

Precocious Idiopathic Primary Osteoporosis in Men: A Case Report

Osteoporose Primária Idiopática Precoce em Homens: Relato de Um Caso

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ABSTRACT

Osteoporosis is a metabolic-based bone disease, which is one of the most frequent osteoarticular comorbidities, especially in countries with older populations, and is associated with an elevated risk of bone fractures with significant morbidity and mortality. We present a case of a 58-year-old man seen at a Primary Care facility complaining of acute low back pain. After persistence of the complaints for 3 weeks, an imaging study with lumbar computed tomography (CT) was performed, showing multiple fractures and rarefaction of bone trabeculation. The diagnosis of osteoporosis was confirmed after bone densitometry with a Z-score of -3.3 in the lumbar spine. The main secondary causes of osteoporosis have been excluded, and no family history is known. The only risk factor found was smoking (37 UMA). The patient was treated with denosumab and cholecalciferol + calcium carbonate. Assessment was requested at a Rheumatology hospital consultation and is now undergoing additional genetic study and monitoring of the disease.

KEYWORDS: Bone Density; Man; Idiopathic Osteoporosis

RESUMO

A osteoporose é uma doença óssea de origem metabólica, uma das comorbidades osteoarticulares mais frequentes, especialmente em países com populações mais idosas, e está associada a um risco elevado de fraturas ósseas com morbidade e mortalidade significativas. Apresentamos o caso de um homem de 58 anos atendido em um centro de cuidados primários com queixa de dor lombar aguda. Após persistência das queixas por 3 semanas, foi realizado um estudo de imagem com tomografia computadorizada (TC) lombar, que mostrou múltiplas fraturas e rarefação da trabeculação óssea. O diagnóstico de osteoporose foi confirmado após densitometria óssea com

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um Z-score de -3,3 na coluna lombar. As principais causas secundárias de osteoporose foram excluídas e não há histórico familiar conhecido. O único fator de risco encontrado foi o tabagismo (37 UMA). O paciente foi tratado com denosumabe e colecalciferol + carbonato de cálcio. Foi solicitada avaliação em consulta hospitalar de reumatologia e encontra-se agora a realizar estudos genéticos adicionais e monitorização da doença.

PALAVRAS-CHAVE: Densidade Óssea; Homem; Osteoporose

INTRODUCTION

Osteoporosis is one of the most common comorbidities in the population, with an estimated prevalence of 10,2%^{1,2} in Portugal, especially above 50 years of age, being increasingly relevant as the population ages in developed countries and this demographic process is being initiated in developing nations. Being more frequent in female patients (RR 6,54),² most common cases in male patients are secondary to other conditions, medications or identifiable causes.³

Idiopathic osteoporosis in men is an uncommon finding and is associated with a higher fracture morbimortality than in women.^{4,5} The lower availability of specific guidelines and scientific evidence for diagnosis and treatment for primary osteoporosis in men creates serious challenges in the management of these patients.

Here is presented a case of idiopathic primary osteoporosis in a men diagnosed in consequence of low-impact vertebral and costal fractures.

CASE REPORT

A 58-year-old male sex cisgendered patient of Portuguese nationality and an active smoking index of 37. Presents no relevant personal and family medical backgrounds and no daily prescriptions for complaints of mechanical back pain for 5 days, starting after a period of atypical physical effort at home. Denies any irradiation for the lower limbs, neurological findings, fever, or any other relevant symptoms. On the physical exam, there was pain at the palpation of lumbar paravertebral muscle masses aggravated by walking and body forced extension, with a bilaterally negative Lasègue test. No other relevant findings were found.

With a diagnostic assumption of acute low back pain without any yellow or red flag findings, the patient was reassured and medicated with cyclobenzaprine 10 mg each day for 5 days and acetaminophen 60 mg each 12 hours for 5 days. A partial reduction of physical effort was recommended, guided by the pain for a brief period.

In the time mediated between the first and seconds

visits, the patient was submitted to an short duration hospital stay in the Cardiology service due to retrosternal anterior chest pain with atypical anginous characteristic (associated with body and thoracic movements, change in posture and with variable duration between seconds and minutes) with dorsal irradiation with a week long duration, accompanied by shortness of breath for medium walking distances and symptom escalation during moderate to intense exercise. The pain did not completely subside with rest.

During this hospital stay, a NSTEMI diagnosis was assumed due to an EKG presenting with a positive R wave in V1 and a broad base T wave in aVF despite persistently negative CK-MB and high sensitivity T troponin, even though there was a record of a slightly elevated high sensitivity I troponin in a previous initial evaluation at the A&E department at a different hospital. Before medical release, the patient underwent a coronary catheterization and a transthoracic echocardiography, revealing no pathological findings. An additional X-ray showed diffuse bilateral hyperinflation in all pulmonary fields. The patient was released from the hospital stay with the introduction of daily AAS 100 mg and atorvastatin 20 mg after a ASCVD calculated risk of 12.6%.

