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Research Article

The Global Pandemic's Detrimental Effect on Osteoporosis Care

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Abstract

Objective: To assess whether restrictions in medical care related to the impact of the Coronavirus 2019 (COVID-19) pandemic affected fracture incidence due to postponed denosumab therapy and to identify ways to adapt to interruptions in osteoporosis therapy during the pandemic.

Methods: We reviewed the records of a 64 year old female diagnosed in 2018 with osteoporosis undergoing treatment with denosumab until the pandemic crisis. We present her case to demonstrate the consequence of delaying denosumab administration, and we reviewed the literature on denosumab.

Results: We found that COVID-19 represents a major and sudden health crisis and that there is no clear answer on which treatment modality is ideal during a global pandemic. There are studies showing that discontinuation of denosumab leads to rapid Bone Turnover Rebound (BTR) and rapid loss of Bone Mineral Density (BMD) potentially leading to an increased incidence of Vertebral Fractures (VF). We found that if a patient is at high risk for secondary fractures the recommendation is to continue denosumab therapy. Our case study demonstrated a potential serious outcome with interrupted or delayed osteoporosis therapy.

Conclusion: This case demonstrates that delaying osteoporosis therapy can be detrimental leading to an increased risk of fractures. We suggest that a temporary delay in scheduled denosumab administration may necessitate an alternative intervention such as starting a bisphosphonate temporarily. We strongly advise continued therapy in high-risk individuals during the COVID-19 global pandemic. Further studies need to be done to determine the optimal treatment in this scenario.

Keywords: Global pandemic; COVID-19; Coronavirus; Osteoporosis

Introduction

Since the Coronavirus 2019 (COVID-19) pandemic "shelter in place" orders have been in effect to reduce transmission of the disease doctors' offices have moved to telehealth visits and halted non-essential treatments. Endocrinologists have delayed treatment with denosumab, a monoclonal human antibody, administered by injection every 6 months in a physician office setting. Denosumab is used to treat osteoporosis and reports have shown rebound Vertebral Fractures (VF) when treatment is delayed. Denosumab use has been temporarily held off partly due to its known increased risk of infection and because many physicians have for a time ceased office visits. We will present a case of interrupted denosumab treatment, the risks of interruption, and options for managing osteoporosis during COVID-19 era restrictions.

Description

A 64-year-old female presented to her orthopedic surgeon in late June 2020 with a 1-month history of right-sided lumbar pain. On imaging, the patient was found to have sustained an acute L1 compression fracture and acute on chronic L2 compression fracture. The patient reported a history of osteoporosis and tachycardia. Medications included Prolia (denosumab), started in 2018, and Verapamil SR. The patient also took calcium and vitamin D supplements. Surgical and family history was non-contributory. The patient stated her injection for Prolia was due in March of 2020 but was postponed due to the pandemic. On physical examination the gait was non-antalgic. Shoulders and iliac crests were level. On palpation, there was tenderness noted at the paraspinous and lumbar region. Paraspinal muscle tone was normal. Muscle testing demonstrated full strength at bilateral hip flexors and ankle dorsiflexion. Patellar and Achilles reflex bilaterally was 2/4. Negative clonus. Sensation was intact. Special testing showed a negative Faberes test on the left side. Straight leg raise testing was negative bilaterally. Previous Dual-energy X-ray Absorptiometry (DXA) from April 2018 showed an L1-L4 T score of -4.3. Recent DXA June 2020 showed an L1- L4 T score of -3.6. Lumbar x-ray showed new compression fracture deformity at L1 and further compression deformity noted at L2. There were degenerative changes throughout but no spondylolisthesis. Subsequently, an MRI was ordered without contrast showing acute to subacute compression fractures of the L1 and L2 vertebral bodies. There was an acute on chronic fracture at L2 from a prior compression noted in 2018 producing a combination of inferior and new superior loss of vertebral body height. There was diffuse lumbar spondylosis without any significant central spinal stenosis. Left foraminal stenosis was noted at L5-S1. There were small left-sided disc herniations at L3-L4 and L4-L5. There were no signs of bone marrow abnormality and no signs of metastatic disease. The patient was recommended for re-initiation of Prolia along with conservative treatment. Several weeks later the patient noted improvement in her back pain.

