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Research article

Domestic fall – related multiple osteoporotic vertebral frac-tures: considerations amid late COVID-19 pandemic (a case on point)

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Abstract: Our purpose was to introduce a case on point of a menopausal woman who suffered a domestic fall with consecutive persistent back pain and reduced mobility, and delayed the presentation amid late COVID-19 pandemic. On admission, she was confirmed with osteoporosis according to DXA (lowest T-score of -5.5) and started zoledronate. She refused further orthopedic intervention and remained on non-invasive long term rehabilitation plan while surveillance of anti-osteoporotic medication was offered to her. Fragility vertebral fractures represent increasingly common issues that require prompt intervention to overall a better prognosis. Late presentation and a first diagnosis of 10 vertebral fractures is a part of real life medicine with consequences amid potential lack of compliance to medication and adherence to a rehabilitation plan with short term and long term effects. Transition to post-pandemic reality still represents a concurrent pitfall to delayed hospitalization.

Keywords: fracture, osteoporosis, vertebra, zoledronate, rehabilitation, pain, surgery, pandemic, fal

Introduction

Treatment - naïve adults with osteoporosis who remain undiagnosed and thus untreated represents a challenging category nowadays due to, on one hand, the need of a multifunctional complex management that includes medical approach with specific anti-osteoporosis drugs and vitamin D supplements, surgical intervention (of orthopedic or neurosurgical type depending on fracture' site), and short/long term rehabilitation plan

in order to address related pain, impaired mobility, overall dysfunctionality, reduced quality of life, as well as, the prevention of other falls or low-trauma events (as risk factors for additional osteporotic fractures) [1-3]. On the other hand, it seems that, despite current overall medical and social progress, approximately one out of three to five individuals who are candidates to therapy according to guidelines are not on long term specific medication against osteoporosis, either by never been offered or by not remaining compliant to a treatment that is recommended for years, if not for lifetime in cases with complicated (severe) primary osteoporosis [4-6].

COVID-19 pandemic has brought us numerous changes, also, with respect to various medical, surgical and social issues [7-9]. While new conditions have been described in relationship with coronavirus infection in virtually all domains, prior known disorders – associated panel has shifted to a different frame due to late hospitalization (regarding a limited admission amid regulations or fear of going out), to a lack of continuing/initiating necessary therapy, or due to unexpected complications while going though infection itself [10-12].

As a matter of fact, osteoporosis field does not represent any exception from other chronic diseases [13-15]. While a decrease of outdoor activities, including walking and other physical exercises, was associated to a lower incidental rate of low trauma fractures, domestic fractures were more frequently reported, as expected, in association to a delay of having a full multidisciplinary evaluation or even a tele-consultation in relationship with a recent indoor fall [16,17]. Overall, the pandemic picture seemed to be aggravating the adherence to osteoporosis – related protocols of diagnostic and treatment; of note, as mentioned, this being already an area with multiple deficiencies in most countries [18,19].

Our purpose was to introduce a case on point of a menopausal woman who suffered a domestic fall with consecutive persistent back pain and reduced mobility, and delayed the presentation amid late COVID-19 pandemic. On admission, she was confirmed with osteoporosis according to DXA and started zoledronate. She refused further orthopedic intervention and remained on non-invasive long term rehabilitation plan while surveillance of anti-osteoporotic medication was offered to her.

2. Results

Blood biochemistry panel showed normal liver and renal function as well as glucose profile, ion and haemogram blood tests. A small total cholesterol increase was confirmed (of 223 mg/dL, with normal upper level below 200 mg/dL). Normal thyroid function and negative thyroid antibodies were identified: TSH (Thyroid Stimulating Hormone) of 1.4 μUI/mL (Normal: 0.35 – 4.95); free T4 (thyroxine) of 10.94 pmol/L (Normal: 9-19); anti-thyroperoxidase antibodies of 0.88 UI/mL (Normal < 5.61) and anti-thyroglobulin of 15.19 UI/mL (Normal < 115).

Mineral metabolism assays showed normal calcium and phosphorus with vitamin D deficiency as reflected by a level of 15 ng/mL of 25-hydroxyvitamin D (25OHD) and normal parathyroid hormone (PTH). Bone turnover markers revealed a small elevation of bone resorption marker serum CrossLaps of 0.89 ng/mL, with normal ranges between 0.33 and 0.782 ng/mL, respectively, of bone formation marker total alkaline phosphatase. (Table 1)

