OLGU SUNUMU CASE REPORT

DOI: 10.31609/jpmrs.2021-84236

Sarcopenia and Frailty Under Teriparatide Treatment: Coincidence or Consequence

Teriparatid Tedavisi Altında Sarkopeni ve Kırılganlık: Tesadüf veya Sonuç

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This study was presented as an oral presentation in 2nd International and 12th Academic Geriatrics Congress, 24-28 April 2019, Antalya, TURKEY

ABSTRACT Osteoporosis is characterized by low bone mass and micro-architectural deterioration of bone tissue and causes increased fracture risk. In patients diagnosed with osteoporosis, anti-osteoporosis treatment should be arranged. Teriparatide is one of the anabolic drugs that reduces the risk of vertebral and non-vertebral fractures. Although, muscle weakness was reported as an adverse effect, to our best knowledge, there is no case presentation that takes attention sarcopenia as an adverse effect of teriparatide treatment. Sarcopenia is a muscle disorder that is related to adverse outcomes and seen in generally older people. Since the same genetic, mechanical, nutritional and endocrine factors may be responsible for the age-related muscle and bone loss, recently, the term of osteosarcopenia has been defined. Herein, we reported a case diagnosed with sarcopenia and frailty after teriparatide treatment and aimed to take attention for the possible relationship between teriparatide and sarcopenia.

Keywords: Osteosarcopenia; teriparatide; bone; muscle; ultrasound

ÖZET Osteoporoz, düşük kemik kütlesi ve kemik dokusunun mikromimarisinin bozulması ile karakterizedir ve kırık riskinin artmasına neden olur. Osteoporoz teşhisi konulan hastalarda, antiosteoporoz tedavisi düzenlenmelidir. Teriparatid, vertebra ve vertebra dışı kırık riskini azaltan anabolik ilaçlardan biridir. Kas güçsüzlüğü yan etki olarak bildirilmesine rağmen bildiğimiz kadarıyla, teriparatid tedavisinin yan etkisi olarak sarkopeniye dikkat çeken bir olgu sunumu yoktur. Sarkopeni, olumsuz sonuçlarla ilişkili olan ve genellikle yaşlı insanlarda görülen bir kas bozukluğudur. Yaşa bağlı kas ve kemik kaybından aynı genetik, mekanik, beslenme ve endokrin faktörler sorumlu olabileceği için, son zamanlarda osteosarkopeni terimi tanımlanmıştır. Burada teriparatid tedavisi sonrası sarkopeni ve kırılganlık tanısı alan bir olguyu sunduk ve teriparatid ile sarkopeni arasındaki olası ilişkiye dikkat çekmeyi amaçladık.

Anahtar Kelimeler: Osteosarkopeni; teriparatid; kemik; kas; ultrason

Osteoporosis (OP) is characterized by low bone mass and micro-architectural deterioration of bone tissue - causing increased fracture risk.[1] The most important aim of the OP management is to reduce the fracture risk and to prevent the fracture and related complications.[2] Hence, bone mineral density (BMD) measurement and fracture risk assessment should be done for patients at risk. In patients diagnosed with OP, anti-osteoporosis treatment should be arranged. While bisphosphonates or denosumab are the initial treatment recommendation, teriparatide and abaloparatide are suggested in postmenopausal women who have OP at very high risk of fracture.[3]

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Peer review under responsibility of Journal of Physical Medicine and Rehabilitation Science.

Received: 04 May 2021 ***Received in revised form:*** 12 Jun 2021 ***Accepted:*** 28 Jun 2021 ***Available online:*** 06 Jul 2021

Teriparatide is one of the anabolic drugs that reduces the risk of vertebral and non-vertebral fractures. Nausea, pain in the limbs, headache, dizziness, transient hypercalcemia, muscle weakness, loss of appetite, unusual tiredness and weight loss are common adverse effects of subcutaneous teriparatide administration.[1] Although, muscle weakness was reported as an adverse effect, to our best knowledge, there is no case presentation that take attention sarcopenia as an adverse effect of teriparatide treatment. For this reason, we aimed to make an awareness for the possible relationship between teriparatide and frailty/sarcopenia.

CASE REPORT

An 83-year-old woman was seen for lower limb muscle weakness, knee pain, fatigue, and unintentional weight loss (more than 10% of the body weight). She had been diagnosed with severe senile OP one year ago when she had been given subcutaneous teriparatide treatment with the following BMD T scores (L1-L4; -4.4, femur neck; -2.7). At that time, her 25-OH vitamin D level was 25.7 ng/mL and parathormone (PTH) level was 76.5 (15-65) pg/mL. She was impaired in daily life activities, especially during standing and climbing stairs. She also declared that her symptoms had started after the OP treatment. Her medical history was otherwise unremarkable.

