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## Dementia due to primary hyperparathyroidism: A lesson learned from delayed diagnosis



### Demencia debida a hiperparatiroidismo primario: lección que se desprende del diagnóstico tardío

Hypercalcemia is a rather common finding (up to 39 cases per 1000 inhabitants<sup>1</sup>), and when detected, a differential diagnosis must be made between hyperparathyroidism and malignancy, which together are responsible for over 90% of all cases. Clinically, hypercalcemia can be the cause of diverse neurobehavioral symptoms, ranging from lethargy, depressed mood, psychosis and cognitive dysfunction.<sup>2</sup> The exact prevalence is not well defined due to the lack of rigorous assessment, the small size of the studies, and the wide variations in the instruments used to assess such disturbances. Depending on both the calcium concentration as well as the speed with which it was acquired, this disease can be life threatening, but yet, treatable during early stages, and thus, a high index of suspicion is required.

We herein report a case of a 78-year-old Caucasian woman who presented in the emergency department with progressive decline of consciousness in the last couple of weeks. Relevant personal history included arterial hypertension, diabetes mellitus type 2, hypothyroidism, osteoporosis, Alzheimer's disease was diagnosed 3 years ago and she was partially dependent in activities of daily living (Global Deterioration Scale – GDS of 6). Our patient also presented with changes in bowel habit since the last 2 years, having undergone a recent endoscopic and CT scan study, revealing only normal findings. Her usual treatments included enalapril–hydrochlorothiazide 20 mg/25 mg od; levothyroxine 25 mcg od, metformine/linagliptine 850 mg/2.5 mg bid and galantamine 8 mg od.

The family revealed that after one month, and after having passed a respiratory tract infection, treated with quinolones during 2 weeks, our patient experienced a progressive deterioration of her general health status, associated with confusion, nausea, vomiting and worsening of her physical dependence.

The physical examination revealed no abnormalities, except for a deterioration of consciousness and a slight dehydration of skin and mucosae. Laboratory workup only showed glucose level of 130 mg/dL [range: 70–100], and corrected calcium level (with protein) of 14.2 mg/dL [range: 8.5–10.6]. The ECG showed a sinus rhythm, without any other conductive abnormalities. The patient was admitted and treatment with intravenous fluids and loop diuretics was initiated. Her usual antihypertensive treatment with hydrochlorothiazide was discontinued.

Forty-eight hours after, she exhibited an acutely cognitive improvement (GDS of 4), together with a normalization of the serum calcium level (10.9 mg/dL). The rest of the analysis revealed phosphorus level of 1.3 mg/dL [range: 2.4–4.1], 25-OH-D level of 4.5 ng/mL [range: 30–74], parathormone of 251.10 pg/mL [range: 10–65 pg/mL], calciuria 150 mg/24 h [range: 100–300]. We performed a point-of-care ultrasound of the thyroid, which showed a well-defined hypo-echoic nodular lesion, measuring

14 mm × 12 mm × 18 mm (H × W × D) and located in the left posterior inferior thyroid lobe (see Fig. 1 and Video 1).

Supplementary Video 1 related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.regg.2015.07.011>.

Hyperparathyroidism due to parathyroid adenoma was diagnosed on the basis of these results. Reviewing the patient's personal history, we noted that the last two years prior to her recent admission, she had presented herself on various occasions to the emergency department, fundamentally with neurological or gastrointestinal symptoms. We also observed elevated calcium levels since 2013 (10.6 mg/dL), without the subsequent initiation of a specific treatment. After obtaining clinical stability, the patient was discharged from the hospital, and she is currently on a waiting list for parathyroid adenoma resection and a neuropsychological reevaluation.

Secondary hypercalcemia caused by parathyroid adenoma can present itself with a wide range of clinical manifestations, although it tends to lead a chronic and mild course, only rarely requiring urgent hospitalization.

In the diagnostic evaluation, ultrasound can be of use, when employed to localize and evaluate parathyroid glands. It's a sensitive, non-invasive and reproducible test, and it permits an evaluation of concomitant thyroid pathology (present in 20–30%), which could modify the surgical treatment.<sup>3</sup> Typically, adenomas are identified as homogenous hypo-echogenic lesions.



**Fig. 1.** Short axis view of the neck showing the left thyroid lobe (LTL), parathyroid adenoma (PTA), internal jugular vein (IJV), carotid artery (CA), and the sternocleidomastoid muscle (SM).

