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Case Report

Pulsed Radiofrequency of the Trigeminal Nerve for Refractory Pain Associated with Medication-Related Osteonecrosis of the Jaw: A Case Report

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SUMMARY

Background: Medication-related osteonecrosis of the jaw (MRONJ) is a severe adverse drug reaction related with exposure to antiresorptive or antiangiogenic agents. Pain control is one of the main treatment goals.
Methods: We report the case of a 63-year-old man with MRONJ who was treated for bone metastases from lung adenocarcinoma. After 11 months of denosumab treatment, he complained of right mandible pain and was diagnosed with stage 2 MRONJ. Although bone necrosis progression was controlled by conservative treatment, the patient still suffered from refractory pain. Pulsed radiofrequency of the mandibular branch of the trigeminal nerve was done for the patient.
Results: Pulsed radiofrequency of the mandibular branch of the trigeminal nerve resulted in successful pain control that remained effective until the patient expired.
Conclusion: This is the first report of using pulsed radiofrequency of the mandibular branch of the trigeminal nerve to treat intractable pain associated with MRONJ.

1. Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is a severe adverse drug reaction that is diagnosed based on the presence of exposed bone in the maxillofacial region after exposure to antiresorptive or antiangiogenic agents for treating osteoporosis or bone metastases in patients with cancer. The management of MRONJ includes medications (antibiotics, anti-inflammatory agents, and analgesics), optimal oral hygiene, wound care, laser therapy, and surgical management in advanced stages. However, there is still limited literature focusing on pain control in patients with MRONJ. To our knowledge, this is the first report that documents successful treatment of refractory pain associated with MRONJ using pulsed radiofrequency of the trigeminal nerve.

2. Case report

Following Institutional Review Board approval (No. 17MMHIS 097e), we report a 63-year-old man who had been suffering with lung adenocarcinoma with multiple bone metastases since 2015, for which he underwent treatment with gefitinib. In addition, since September 2015, piroxicam 20 mg sachets and acetaminophen 325 mg/tramadol hcl 37.5 mg tab were prescribed for treating metastatic bone pain. From November 2015 to September 2016, denosumab 120 mg was administered monthly to prevent skeletal-related events associated with bone metastases. In September 2016, the patient visited the oral and maxillofacial surgeon due to right mandible pain and difficult chewing. Intraoral examination revealed soft tissue swelling and tenderness over the right lower edentulous ridge without pus formation. Periapical radiography revealed necrotic bone over the lower right alveolar ridge. He was diagnosed with stage 2 MRONJ, and therapies comprising oral antibiotics (amoxicillin trihydrate 80 mg/ml and clavulanate potassium 11.4 mg/ml syrup 15 ml for every 12 hours), chlorhexidine gargling, and oral cleaning were initiated. Denosumab was discontinued.

Due to persistent right mandible pain, the patient sought care at a pain clinic in October 2016. The numeric pain rating scale (NRS) for pain was found to be 6–8 of 10 when resting. Fentanyl patch 12 μg/h and sublingual buprenorphine 0.2 mg were prescribed initially, which decreased the NRS to 3–5 after 1 week. He received clodronate instead of denosumab in October 2016 and resumed denosumab 2 months later because of improvement in his MRONJ, and oral antibiotics was discontinued in November 2016. The patient complained that the right mandible pain exacerbated since December 2016, and hence the dosage of fentanyl patch was increased to 25 μg/h. However, he showed only little improvement. Accompanied with exacerbated right mandible pain, he suffered from difficult chewing, and poor oral hygiene was noted. Pus formation over the right lower edentulous ridge was observed, and thus oral antibiotics syrup (amoxicillin trihydrate 80 mg/ml and clavulanate potassium 11.4 mg/ml syrup 15 ml for every 12 hours) was prescribed and continued to January 2017. In December 2016, we performed a diagnostic block of the mandibular branch of the trigeminal nerve with lidocaine. The injection technique has been

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described in a previous study.[1] The NRS decreased from 5 to 2 immediately but lasted for only 30 min.

In January 2017, we performed pulsed radiofrequency therapy of the mandibular branch of the trigeminal nerve. The radiofrequency cannula tip was placed at the infratemporal surface of the greater wing of the sphenoid bone, immediately anterior to the foramen ovale, under fluoroscopic guidance (Fig. 1) and further verified by nerve stimulation. The radiofrequency neuromodulation was performed three times at 48 °C for 360 s.

