Acta Biomed 2020; Vol. 91, S. 14: e2020005 DOI: 10.23750/abm.v91i14-S.10785

Case Report

Distrectual osteosarcopenia in limb disuse: case report and mini literature review

Filoni Gabriele, Di Lonardo Michele, Mandile Giovanni, Andreani Lorenzo, Falossi Francesca[1], Franchi Alessandro[2], Bottai Vanna, Capanna Rodolfo

2nd Orthopedic and Traumatologic Clinic, University of Pisa, Pisa, Italy
[1]Orthopedic Rehabilitation Department Section, University of Pisa, Pisa, Italy
[2]Division of Surgical, Molecular and Ultrastructural Pathology, University of Pisa, Pisa, Italy

Abstract: Osteosarcopenia is a new concept and it is the association of osteoporosis and sarcopenia. Both of these pathologies are more frequent in elderly people and generally affects all the skeleton increasing risk of falls and fractures, loss of global function, fragility, and mortality, and also surgical failures. The coexistence of these conditions derives from a close relationship, not only anatomical, between bone and muscle tissues. Sometimes they can involve only a skeleton segment, due to a local disuse, causing a different form of sarcopenia. In this clinical case, Authors describes a case of isolated lower limb osteosarcopenia in a young non-osteoporotic patient, due to a prolonged limb disuse, complicated by surgical treatment failure for previous pathology, diagnosed by clinical, laboratory, instrumental and histopathological exams.

Keywords: Osteoporosis, osteosarcopenia, disuse, BMU

Background

Sarcopenia and osteoporosis are chronic conditions, which are frequently associated in patients, especially older people, with prolonged periods of disuse or reduction of normal daily activity. Their association is defined as osteosarcopenia, described for the first time by Duque and colleagues[1]. They described osteosarcopenia as an unique syndrome characterized by simultaneous low bone density (osteoporosis) and together with low mass and function (sarcopenia). It affects especially elderly people with a prevalence increasing together with aging. It results in a greater number of important clinical consequences such as falls, bone fractures and hospitalizations.

Most of time osteosarcopenia affects all the skeleton, especially lower limbs. Sarcopenia is a progressive loss of skeletal muscle tissue and reduced muscle function that, from a clinical point of view, translates to a negative impact on daily activities, with an higher risk of falls[2]. Osteoporosis is defined as a bone disease in which the bone microarchitecture fades and bone mineral density (BMD) reduces with mineralometric T score equal to or less than -2.5 standard deviations below the peak bone mass of a young healthy cohort patients. The resulting bone fragility is the cause of an higher risk of fractures that could occur even after a low intensity trauma[3]. In most of cases is age and sex related (primary osteoporosis) but it can be also caused by different kind of clinical situations such as primary hyperparathyroidism, corticosteroids drug assumption anorexia. Osteoporosis and sarcopenia are both multifactorial pathologies and share various pathophysiological pathways. Such as osteoporosis and sarcopenia, in addition to age, there are many other risk factors that play a role in the development of osteosarcopenia: genetic polymorphisms, endocrine disorders, malnutrition, obesity and

use of corticosteroids drugs are related to bone and muscle loss. The shared risk factors are not the only mechanisms explaining synchronous loss of bone and muscle mass. Clinical research suggests a combination between the two tissues, with the fat being a major player influencing this interaction. In the past, fatty infiltration of muscles and bones was interpreted as a natural phenomenon linked to aging, it is now known its specific role in osteosarcopenia onset.

Finally, the existence of mechanically, physically and biochemically interactions defines BMU (Bone Muscle Unit) [4]–[6]. Both bone and muscle are adaptive tissues, changing their mass and strength in response to mechanical loading. Therefore, mechanical stimulus is essential for the health of both tissues and thus decreased level of physical activity may shift the frail balance in favor of muscle degradation and bone reabsorption, this occurs in patients forced to a prolonged disuse over time. A positive correlation is observed between the two tissues, with higher lean body mass associated with increased BMD and vice versa.