A recently published study analyzed a series of cases with hypercalcemia attended in the emergency department.<sup>4</sup> They found that up to 81% of patients were symptomatic, although only 3.5% were diagnosed with hyperparathyroidism and up to 24% of patients had no follow-up plan at the time of discharge. With an estimated prevalence of 20%, we are probably dealing with an underdiagnosed disease.

Global cognitive decline in the elderly due to parathyroid adenoma it is remarkably underdiagnosed, since changes in behavioral and cognitive function are usually attributed to aging, dementia and frailty, which makes the diagnosis challenging. Nevertheless, because many of these patients could benefit from a medical or surgical treatment, as was the case in our patient, it would be advisable to integrate emergency department and care pathways and protocols, in which point-of-care ultrasound could be of great importance to standardize practice.

#### Conflict of interest

No potential conflicts of interest were disclosed.

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#### Repercusión de la somnolencia sobre la calidad del equilibrio y la marcha



#### Sleepiness repercussion on gait and balance

La somnolencia diurna afecta de forma directa a la capacidad funcional<sup>1</sup> de los mayores, produciendo limitaciones tanto a las actividades físicas como a las mentales.

Algunos autores han propuesto una posible relación entre la disminución del equilibrio y el sueño<sup>2</sup>, sin embargo, no ha sido analizada la posible repercusión de la somnolencia diurna con el deterioro de la marcha y el equilibrio. El objetivo de este estudio es evidenciar la asociación existente entre somnolencia diurna y alteración del equilibrio estático y dinámico en personas mayores de 70 años. Se realizó un estudio descriptivo trasversal en población mayor de 70 años de la ciudad de Granada entre los meses de enero y abril de 2015. La somnolencia diurna se evaluó con la escala de somnolencia de Epworth<sup>3</sup> y la puntuación total oscila entre 0–24, valores mayores a 10 indican exceso de somnolencia durante el día.

El equilibrio estático y dinámico se evaluó con el Mini Balance Evaluation System Test (Mini-BESTest). El test posee diferentes pruebas que evalúan de forma sistemática el equilibrio tanto estático como dinámico. Obteniendo una puntuación máxima de 28 y una puntuación mínima de 0, siendo mayores puntuaciones mejor equilibrio y menor riesgo de caídas<sup>4</sup>.

La calidad del equilibrio y la marcha también se evaluó mediante la escala de Tinetti. Consiste en 2 subescalas: una de equilibrio, con una puntuación máxima de 16 puntos, y otra de marcha, con una puntuación máxima de 12 puntos<sup>5</sup>.

Se evaluaron un total de 108 sujetos residentes en la comunidad con una media de edad de  $80,12 \pm 6,413$  y de los cuales el 67,6% eran mujeres. De los sujetos evaluados 44 presentaron valores de somnolencia significativa en el cuestionario Epworth y 64 presentaron valores normales.

Las variables equilibrio y calidad de la marcha analizadas por grupo de somnolencia presentaron diferencias significativas en

la escala Tinetti con peores valores para el grupo somnolencia ( $p < 0,05$ ).

En cuanto a la escala Mini-BESTest se encontraron valores significativamente peores para el grupo somnolencia respecto al no somnolencia ( $13,05 \pm 5,373$  y  $16,059 \pm 3,26$ ,  $p = 0,032$  respectivamente).

Nuestros resultados confirman investigaciones previas<sup>6,7</sup> en las que se han propuesto factores adicionales a los musculoesqueléticos como los psicológicos y cognitivos sobre el riesgo de caídas.

La asociación entre las alteraciones del sueño y el riesgo de caídas han sido investigadas anteriormente<sup>8</sup>. Stone et al. llevaron a cabo un estudio que evidenció una asociación directa entre el insomnio y el riesgo de caídas.

Otros estudios que han analizado la relación entre somnolencia y alteraciones del equilibrio y marcha en personas mayores institucionalizadas presentan resultados controvertidos<sup>9,10</sup>. En nuestro caso la población estudiada mostró diferencias significativas entre grupos de somnolencia, esto puede explicarse por la evaluación pormenorizada y presencial desarrollada en nuestro estudio respecto a otros anteriores cuya exploración ha sido de carácter genérico.

Como limitación en nuestro estudio hay que incluir el método de evaluación de la somnolencia utilizado, que en otros casos ha sido el test de latencias múltiples, sin embargo, este presenta un elevado coste frente a la gran validez de la escala Epworth.

Como conclusión, podemos decir que las personas con más de 70 años que presentan somnolencia diurna significativa poseen alteraciones del equilibrio estático, dinámico, y de la calidad de la marcha comparadas con las que no presentan somnolencia.

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