Discussion

This case demonstrates the effect of a global pandemic on clinical medicine and prescribing characteristics of denosumab. Due to the pandemic, our patient had a temporary interruption of

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her previously scheduled denosumab injection and subsequently suffered two new VF. The consequences of delaying or interrupting treatment in high-risk populations have led to increases in VF, morbidity, and healthcare spending. With recent surges in different parts of the nation, a collaborative effort needs to be put into place to prevent subsequent fractures. Our discussion will address a new treatment approach in the setting of the COVID-19 pandemic as pertaining to denosumab therapy. Since the beginning of the COVID-19 global pandemic, patient care has adjusted to new social distancing guidelines. Schedules in clinics are absent or reduced to only what is deemed urgent. Telehealth has expanded but does not include the administration of injectable medications and infusions. Radiology departments are limiting imaging to essential testing only. Thus, imaging modalities such as DXA scans are being performed on a limited basis. Additionally, health care providers are delaying DXA scans and patients are reluctant to schedule DXA scans or are deferring DXA scans to reduce the risk of COVID-19 exposure [1,2]. We urge patients who are at high risk for fracture and not on treatment to continue imaging modalities with proper precautions. Decreased immunity during COVID -19 pandemic is a cause for concern. Theoretically, since denosumab is a known immune modulator it can increase the risk of infections. A recent meta-analysis performed on randomized control trials showed that denosumab has a higher incidence of GI and ENT infections. Despite the increased risk of infections, denosumab did not change mortality. Furthermore, the study confirmed that in comparison to other osteoporosis agents, such as PTH analogs and bisphosphonates, there was no increased risk of infection [3]. During the pandemic, we recommend the continuation of denosumab since infection risk is similar to other agents and infections are not life-threatening. Due to the pharmacokinetics of denosumab, discontinuation leads to rapid bone turnover leading to increased incidence of VF [4]. Unfortunately, delaying osteoporosis treatment can lead to new fractures as demonstrated in our case report. Denosumab, a human monoclonal antibody, prevents bone resorption, increases bone mineral density, and reduces the risk of fractures. As mentioned, any delay in treatment can increase the risk of bone turnover leading to rebound VF. A 2017 Journal of Clinical Endocrinology and Metabolism case series showed 9 cases of rebound fracture after stopping denosumab. VF was noted to occur rapidly after treatment was suspended, approximately 9-16 months after the last injection. The case series suggested bisphosphonate use, before or after, denosumab may reduce bone turnover. Furthermore, the study suggested the use of bisphosphonates if denosumab injection cannot be administered [5]. Based on available data, we recommend the use of bisphosphonates if denosumab therapy must be delayed. Lastly, if a patient is at high risk for repeat fracture, the recommendation is to continue treatment. Studies suggest that the strongest predictors of fracture after stopping therapy are older age and bone mineral density at discontinuation. Women with a hip T score below -2.5 after 3 years of therapy, who are older, and non-adherent to recommendations are at the highest risk for new fractures and thus should receive continued therapy for osteoporosis. This case highlights the need to adapt to how we administer osteoporosis medications during the pandemic. The National Osteoporosis Foundation (NOF) has released options for treatment as they recognize the impact of delaying denosumab therapy. The NOF statement reviews new Medicare options to continue treatment. Medicare is now allowing the injection of osteoporosis drugs via two new methods in the home setting: 1. Health Care Providers can administer the medication in the patient's home 2. The patient can be deemed homebound allowing for services that include injections at home. Although both methods seem similar, the billing may vary. Therefore, it is important to clarify with Medicare before treatment. Due to the COVID-19 pandemic, Amgen, maker of the brand name Prolia (denosumab), has given a temporary allowance for injection of Prolia by the patient or his/her caregiver. We recommend that if needed, denosumab can be administered by alternative methods. However, it is imperative to discuss with the patient to determine which technique is safest and covered by insurance. The burden of suspending osteoporosis therapy is not only clinically detrimental but also a major public health issue. In 2015, two million Medicare patients sustained over two million fractures; the majority of these fractures were in women. Unfortunately, 90% of those that suffered hip fractures were hospitalized and 30% died within a year. Secondary fractures cost Medicare 6.3 billion dollars. However, 50% of repeat fractures can be mitigated with treatments that are well tolerated. If secondary fractures were reduced by approximately 20%, it is estimated this could save 1.2 billion Medicare dollars [6]. In addition to the economic impact associated with repeat fragility fractures, patients present with more debilitating complications. Subsequent fractures are associated with a higher spine deformity, an increased spinal kyphotic angle and severe back pain [7]. These clinical manifestations can result in both acute and chronic effects on patients' quality of life and overall well-being. We urge physicians to continue the treatment of osteoporosis during the pandemic to prevent further healthcare burden. This case demonstrates the effect of a global pandemic on clinical medicine in regards to the prescribing characteristics of denosumab. The aforementioned hurdles have created a challenge in identifying new osteoporosis cases, evaluation of osteoporosis management, and continuation in the administration of injectable medications whose effectiveness relies on adherence to regular interval dosing. With recent surges of COVID-19 cases in different parts of the nation, a collaborative effort needs to be put into place to prevent subsequent fractures [1]. In summary, if a patient is at high risk for repeat fracture, the recommendation is to continue denosumab treatment [4]. If halting denosumab temporarily, we urge physicians to start another osteoporosis agent such as bisphosphonates [5]. We believe that adopting a new approach to osteoporosis therapy will prevent further fractures and hospitalization during the COVID-19 global pandemic.

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