The patient experienced immediate pain relief after the pulsed radiofrequency treatment, and the NRS reached 3–5 after 1 week and then gradually decreased to 0–3 without significant complications. The fentanyl patch 25 μg/h and piroxicam 20 mg sachets were maintained for treating headache, which was suspected to be caused due to skull metastasis. The right mandible pain did not recur ever since the pulsed radiofrequency treatment. Also, neither progression of jaw necrosis nor pus formation over the right lower edentulous ridge was noted. Unfortunately, the patient expired due to sepsis and multiorgan failure in July 2017.

3. Discussion

The treatment goals of established MRONJ include control of pain and secondary infection and prevention of bone necrosis progression. Considering the benefit of reducing skeletal-related events, the continuation of antiresorptive therapy has been supported and prioritized in oncology patients.[2] For patients with stage 2 MRONJ, conservative treatments, including systemic antibiotics, oral antibacterial mouth rinse, and pain control, are considered as the first-line strategies. Surgical treatment such as debridement or bone resection could be considered if the MRONJ is refractory to conservative treatment. However, cessation of antiresorptive agents for at least 3 months is recommended if operation is considered. Patients who depend on the benefits of antiresorptive agents, or those who have higher perioperative risks, may not be suitable candidates for operation.[3] Hyperbaric oxygen therapy can also be considered as an adjunct to other therapies for symptomatic relief.[4] However, it can be used only in cancer-free patients. Currently, there is a lack of studies describing trigeminal nerve block for pain control in patients with MRONJ.

The patient in the present case report had no bone necrosis progression after antibiotic treatment, and hence surgical treatment was not considered by the oral and maxillofacial surgeon. However, the right mandible pain persisted, which interfered with his life quality and caused difficult chewing and swallowing. Previous research has demonstrated that conventional radiofrequency is an effective method to treat trigeminal neuralgia, and severe adverse effects such as sensory loss, dysesthesia, and anesthesia dolorosa exist. The effect of pulse radiofrequency usually does not last long, but high-voltage and extended duration may improve the outcome.[5] Since conservative treatment failed to alleviate the patient's pain, we chose pulsed radiofrequency for neural modulation.

To our knowledge, this is the first report demonstrating the successful control of refractory pain associated with MRONJ achieved using pulsed radiofrequency of the mandibular branch of the trigeminal nerve. The effect lasted for 6 months until the patient expired without severe adverse events. Pulsed radiofrequency may be considered in patients with refractory pain associated with MRONJ who are not suitable candidates for surgical treatment. Further investigation is needed to determine the timing of intervention, patient selection, and appropriate regimen.

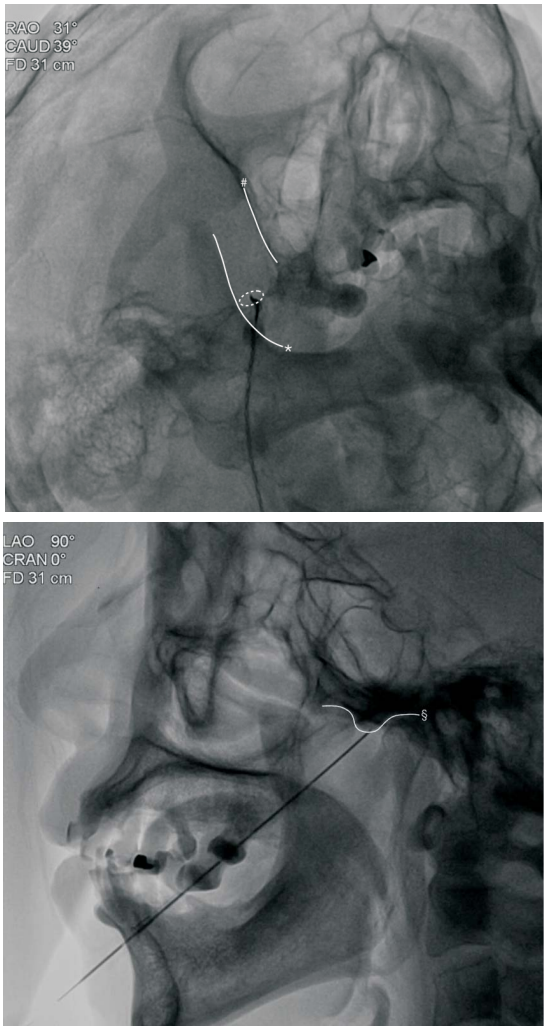

Fig. 1. Under fluoroscope, the radiofrequency cannula tip was placed at the infratemporal surface of the greater wing of the sphenoid bone, immediately anterior to the foramen ovale. Dash line: foramen ovale. * Medial border of the mandibular ramus. # Lateral border of the maxilla. § Skull base.

Conflict of interest

There is no conflict of interest to declare.

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