Even if muscle degradation and bone resorption usually occur in a generalized manner, these can be limited to a specific body district, especially if this district is less used due to pathologies that limit its activity and motility[7]. Several studies describes an higher incidence of sarcopenia in patients presenting prior fragility fractures, especially in femoral fractures[8], [9], but also in osteoporotic ones, and in patients with frequent falls in clinical personal history[10], [11]. The prevalence of osteosarcopenia in eighties is 10,4% in men and 15,1% in women[12]. The most common definition of osteoporosis is based on the T-score for BMD as assessed by DXA at the femoral neck and spine; osteoporotic value is defined as a BMD 2.5 SD or more. Other risk factors should be also considered according to FRAX[3].

The diagnosis of osteosarcopenia includes history (i.e. previous medical and social conditions, falls, fractures, and drug anamnesis), risk factor identification, physical assessments (grip strength, sit to stand test and others) and targeted investigations like blood samples to exclude secondary forms and other instrumental techniques as bioelectrical impedance analysis (to estimate fat-free mass), peripheral quantitative computerized tomography and others[13]. Treatment of osteosarcopenia is based on resistance exercise, useful in stimulating osteoblastogenesis and muscle protein synthesis, dietary supplementation such as correct intake of protein, calcium and Vitamin D[14], [15]. No specific pharmacological agents for sarcopenia treatment haven't yet been developed, in contrast of treatment of osteoporosis, even if some drugs such as denosumab seems to show positive effects on bone and muscles[16].

Actually osteosarcopenia describes only a systemic disease which consist in the association between generalized osteoporosis and sarcopenia, especially in elderly patients, exiting in a global frailty condition. No studies are reported about the possibility that osteosarcopenia can affect only a part of the skeleton that could be defined as "distrectual osteosarcopenia".

The aim of this article is to show that osteosarcopenia is not only a systemic disease but, in some case, especially when associated important loss of function and activity, can also appear as a localized form of pathology.

Case Report

A 43 years old, Latin American woman, right-handed, height 170cm, weight 106 kg, without relevant comorbidities except for obesity, suffered a pathological fracture of her right femur in May 2018. Consequentially she was treated with the resection of the fragment involved in the fracture and its substitution with a cylindrical-shaped implant of bone cement, stabilized with double carbon-PEEK fiber plates. The pathologist report was positive for malignant PECome tumor, a low-grade neoplasm, without any indication for further treatment. After a couple years of wellness, even though the function of the right low limb was reduced, the patient suffered in January 2020 a sudden atraumatic pain localized on the synthesized zone; After a radiological exam, implant failure was diagnosed (figure 1). As a routine follow-up was performed, a series of instrumental exams was carried out, comprehensive femur X-Ray, a PET-CT with FDG and chest CT scan in March 2020, which evidenced some pulmonary nodules of a probable metastatic nature. New surgical treatment was