The patient was re-evaluated two weeks after the release from the hospital stay described above, keeping the complaints of low back pain and anterior chest pain aggravated by changes in body posture and upper body movements. At this time, he was under a symptomatic prescription of ibuprofen 600 mg and paracetamol 1000 mg – without any major improvement of the pain or functional limitations, maintaining the incapability to work during this time span.

Given the maintenance of the low back pain for more than 4 weeks in disregard of symptomatic medication and behavioral changes, a CT scan of the dorsal and lumbar regions was requested, demonstrating the following:

“Multiple dorsal vertebral fractures (T5-T12) with a slight anterior wedging of the vertebral body of T5, moderate anterior wedging of the vertebral bodies

of T6-T8 and slight depression and anterior wedging of the superior platform of T12 vertebral body. Bone marrow edema at the level of T5. At T8, indications of linear focus of intravertebral vacuum in relation to fracture with vertebral platform distraction fracture. Hyperkyphosis at the segment between T4 and T9 as result of the anterior wedging between T5 and T8. General rarefaction of bone density"

Additionally, a series of rib projections X-rays were prescribed as well as a bone densitometry, revealing multiple stress rib fractures in the anterior margin of the central ribs and confirmed the suspected diagnosis of osteoporosis with a Z score of -3.3 and a T score of -2.5.

Due investigation of secondary causes was prosecuted with the prescription of several studies, with the following relevant results:

- Vitamin D 18 ng/dL (N>20 ng/dL)
- Slight isolated hypocalciuria
- Whole body scintigraphy: hypercaptation in the projection of T4-T5 and T7 with foci of hypersignal along the proximal epiphysis of the right humerus and at the anterior margin of the 6th rib – compatible findings to stress fractures
- Remaining blood studies within normal range (Mg²⁺, renal function, liver function, TSH, T4L, free cortisol, ACTH, iron studies, alkaline phosphatase, total and free testosterone, FSH and LH, PTH, B9, B12, urinary calcium, beta-2-microglobulin, beta-crosslaps, ECA, proteinogram with electrophoresis and osteocalcin)

The patient was medicated with calcium carbonate 1500 mg + cholecalciferol 144 U.I. id, denosumab 600 mg/1 mL each 6 months.

He was then referred for evaluation for Rheumatology and Endocrinology at the reference hospital, where the patient continues to be accompanied now with further and more advanced investigations, including genetic studies.

DISCUSSION

Osteoporosis is a common osteo-articular disease related to a progressive diminishment of the bone mineral density (DMD), inducing a pathologic change in the internal microstructure of skeletal bones, leading to an augmented risk of vertebral and extra-vertebral fractures.

Despite the diagnosis of osteoporosis (being it primary or secondary) being mostly established after events of low-impact vertebral and extra-vertebral fractures at an advanced age, the change in bone microstructure precedes the clinical manifestations for years to decades. The reduction of DMD, when progressive and without pathological consequences, is a physiological phenomenon of normal human aging, starting right after the peak on DMD reached between 18 and 25 years of age. Although peak DMD is reached at around the same age in biological males and females,⁶ bones in male subjects have a 30% wider diameter and a significantly higher DMD, making it harder and questionable to use the common cut-offs for the evaluation of bone density rarefaction, based mostly on women populations.

A Portuguese national study published in 2016 points to an estimated prevalence of osteoporosis around 10.2% in the general population, with a stark preference for females (17.0%) with a risk 6.54 times higher than in males (2.6%). This data for the Portuguese population was mostly in line with that from other European countries with aging populations, such as Spain, France or Italy.⁷

Osteoporosis affects mostly postmenopausal women (with an estimated prevalence around 49.5% in the Portuguese population segment above 65 years), but the existence of multiple risk factors for the reduction of DMD increases the risk of precocious manifestations. As well as in females, the prevalence of osteoporosis in men increases progressively with the advance of age.⁸

Primary osteoporosis (PO) corresponds to the cases of osteoporosis diagnosed in the absence of secondary causes of the disease, classifying it into two big groups: involutive PO (further distinguished between types I and II, respectively, postmenopausal PO and senile PO) and idiopathic PO.

The diagnosis of idiopathic PO in young segments of the population is rare in the absence of cumulative risk factors, especially in men,^{9,10} in whom secondary causes are diagnosed up to 60%.^{10,11}

After a confirmed diagnosis of PO through bone densitometry, the FRAX®Port (fracture risk assessment tool) shall be calculated, in case it has not been done recently, to evaluate the risk of major osteoporotic fracture events and the need to introduce directed therapeutic strategies. In case of previous events of osteoporotic fractures in the last 10 years (vertebral and/or extra vertebral, especially femur and pelvic

fractures) a therapeutic approach is indicated independently of the FRAX®Port estimated risk.

