. Reportamos un caso de EC diagnosticada en un hombre de 30 años, asintomático, sin deficiencia de vitamina D. Sus niveles séricos: calcio total 9,2 mg/dl, 25-hidroxivitamina D 36 ng/dl, hormona paratiroidea 112 pg/ml, inmunoglobulina A (IgA) total 42 mg/dl y anticuerpos anti-transglutaminasa tisular (tTG) IgA 22 U/ml. Biopsia duodenal por endoscopia confermó el diagnóstico de EC. El paciente

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empezó una dieta libre de gluten. Después de seis meses, el paciente presentó calcio total 9,5 ml/dl, 25-hidroxivitamina D 42 ng/dl y hormona paratiroidea 48 pg/ml. En la mayor parte de los pacientes con hormona paratiroidea elevada y calcio sérico normal, el historial clínico, la evaluación de la función renal y las mediciones de vitamina D, fósforo y calciuria definen la causa del hiperparatiroidismo secundario. No obstante, en los pocos casos en los cuales esa investigación inicial es negativa, incluso los individuos asintomáticos deben ser examinados para anticuerpos para EC antes que el diagnóstico de hiperparatiroidismo primario normocalcémico sea establecido.

Palabras clave: *hiperparatiroidismo primário; hiperparatiroidismo secundario; enfermedad celíaca.*

INTRODUCTION

It is known that many patients with primary hyperparathyroidism (PHP) do not exhibit hypercalcemia. However, PHP with normal serum calcium is also associated with complications[1], and patients with this condition would benefit from surgical treatment[1]. A current challenge is the correct diagnosis of normocalcemic PHP[1, 2]. This diagnosis is done based on the combination of elevated parathyroid hormone (PTH) and normal serum calcium, both total calcium corrected for albumin and ionic calcium, in more than one measurement, and after the exclusion of causes of secondary hyperparathyroidism (SHP)[1-6]. There is consensus regarding the need to exclude the following causes of SHP: vitamin D deficiency, renal dysfunction, medications, hypercalciuria, and intestinal malabsorption[1, 3-6]. None of the current consensus statements makes it clear how this last cause should be ruled out, whether only clinically or also by complementary investigation of asymptomatic patients, and even in the absence of associated vitamin D deficiency[1, 3-6].

Although SHP is a known complication of celiac disease (CD), there is no formal recommendation to investigate CD in patients with elevated PTH and normal blood calcium if they are asymptomatic, especially if they do not have hypovitaminosis D[1,6]. Even in patients with vitamin D deficiency, investigation for CD is only recommended if vitamin levels do not increase during replacement therapy[7].

CASE REPORT

A prospective study[2], in which calcium and PTH were measured in 676 adults (age ≥ 18 year) without a history of fracture, nephrolithiasis or symptoms of hypercalcemia, identified 222 individuals with elevated PTH and normal total and ionic calcium concentrations (confirmed in two measurements). Known causes of PTH elevation were identified in 216 patients, including: a) medications (diuretics, lithium, bisphosphonate, denosumab, recombinant PTH, corticosteroid); b) suspected or known malabsorption syndrome; c) 25-hydroxyvitamin D < 30 ng/dl; d) estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2; e) hypercalciuria; f) hyperphosphatemia. Six patients without an apparent cause for PTH elevation, none of them with gastrointestinal or suspicious symptoms of CD, had their anti-tissue transglutaminase (tTG) IgA and total IgA antibodies measured.

CD was diagnosed in a 30-year-old asymptomatic man without vitamin D deficiency, who had total calcium 9.2 mg/dl (ref.: 8.4-10.4), ionic calcium 4.8 mg/dl (ref.: 4.4-5.4), 25-hydroxyvitamin D 36 ng/dl, PTH 112 pg/ml (ref.: 12-65), total immunoglobulin class A (IgA) 42 mg/dl (ref: 70-400), and tTG IgA 22 U/ml (reagent > 10); human leukocyte antigen testing was positive for DQ2 alleles associated with CD, and a duodenal biopsy by endoscopy showed moderate villous atrophy and lymphocytosis, confirming CD diagnosis. The patient started a gluten-free diet that was strictly maintained. After six months, the patient had total calcium 9.5 mg/dl, ionic calcium 5.2 mg/dl, 25-hydroxyvitamin D 42 ng/dl, and PTH 48 pg/ml.

DISCUSSION

In most patients with elevated PTH and normal blood calcium, clinical history, assessment of renal function, vitamin D and phosphorus measurement, and calciuria define the cause of SHP. However, in the few cases in which this initial investigation is negative, even asymptomatic individuals should be tested for CD antibodies before the diagnosis of normocalcemic PHP is made.

DECLARATION OF INTEREST

The authors declare no conflict of interest.

COMPLIANCE WITH ETHICAL STANDARDS

The study was approved by the Research Ethics Committee of our institution.

REFERENCES

1. Cusano NE, Cipriani C, Bilezikian JP. Management of normocalcemic primary hyperparathyroidism. Best Pract Res Clin Endocrinol Metab. 2018; 32: 837-45.

2. Rosário PW, Calsolari MR. Normocalcemic primary hyperparathyroidism in adults without a history of nephrolithiasis or fractures: a prospective study. Horm Metab Res. 2019; 51: 243-7.

3. Eastell R, Brandi ML, Costa AG, et al. Diagnosis of asymptomatic primary hyperparathyroidism: proceedings of the Fourth International Workshop. J Clin Endocrinol Metab. 2014; 99: 3570-9.

4. Wilhelm SM, Wang TS, Ruan DT, et al. The American Association of Endocrine Surgeons guidelines for definitive management of primary hyperparathyroidism. JAMA Surg. 2016; 151: 959-68.

5. Khan AA, Hanley DA, Rizzoli R, et al. Primary hyperparathyroidism: review and recommendations on evaluation, diagnosis, and management. A Canadian and international consensus. Osteoporos Int. 2017; 28: 1-19.

6. Fileihan GEH, Silverberg SJ. Primary hyperparathyroidism: diagnosis, differential diagnosis, and evaluation. UpToDate [Internet]. Available at: www.uptodate.com/contents/primary-hyperparathyroidism-diagnosis-differential-diagnosis-and-evaluation.

7. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al.; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011; 96: 1911-30.

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