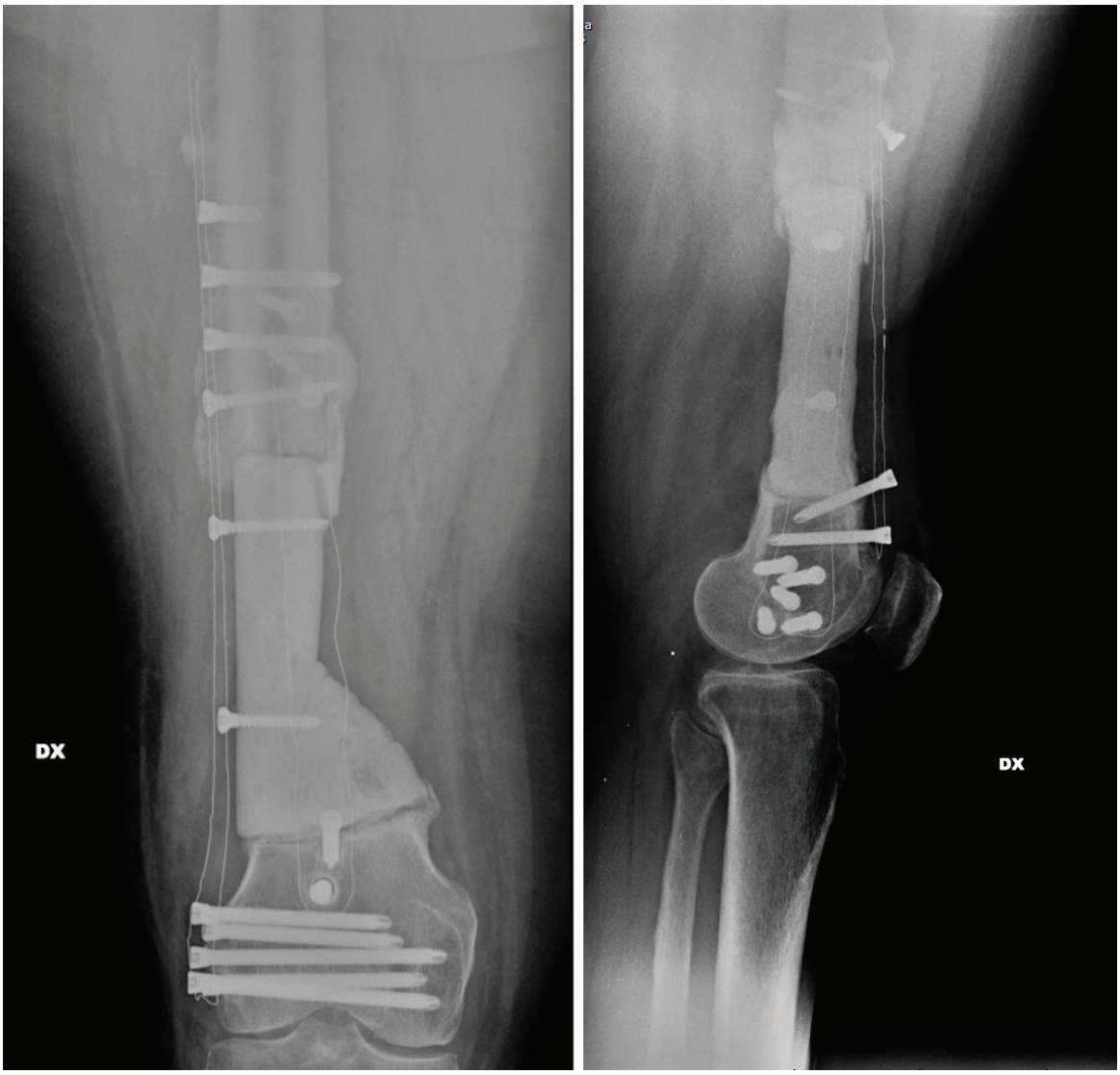


Figure 1. Implant Failure X-Ray

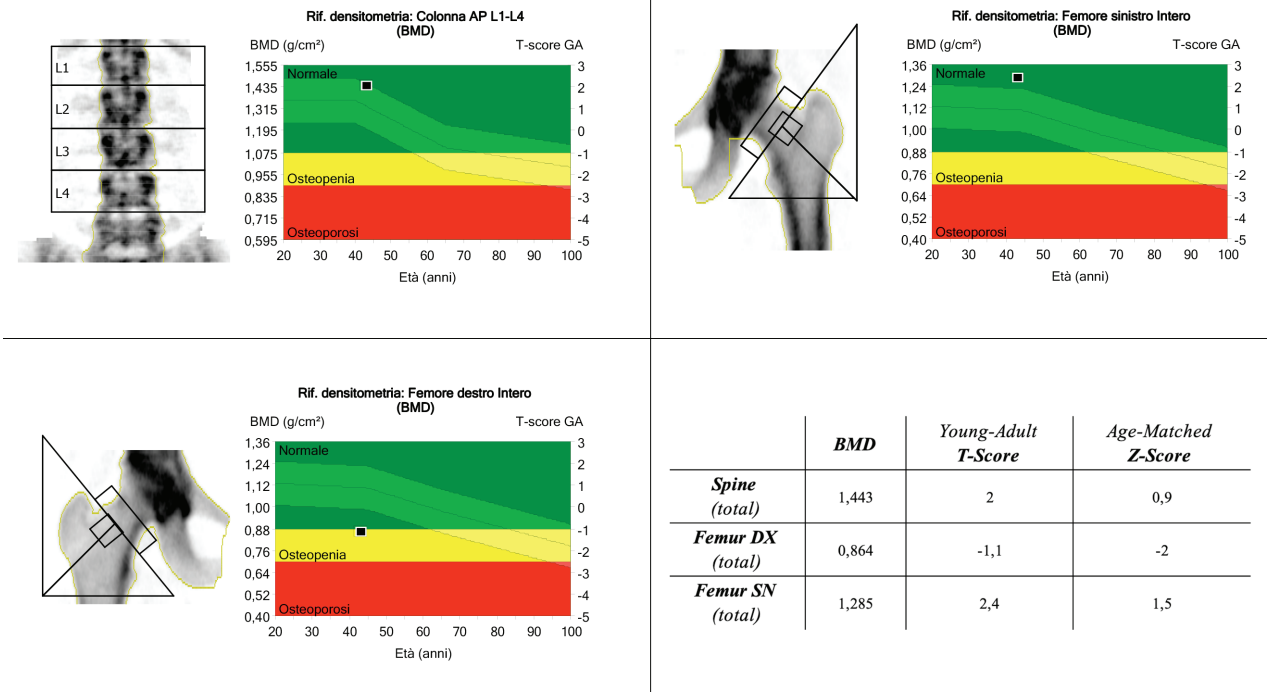
performed with distal femur resection and implantation of a megaprosthesis implant. The histological exam, in the latter case, was positive for malignant PEComa tumor. During the hospitalization a specific anamnestic collection focused on the bone fragility and osteoporotic risk factors was performed in addition to routine laboratory tests for bone metabolism (protein electrophoresis, complete blood count, 24-hour urine calcium excretion and creatinine levels, serum level of calcium, albumin, phosphorus, vitamin D, alkaline phosphatase, blood urea nitrogen and creatinine) and densitometric bone evaluation of lumbar spine and both hips. It was also performed a biopsy from quadriceps muscle of both legs. No personal or familiar risk factors for generalized osteoporosis were highlighted. Laboratory test showed only a slightly increased PTH (43 ng/L ; normal values 8 ng/L -40 ng/L). Hand grip test was performed and no significant differences between right and left side were appreciated, with values comparable with the mean ones in relation to age and sex[17]. Stand up and go test couldn't be performed because of the prior important disability due to the pathological condition of the affected leg. DXA screen showed normal values in all districts except for hip region on affected limb