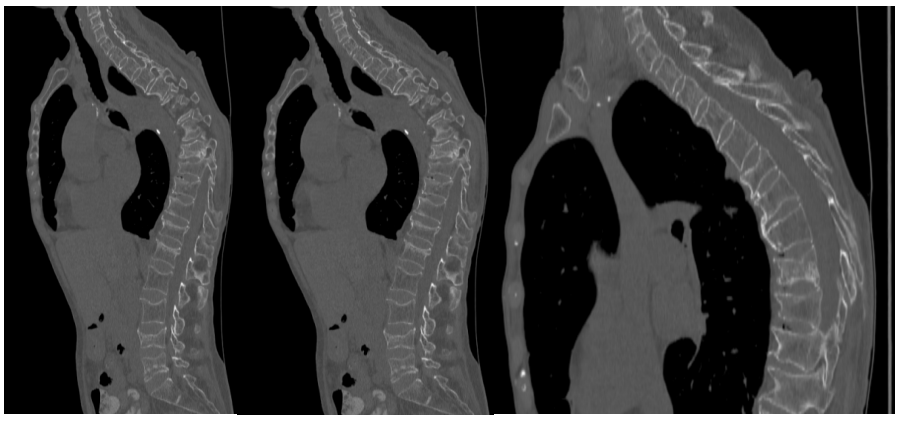
Table 1. Mineral metabolism assessments on a 68-year-old female admitted with cascade vertebral fractures without a prior diagnosis of osteoporosis

Parameter	On point value	Normal ranges	Unit
	Blood biochemistry panel		
Total serum calcium	9.66	8.4-10.3	mg/dL
Ionic serum calcium	4.1	3.9-4.9	mg/dL
Phosphorus	3.56	2.5-4.5	mg/dL
	Hormones of calcium-phosphorus metabolism		
25-hydroxyvitamin D (25OHD)	15	>30	ng/mL
Parathormone (PTH)	45.24	15-65	pg/mL
	Blood bone turnover markers (formation)		
Osteocalcin	31.13	31.13	ng/mL
Total alkaline phosphatase	131	38-105	U/L
P1NP	76.8	20.25-76.31	ng/mL
	Blood bone resorption marker		
CrossLaps	0.89	0.33-0.782	ng/mL

Further investigations were done for osteoporosis that was confirmed in terms of identifying multiple vertebral fractures (N=10 vertebras) at plane profile X-Ray of thoracic – lumbar region and computed tomography scan (with intravenous contrast) as well as central DXA with lowest T-score at lumbar L1-L4 level of -5.5 (BMD of 0.519 g/sqcm, and Z-score of -3 SD). (Figure 2)

Figure 2. Computed tomography (intravenous contrast) on a 68-year-old woman with first diagnosis of fractures at the level of thoracic vertebras, namely, T5 (1.4 cm), T6 (1.89 cm), T7 (1.42 cm), T8 (1.2 cm), T9 (1.2 cm), T10 (1.22 cm), T11 (1.69 cm), and T12 (1.54 cm) and lumbar vertebras L4 (1.27 cm) and L5 (2.12 cm).

a. Sagittal plan (different sections)



b. Frontal plane

The patient was offered 2000 UI daily cholecalciferol and 5 mg zoledronate per year. No post-acute side effects following the injection were registered. Periodic checkup was recommended in addition to non-pharmacological rehabilitation plan. She refused an orthopedic/neurosurgical evaluation, neither to be followed at a local rehabilitation center. Upon vitamin D replacement and 25OHD correction that was expected in at least 3 months a switch to a lower maintenance dose of daily 1000 UI cholecalciferol is advisable. Lifelong surveillance of skeletal health is mandatory.

3. Discussions

This case on point highlights several aspects of major importance as following:

3.1. Late diagnosis of the vertebral fractures

First of all, the mentioned female patient suffered vertebral fractures cascade, but continued her domestic activities despite intense back pain. She delayed the presentation to the hospital thus the timing of intervention since being a suitable candidate to initiate an adequate medication (therapy against osteoporosis and vitamin D supplementation) in addition to a rehabilitation program [20,21].

Low-trauma vertebral fractures may be caused by primary (menopausal or age – related) osteoporosis as here, but a traumatic event should be an additional factor as well to a secondary osteoporosis [22].

The severity profile of these multiple vertebral fractures in this case required a differential diagnosis with other secondary causes of osteoporosis such as primary hyperparathyroidism or hyperthyroidism, but also to a primary or secondary malignant bone condition [23-27]. Other causes of secondary osteoporosis, such as prolonged corticosteroid therapy or an autoimmune thyroid pathology, were considered and excluded. [28, 29]. The investigations we performed were clear of excluding other forms of bone damage other than severe primary osteoporosis (normal parathyroid hormone, and thyroid function, and no endogenous Cushing's syndrome, etc.). However, lifetime surveillance is mandatory.

This late presentation after months of dysfunctionality and impaired quality of life does not represent an unusual scenario nowadays; in many rural areas of different geographic regions a limited access to investigations and therapy is reported, an aspect that was aggravated by the pandemic circumstances thus requiring prompt public health strategies [30-32].

3.2. Anti-osteoporosis drug selection

In this particular case, an alternative to zolendronate was represented by subcutaneous teriparatide that acts as bone forming agent with a statistically significant intervention

regarding fracture risk reduction, particularly at vertebral level, in both naïve individuals and those with previous medication against osteoporosis, regardless they underwent surgical cure of fragility fractures [34,35].