According to the Portuguese Society of Rheumatology, who writes national recommendations,¹² it is stated that:

General measures such as adequate diet, vitamin D supplementation exercise and fall prevention strategies are recommended for all people with risk factors, regardless of DEXA and FRAX risk

Therapeutic regimes for all people with at least one fragility hip fracture and/or at least one symptomatic vertebral fracture and/or two or more fragility fractures (whatever symptoms and locations)

Therapeutic regimes in all people with an estimated FRAX risk equal or above 9.0% with DEXA or 11.0% without DEXA for a major osteoporotic fracture over 10 years and/or equal or above 3.0% with DEXA or 2.5% without DEXA for a hip fracture over 10 years

There is not an established and validated consensus regarding the therapeutic approach to osteoporosis in males (contrarily to the case of postmenopausal osteoporosis), even though a recent guideline directed to osteoporosis in men was proposed,¹³ creating the need for an individual based decision according to each patient's individual characteristics and the most recent scientific evidence available.

The supplementation with vitamin D from 800 to 1200 UI per day in one or two daily intakes or the adequate alternative intake of calcium (in needed with supplementation) in order to maintain blood cholecalciferol levels equal or above 25-30 ng/mL is an approach with extensive and validated evidence and recommendation.¹⁴

Other strategies, especially directed to the most common risk factors, appear to gather a broad base of scientific support, nominally smoking cessation, directed prescription of physical exercise regularly and with a strengthening of the muscle axis around the hips and lower limbs as well as reduction in the intake of alcohol and sedatives.^{15,16}

As well as in menopausal women, bisphosphonates are defined as the first-line treatment strategy after the supplementation of calcium and vitamin D, usually used in combination with. Between several active substances in the class of antiresorptive medications, alendronate 10 mg per day or 70 mg per week is the most studied in men.^{15,17} Risendronate 35 mg per week was already studied in the context of male osteoporosis with significantly positive results¹⁸ in the reduction

of vertebral and extra vertebral osteoporotic fractures, in line with the findings in studies with postmenopausal women. The reduction in osteoporotic vertebral risk fractures in men with PO with the use of intravenous zoledronate 5mg per year also has solid studies, even though the effect on extra vertebral fractures is not yet been established.^{19,20}

In recent years, the use of denosumab has been increasing as an alternative to bisphosphonate antiresorptive medications, including in the Primary Care setting. There is, however, some resistance to its initial prescription in non-hospital sets, due to putative security concerns.²¹ Albeit being a monoclonal antibody, denosumab had confirmed its security and non-inferior²² or even superior efficiency^{23,24} to bisphosphonates in the reduction of osteoporotic vertebral and extra vertebral fractures,²⁵ with a weekly intake of 60 mg subcutaneously and with a concomitant supplementation with calcium and vitamin D.²⁶ Denosumab may be a useful option in cases of PO with low DMD or with an insufficient response to optimized treatment with bisphosphonates, especially in patients who value the weekly intake opposite to a daily compromise.

As well, the use of teriparatide has been increasingly appointed as an adequate option for PO with DMD severely reduced or associated with major fracture while under antiresorptive therapy.^{27,28} Opposite to bisphosphonates and denosumab, teriparatide is the only pharmacological agent formally approved for the use in male osteoporosis worldwide²⁷ with a 30 to 40 µg daily dose with a concomitant supplementation with calcium and vitamin D. It has demonstrated efficiency in the reduction of risk fractures and with increasing bone density in both vertebral and extra-vertebral contexts.

In the absence of identified secondary causes, there is no place for directed, specific corrective measures.

CONCLUSION

The diagnosis and management of osteoporosis in men is a challenging job, due to its rarity in the general population, the rarity of medical consensus or guidelines specifically concerning osteoporosis other than the postmenopausal type,²⁹ and the lack of evidence for the efficiency and dosage regimes for drugs commonly used for osteoporosis treatment. Aggravating this scenario, the absence of any meaningful cluster of risk factors as well as potential secondary causes further complicates the case, raising serious difficulties in performing a diagnosis before the first clinically sig-

nificant events, more commonly, major fractures with significant morbidity and mortality associated.

This case report demonstrates the need for the development of specific guidelines for the diagnosis as management of osteoporosis in men and further studies for the validation of several drugs used in common practice with increased evidence for the use in men with osteoporosis with increasing safety and confidence. Despite the lack of solid and specific clinical orientations, the initial management should be same as any other case of suspected and confirmed osteoporosis, focusing on the objective measurement of bone marrow density, the exclusion of major asymptomatic fractures and potential secondary causes, addressing them as well as clusters of risk factors in an individualized manner. Patients without evident etiopathology, cases of osteoporosis in men and diagnosis in younger than expected ages (e.g., before 50 years of age) should always be readily referred for additional studies and differentiated management in the local hospital for Endocrinology and/or Rheumatology.

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