(figure 2). The histological examination of the muscular biopsy showed a partial adipose substitution of muscular fiber, the presence of fibro-adipose stripes and partial muscular atrophy only on the affected leg (figure 3).

Discussion and Conclusion

Osteosarcopenia is a pathological condition, recently described, that consists in association between osteoporosis and sarcopenia. Osteoporosis is a pathology of skeleton but in some cases, it can afflicts only specific district (localized forms). The latter case is described in literature only related to lower limbs[18]. There are primary and secondary osteoporosis, including disuse osteoporosis [19]. Disuse osteoporosis is a secondary form of osteoporosis affecting specific skeleton sites and caused by loss of function. Nowadays no studies suggest that, in some cases, disuse osteoporosis can be associated with distrectual condition of muscle degradation fibres and consequent decreased muscle strength and performance, limited to a specific zone. In this case report, Authors points out that localized disuse osteoporosis can be associated with sarcopenia, determining a condition of local osteosarcopenia regardless of coexistence of generalized osteoporosis. In our case laboratory tests for bone metabolism and mineralometric exam excluded primary and secondary forms of osteoporosis (except for a slight secondary hyperparathyroidism due to low daily calcium intake). Furthermore, densitometric exams highlighted the presence of local reduced value of T-score and Z-Score on the affected side. Histological exams confirmed the presence of local tissue alterations such as a partial adipose replacement of the muscle fibres, the presence of fibro-adipose stripes and a partial muscle atrophy in the limb affected by disuse. Hand grip test results were normal for both hands. Stand up and go test couldn't be performed because of the prior disability.

The clinical case shows that localized forms of osteosarcopenia exists and a correct diagnosis and treatment can be useful to prevent the occurrence of fragility fractures but also to optimize surgical treatment and prevent surgical failures. Nevertheless, nowadays there aren't specific guidelines to treat local osteosarcopenic diseases and more studies are necessary to identify a correct treatment strategy.



