Denosumab/ibandronic acid/zoledronic acid

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Medication-related osteonecrosis of jaw: case report

A 77-year-old woman developed medication-related osteonecrosis of jaw (MRONJ) during treatment with denosumab, ibandronic acid and zoledronic acid for osteoporosis and invasive ductal breast cancer with bone metastases [*not all dosages stated; time to reaction onset not clearly stated*].

The woman presented with MRONJ of the mandible in April 2014 to current facility. She had been diagnosed with invasive ductal breast cancer in November 2000 followed by bone metastases and a pathological right femoral neck fracture. In February 2001, she had received neoadjuvant therapy with docetaxel and doxorubicin followed by breast conserving surgery and lymphadenectomy. Finally, she had received cyclophosphamide, fluorouracil and methotrexate combined with exemestane. Subsequently, she developed severe osteoporosis leading to recurrent sintering fractures of lumbar and thoracic vertebral bodies followed by multiple stabilizing surgeries. Thereafter, she received oral ibandronic acid [Bondronat] from March 2001 to August 2003 followed by IV zoledronic acid until November 2013. In December 2013, she started receiving SC denosumab 120mg monthly. On current presentation in April 2014, she showed exposed oral jawbone in region 38 and 37 at the lingual rim of the mandible. She reported pain and showed signs of moderate infection (stage 2 MRONJ).

The woman was treated with unspecified antibacterials for 3 weeks resulting in improvement in infection. Additionally, local mouth rinses with chlorhexidine and green tea were recommended. In July 2014, she discontinued denosumab therapy, followed by a single application in September 2014. Due to necessity of oncological treatment, she restarted on denosumab and exemestane in November 2014. Until 2018, she continued with local mouth rinses. Due to signs of boosted infection and acute pain, she was treated with sultamicillin for short period for a total of nine instances. She still preferred conservative treatment over surgical therapy. In April 2018, examination showed bone exposure in regions 36 to 38 of the lower left jaw and a fistula and palpable bone at the right molar in region 46. The panoramic radiograph revealed a mandibular involvement with diffuse radiopaque areas between radiolucent areas. In May 2018, an ^{18}F-fluoride positron emission tomography/computed tomography (PET/CT) of the jaw showed substantially increased ^{18}F-fluoride uptake in regions 38 to 47 of the mandible with a focal gap in region 36, with medullary sclerosis and cortical thickening with confluent periosteal reaction and focal cortical erosion in the regions 37 to 42, whereas the regions 43 to 47 were only subtly sclerotic without cortical thickening. These findings were consistent with stage 3 MRONJ. She was admitted to hospital and was treated with ampicillin/sulbactam and metronidazole with resolution of pain within 3 days. After 4 days, she was discharged on sultamicillin. She received sultamicillin for 45 days in total. A follow-up ^{18}F-fluorine PET/CT scan in September 2018 revealed no changes in regions 38 to 42, whereas the bony sclerosis was slightly increased in regions 43 to 47 with a slight reduction of ^{18}F-fluoride uptake. These findings were consistent with clinical stage 1 MRONJ. Conservative treatment with local mouth rinses was continued until April 2019 when an extraoral fistula appeared at the left mandible. Observation followed until June 2020 and follow-up was not possible due to COVID-19 infection risk. Currently, she was clinically stable with low infection signs and moderate purulent discharge at the extraoral fistula. In November 2019, denosumab was discontinued and exemestane was continued.

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