However, the patient refused daily administration *via* self-injection and further difficulties of endocrine surveillance with regard to teriparatide protocol were noted thus the lack of adherence and potential deficiencies of subject' compliance did not allow the drug initiation. Oral bisphosphonates represented an alternative which was not feasible due to a history of ulcer. Also, denosumab was a valuable solution; however, the requirement of continuing the drug or switching to bisphosphonates as long term plan might have been a problem with respect to the lack of compliance in this case on point [5,36].

As long term recommendations, an annual DXA-BMD re-assessment is necessary, but recent studies showed the anti-fracture efficacy of 5 mg zoledronate is extended more than 12 -18 months up to 3 - 5 years in naïve and prior treated osteoporotic menopausal females [37-39].

3.3. Rehabilitation plan

The female subject refused further orthopedic/neurosurgical investigations such as kyphoplasty or vertebroplasty and at home plan of rehabilitation was taken into consideration noting that she did not have access to a larger hospital nearby her home. While the benefits of kyphoplasty on overall mortality in seniors are not unanimously recognized [40], multiple vertebral fractures of one individual represent a major burden of the patient and generally of health care systems. A recent meta-analysis showed that lack of exercise following vertebral augmentation doubled the risk of incidental vertebral fractures while daily exercise associated benefits for pain reduction, improved functionally, and reduced risk of re-intervention [41].

Non-pharmacological rehabilitation management in cases of vertebral fractures was also applied *via* virtual medicine amid COVID-19 pandemic depending on fracture's stability, and individual medical and surgical profile of co-morbidities [41-43]. It generally includes pain medication, physiotherapy, and manual therapy, educational components with respect to lifestyle intervention, diet, daily habits, and physical exercise, both a theoretical training and mindfulness/medical yoga for the subjects with stable fractures, with an adjustment depending on short and long term plan for osteoporosis and associated fractures [42-44].

Long term considerations with respect to osteoporotic vertebral fractures should be regarded at multiple levels. The condition associates back pain, impairment of daily activities and sleep, psychological stress, reduced social wellbeing and affected quality of life [45]. Prolonged immobilization might aggravate further bone loss [46]. Severe thoracic fractures might prove detrimental to respiratory function [47]. Overall wellbeing and maintaining an active live contribute to a supplementary reduction of other important elements like sarcopenia and frailty that are risk factors for falls [48].

Enough evidence already showed us that the risk of a second (additional) fracture after first one/ones is higher within the first two years following the initial event thus the importance of prompt pharmacologic and non-pharmacologic interventions to address the re-fracture risk. In seniors, the risk of "silent" fractures requires a continuous vigilance [49-51].

Of note, the subject on point showed vitamin D deficiency that was not severe, neither associated secondary hyperparathyroidism (less likely to correlate with very low T-score as seen in sever osteomalacia) [52]. Hypovitaminosis D seems rather usual in aging population nowadays, especially upon pandemic regulations, and it requires adequate replacement [53]. In case of no response to vitamin D supplementation and intravenous bisphosphonates, as, for instance, suppression of bone turnover markers, a bone biopsy should be advised [54].

Overall, as recently specified by International Osteoporosis Foundation (IOF) – associated Rehabilitation Working Group, post-fracture strategies are multimodal, "inter-reliant", centered on one individual' specific needs and real life conditions, thus requiring a continuous and dynamic adjustment [55].

4. Materials and Methods

The case' data are provided upon signed informed consent by the patient. She agreed to anonymous presentation of her medical data. We provided a large panel of data with respect to mineral metabolism assessment, including bone turnover markers, bone mineral density (BMD) and associated T-score based on central Dual-Energy X-Ray Absorptiometry (DXA) according to a GE Lunar Prodigy device and computed tomography (CT) scan.

This was a 68-year-old, nonsmoking female who was admitted for persistent back pain since last months. She was referred by her primary physician with suspected osteoporosis amid late months of COVID-19 pandemic. She suffered a domestic fall as starting point of her pain and delayed to seeking for medical assistance. Moreover, in the meantime she continued to take care of her mother who was terminally ill as a single self-care provider. Her personal medical history was irrelevant with regard to the bone health. She entered surgical menopause by the age of 45 years for a benign uterine fibroma. She was known with high blood pressure since last 2 decades that was controlled under anti-hypertensive medication; she received a diagnosis of gastric ulcer 15 year prior, and was known with high cholesterol. On admission, the body mass index was of 21 kgs/sqcm, and no particular phenotype was identified.

5. Conclusions

Fragility vertebral fractures represent increasingly common issues that require prompt intervention to overall a better prognosis. Late presentation as seen in this case on point diagnosed for the first time with 10 vertebral fractures is a part of real life medicine with consequences amid potential lack of compliance to medication and adherence to a rehabilitation plan with short term and long term effects. Transition to post-pandemic reality still represents a concurrent pitfall to delayed hospitalization.

Abbreviations

BMD	bone mineral density
CT	computed tomography
25OHD	25-hydroxyvitamin D
DXA	Dual-Energy X-Ray Absorptiometry
IOF	International Osteoporosis Foundation
PTH	parathyroid hormone (parathormone)
TSH	Thyroid Stimulating Hormone
T4	thyroxine

Supplementary Materials: Not applicable

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