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Original article

High frequency of asymptomatic hyperparathyroidism in patients with fibromyalgia: random association or misdiagnosis?

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ARTICLE INFO

Article history:

Received 30 October 2015

Accepted 31 January 2016

Available online xxx

Keywords:

Fibromyalgia

Hyperparathyroidism

Musculoskeletal pain

Hypercalcemia

ABSTRACT

Fibromyalgia (FM) and hyperparathyroidism may present similar symptoms (musculoskeletal pain, cognitive disorders, insomnia, depression and anxiety), causing diagnostic confusion.

Objectives: To determine the frequency of asymptomatic hyperparathyroidism in a sample of patients with FM and to evaluate the association of laboratory abnormalities to clinical symptoms.

Methods: Cross-sectional study with 100 women with FM and 57 healthy women (comparison group). Parathyroid hormone (PTH), calcium and albumin levels were accessed, as well as symptoms in the FM group.

Results: In FM group, mean serum calcium (9.6 ± 0.98 mg/dL) and PTH (57.06 ± 68.98 pg/mL) values were considered normal, although PTH levels had been significantly higher than in the comparison group (37.12 ± 19.02 pg/mL; $p = 0.001$). Hypercalcemic hyperparathyroidism was diagnosed in 6% of patients with FM, and 17% of these women exhibited only high levels of PTH, featuring a normocalcemic hyperparathyroidism, with higher frequencies than those expected for their age. There was no significant association between hyperparathyroidism and FM symptoms, except for epigastric pain, which was more frequent in the group of patients concomitantly with both diseases ($p = 0.012$).

Conclusions: A high frequency of hyperparathyroidism was noted in women with FM versus the general population. Normocalcemic hyperparathyroidism was also more frequent in patients with FM. Longitudinal studies with greater number of patients are needed to assess whether this is an association by chance only, if the increased serum levels of PTH are part of FM pathophysiology, or even if these would not be cases of FM, but of hyperparathyroidism.

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<http://dx.doi.org/10.1016/j.rbre.2016.03.008>

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Frequência elevada de hiperparatireoidismo assintomático em pacientes com fibromialgia: associação ao acaso ou erro diagnóstico?

R E S U M O

Palavras-chave:

Fibromialgia

Hiperparatireoidismo

Dor musculoesquelética

Hipercalcemia

A fibromialgia (FM) e o hiperparatireoidismo podem apresentar sintomas semelhantes (dores osteomusculares, distúrbios cognitivos, insônia, depressão e ansiedade) e causar confusão diagnóstica.

Objetivos: Determinar a frequência de hiperparatireoidismo assintomático em uma amostra de pacientes com FM e avaliar a associação das alterações laboratoriais com a sintomatologia.

Metodologia: Estudo transversal com 100 mulheres portadoras de FM e 57 mulheres saudáveis (grupo de comparação). Foram pesquisados os níveis de paratormônio (PTH), cálcio e albumina, além da pesquisa de sintomas no grupo com FM.

Resultados: No grupo com FM, os valores médios de cálcio sérico ($9,6 \pm 0,98$ mg/dL) e de PTH ($57,06 \pm 68,98$ pg/mL) foram considerados normais, embora os níveis de PTH tivessem sido significativamente maiores do que no grupo de comparação ($37,12 \pm 19,02$ pg/mL; $p = 0,001$). O hiperparatireoidismo hipercalcêmico foi diagnosticado em 6% das pacientes com FM e 17% delas apresentaram apenas PTH elevado, o que caracterizou o hiperparatireoidismo normocalcêmico, frequências maiores do que esperada para a faixa etária. Não houve associação significativa entre hiperparatireoidismo e sintomas da FM, com exceção da epigastralgia, que foi mais frequente no grupo de pacientes com as duas doenças concomitantes ($p = 0,012$). **Conclusões:** Houve frequência elevada de hiperparatireoidismo em portadoras de FM quanto à população geral. Hiperparatireoidismo normocalcêmico também foi mais frequente em pacientes com FM. Estudos longitudinais e com maior número de pacientes são necessários para avaliar se trata-se apenas de uma associação ao acaso, se as elevações séricas do PTH fazem parte da fisiopatologia da FM ou, ainda, se não seriam casos de FM, e sim de hiperparatireoidismo.

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Introduction

Primary hyperparathyroidism (PHP), a disease caused by a hyperactive parathyroid and consequent hypercalcemia, is associated in 85–90% of cases, to the presence of solitary gland adenomas, occurring most commonly in people aged over 50 and in women in post-menopause, with a prevalence of 0.78% for the general population. Although the clinical presentation is variable, the asymptomatic hypercalcemia form is the most common (50–80%).^{1,2}

Fibromyalgia (FM) is one of the most common rheumatic disorders, affecting approximately 2–8% of the population, depending on the diagnostic criteria used for its classification.³ FM affects specially young women (30–55 years old),⁴ but with the use of new classification criteria,⁵ the prevalence in men has increased.⁶ Its main feature is a diffuse and chronic musculoskeletal pain associated with symptoms such as fatigue, sleep disturbances, morning stiffness, diffuse paresthesias, a subjective feeling of edema, cognitive disorders, depression and anxiety.⁷ The cause of FM is unknown, but its development is associated with a disorder of central nervous system regulation with respect to pain. So far, no significant laboratory abnormalities were identified in FM patients.⁸

Fatigue, arthralgia, myalgia, sleep disturbances, depression, anxiety and memory impairment – common symptoms

in patients with FM – are part of the nonspecific symptoms in patients with PHP. Asymptomatic PHP is understood as that case in which laboratory changes are occurring, with elevated serum levels of parathyroid hormone (PTH) and calcium, without the presence of the classic manifestations of PHP, for instance, severe hypercalcemia, cystic fibrous osteitis and advanced kidney disease.² Starting in the 70s, with the acquisition of new knowledge and with improved techniques for the determination of calcium and PTH, it was observed that PHP is a common disorder, and usually has no serious or specific symptoms.² In a series of 124 cases of PHP evaluated in the city of Recife (Brazil), 47% had no symptoms related to the disease, while 25% suffered from cystic fibrous osteitis, 25% exhibited kidney stones without bone involvement, and 2% presented with typical neuropsychiatric syndrome.⁹

Another study involving 4207 patients aged over 18 in public and private endocrinology centers in Recife (Brazil), found a prevalence of 0.78% (95% CI, 0.52 to 1.04) of PHP, of which 81.8% were asymptomatic.¹⁰ The ratio between women:men was 7.2:1, the mean age was 61 ± 16 years and 89.7% of affected females were postmenopausal. Among the typical manifestations of PHP, fibrous osteitis was present in 6.1% of cases, nephrolithiasis in 18.2%, and acute neuropsychiatric syndrome in 3%. The prevalence of nonspecific symptoms was 51.5% for fatigue and 39.3% for muscle weakness.¹⁰

A former study also conducted in Recife (Brazil) determined a prevalence of 1.3% of PHP in postmenopausal women. Of

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