Physical examination revealed quadriceps muscle weakness (4/5 bilaterally). Complete blood count, erythrocyte sedimentation rate, C-reactive protein, creatine kinase levels, liver/renal/thyroid functional tests were all within normal ranges. 25-OH vitamin D level was 16.9 ng/mL and PTH level was 56.5 (15-65) pg/mL. Parathyroid ultrasonography (US) was normal. Nerve conduction studies and electromyography were also unremarkable. US imaging revealed muscle thicknesses of 13 mm for rectus femoris and 6 mm for rectus abdominis. Bioelectrical impedance analysis showed that fat mass was 31.7%, and skeletal muscle mass index was 7.8 kg/m^2. Grip strength and gait speed were 19 kg and 0.74 m/sec, respectively. The normal cut-off values were given in Table 1.[4-6] Echocardiography revealed tricuspid valve regurgitation and ejection fraction was 63%. Control BMD T scores were as follows; L1-L4; -4.0, femur neck; -3.3. She was diagnosed with sarcopenia and frailty possibly due to teriparatide treatment.[7,8] The treatment was changed to i.v. zoledronic acid 5 mg/year together with calcium and vitamin D replacement. Progressive resistive exercises for quadriceps and abdominal muscles were prescribed as well.

The patient was informed about the case report and informed consent form was obtained.

DISCUSSION

Teriparatide is an anabolic hormone analogue used in the treatment of severe OP. In the current literature, there is only one case who had muscle weakness (myopathy) after teriparatide usage for OP treatment.[9] Patients with secondary hyperparathyroidism due to chronic uremia may have symptoms of myopathy. Muscle dysfunction is generally attributed to excessive PTH levels.[10] It was shown that both intact PTH and its amino-terminal fragment increase muscle proteolysis and the release of alanine and glutamine.[11] In addition, excessive PTH inhibits long-chain fatty acids oxidations and reduces the energy source required for skeletal muscle and myocardium. PTH affects energy metabolism at different stages such as production, transport and usage.[10] Therefore, it may influence muscle tissue and may cause muscle disorders such as weakness, myopathy, and sarcopenia.

TABLE 1: Cut-off values that are used for the evaluated parameters.

Parameters	Female	Male	Reference
Grip strength	20 kg	30 kg	Cruz-Jentoft AJ et al.[4]
Gait speed	0.8 m/s	0.8 m/s	Cruz-Jentoft et al.[4]
SMI	7.4 kg/m^2	9.2 kg/m^2	Bahat et al.[5]
RF thickness	16 mm	20 mm	Minetto et al.[6]

RF: Rectus femoris muscle; SMI: Skeletal muscle mass index.

Sarcopenia is defined as age-related loss of muscle mass and function that is related to adverse outcomes in generally older adults. Thus, for the diagnosis of sarcopenia, muscle mass and muscle function should be evaluated.[4] In addition, specific muscle thicknesses can also be assessed in sarcopenia. Rectus femoris muscle thickness <16 mm for females (<20 mm in males) was diagnosed as low muscle mass.[6] In our case, although laboratory and electromyography findings were normal, regional (i.e. anterior thigh and abdominal) muscle measurements and functional parameters were low. Accordingly, she was diagnosed with sarcopenia and also frailty. Although it is not a common adverse effect of teriparatide, we should keep muscle disorders in mind, especially in patients at risk for secondary hyperparathyroidism, and sarcopenia/frailty.

In recent years, older people who have the combination of low BMD and low muscle mass, strength, and/or physical function have been defined as osteosarcopenia.[12] The same genetic, mechanical, nutritional and endocrine factors may be responsible for the age-related loss of muscle and bone masses.[12] It has been reported that the prevalence of osteosarcopenia varies between 4.7% and 40% in different populations.[13] Although there is no accepted treatment so far, adequate levels of calcium, vitamin D, protein intake and regular exercise treatment are highly recommended.[12] In a 3-year follow-up study, although the authors have stated that denosumab improves muscle mass and strength in postmenopausal women with OP, randomized controlled studies are needed for further evidence.[14]

Although we were not able to exclude a possible diagnosis of sarcopenia in our patient before the teriparatide treatment and although we did not have any detailed regional or total skeletal muscle mass measurements; we propose that teriparatide treatment might have induced/accelerated the development of sarcopenia and frailty. Moreover, vitamin D deficiency and secondary hyperparathyroidism are common in the older people.[15] Although the relationship between teriparatide and sarcopenia/frailty is not well established, the mechanism of PTH on the catabolism and energy metabolism of muscle may be responsible for the possible side effects. Therefore, patients who are treated with teriparatide and who are not followed closely can be at risk of adverse effects. To this end, clinicians prescribing teriparatide treatment should consider such a possibility and perform screening studies accordingly. For sure, prospective studies will clarify this situation.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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