	BMD	*Young-Adult* ***T-Score***	*Age-Matched* ***Z-Score***
Spine *(total)*	1,443	2	0,9
Femur DX *(total)*	0,864	-1,1	-2
Femur SN *(total)*	1,285	2,4	1,5

Figure 2. DXA exam (from left to right: spine, left femur, right femur, DXA values)

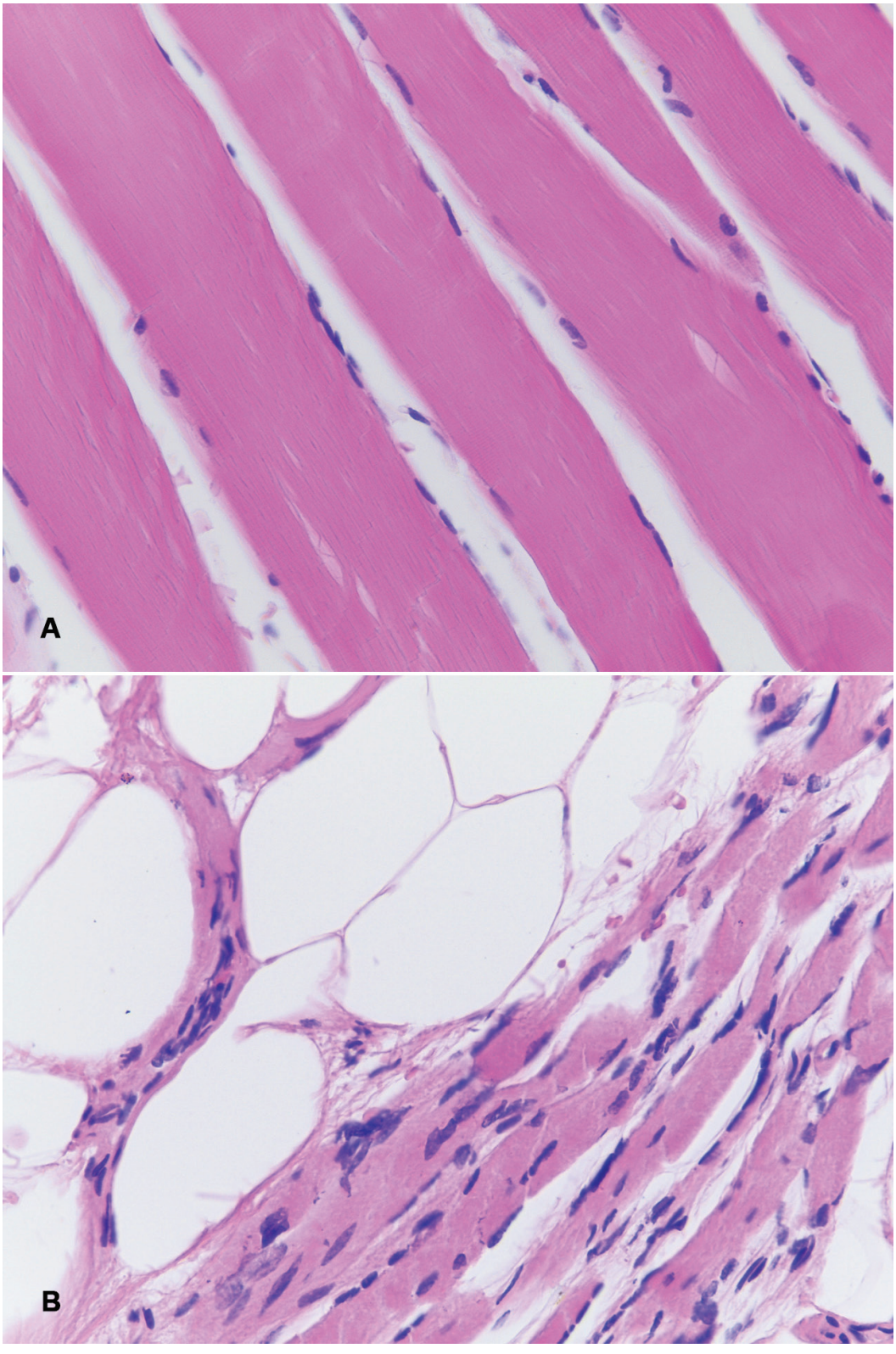


Figure 3. Presence of fibro-adipose stripes and a partial muscle atrophy in the limb affected by disuse (A: Left Femur, B: Right Femur)

"Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article".

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Received: 10 October 2020 - Accepted: 20 November 2020
Corresponding Author:
Gabriele Filoni
via Paradisa 2
56121 Pisa (PI) – E-mail: g.filoni@gmail.com
Fax 050993415