

Case report of a spontaneous occurrence of MRONJ

Abstract

This is a case report of a patient with bone cancer who developed medicine-related osteonecrosis of the jaws (MRONJ). The case management, lesion progression, sequestration and sequelae are discussed.

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Introduction

This 68-year-old male developed a lesion of medicine-related osteonecrosis of the jaws (MRONJ) on the lingual surface of the right posterior mandible. The patient had renal cancer five years prior to the appearance of the MRONJ lesion. Following removal of the right kidney, a scan showed that renal cancer nodules had spread to involve the ribs. This was treated with various forms of chemotherapy and he had been on intravenous zoledronate (Zometa) for approximately two months prior to the appearance of the lesion.

Zoledronate is one of the bisphosphonate group of medicines. Bisphosphonates are used in the treatment of osteoporosis and in the prevention of bone complications from cancers. In this case, the zoledronate was used to lower abnormally high blood calcium levels. Here it has the double benefit of reducing the amount of calcium release from the bones into the bloodstream and helping to reduce cancer spread.

In 2003 Marx reported avascular necrosis of the jaws following treatment with zoledronate.¹ Since then there have been numerous scientific publications on MRONJ. A recent review article by Cooney *et al.* in this journal summarises the aetiology, risk factors, incidence and preventive strategies of MRONJ.²

The Cochrane Database of Systematic Reviews examined interventions for managing MRONJ. However, it concluded that at present there is not a sufficient evidence base to support any specific treatment strategy.³ Pichardo and van Merkesteyn have outlined a surgical approach for treating MRONJ. In their cohort study, they achieved a high success rate with a combined surgical and antimicrobial treatment protocol. After a five-year follow-up of their cases, they concluded that their combined surgical and antibiotic protocol is the treatment of choice at all stages of bisphosphonate-related osteonecrosis of the jaws (BRONJ).⁴

This patient was managed conservatively in a general dental practice setting, with hygiene visits every four to six weeks combined with daily use of chlorhexidine mouthwash.

Case

This 68-year-old male is a non-smoker. He had renal cancer five years prior to

this point with surgical removal of his right kidney in 2015. Follow-up scans showed localised spread of the renal cancer nodules to the pleural space and the adjacent ribs.

Initial drug treatment was with Sutent, which is a targeted therapy for renal cancer. This continued for approximately one year. This was followed by another year on nivolumab from August 2016 to July 2017. Nivolumab is an immunotherapy drug, which uses principles of the immune response to fight cancer. The patient was then returned to Sutent treatment for another year. In November 2018 he developed hypercalcaemia. This was treated with monthly intravenous administrations of zoledronate for two months. His current treatment is now cabozantinib 40mg, which is proving very successful in his case management. This is a targeted chemotherapy drug that works by slowing or stopping cancer cells. He also takes 2mg dexamethasone (a corticosteroid) daily. During the course of the examination in December 2018, a small area of what appeared to be exposed bone was noticed on the lingual surface of the right mandible. The lesion was on an edentulous area anterior to the last standing molar (**Figure 1**). The lesion was asymptomatic. A dental panoramic radiograph was taken, which revealed no abnormality, but it did show some areas of increased radiopacity in the edentulous bone superior to the mylohyoid ridge (**Figure 2**).

The patient was made aware that he had a potentially severe adverse drug reaction. Clinical photographs and dental findings were communicated with his oncologist. His medication was not changed by the oncologist, as his current medications were managing his cancer and his quality of life, and there had been some challenges in achieving this. The patient was reluctant to seek the opinion of a specialist oral surgeon and it was agreed that he could be managed conservatively in the general dental practice setting.



FIGURE 1: December 21, 2018. Initial appearance of lesion.



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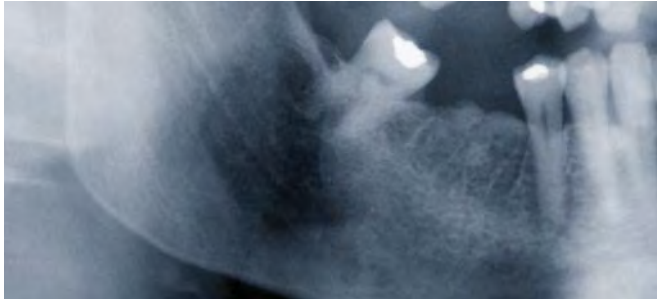


FIGURE 2: Radiographic appearance.



FIGURE 3: March 2019.



FIGURE 4: April 2019.

The treatment plan was for daily chlorhexidine mouthwash and monthly hygiene visits and review. On each subsequent hygiene visit the lesion was monitored and a photograph was given to the patient to aid communication with the oncologist.

By March 2019 the lesion had progressed to give two distinct peaks of exposed, very white bone (**Figure 3**). The exposed bone did not cause pain but was a minor irritant to the tongue. In April 2019 the peaks of the exposed bone had joined up to display approximately 15mm x 5mm of sequestrum (**Figure 4**). On the October 2019 visit, it was noted that the protruding bone appeared loose to probing. The bone separated from the mandible and left an erythematous ulcerated area (**Figure 5**). This procedure was done without local anaesthetic as the sequestrum of bone was ready to come away. The



FIGURE 5: October 2019.

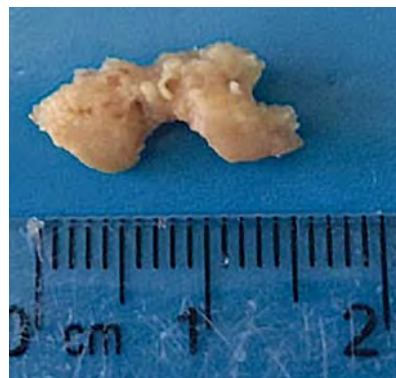


FIGURE 6: Sequestrum.



FIGURE 7: December 2019.

sequestrum measured approximately 15mm by 5mm and was sent for histological analysis (**Figure 6**). The histology report stated that it was "a fragment of necrotic/non-viable bone showing abundant bacterial overgrowth".

The December 2019 visit showed healing of the bone defect leaving a deep concavity with mucosal coverage. However, a new area of bone sequestrum had appeared mesial to the initial lesion (**Figure 7**). A further dental panoramic radiograph was taken to check for any further pathology and to check the roots of the molar. Nothing abnormal was noted (**Figure 8**).

Discussion

Initially, it is important for the dentist to rule out that the lesion is a metastatic

spread of the renal cancer or a mouth cancer. Together, the clinical examination, medical history and communication with the oncologist all aid the diagnosis of MRONJ.

MRONJ is more commonly associated with extractions and dental treatment.⁵ However, this lesion could be considered to have developed spontaneously following a short period of intravenous zoledronate to treat hypercalcaemia. Cooney *et al.* provided a useful table of risk factors in their recent publication.² The medical history suggests that while the MRONJ lesion may have been precipitated by intravenous Zometa, the risk of developing MRONJ is potentiated by concomitant therapy with corticosteroids and the underlying medical condition involving therapy for the malignancy. Khominsky and Lim describe a case report of a similar presentation to this one. In it they query that the lesion should be called spontaneous, as it occurs at the mylohyoid ridge. They consider that an area of underlying protruding bone is a causative factor.⁶ In this case, radiographic evidence suggests that the lesion is superior to the mylohyoid ridge.

In the Khominsky and Lim case the patient reported discomfort after four months and a sequestrectomy was performed under local anaesthetic.⁶ Luckily in this case the sequestrum came adrift with time.

The Cochrane Review describes the treatment regime used in this case as “standard care”, i.e., regular check-up visits combined with the use of chlorhexidine mouthwash. The review compared standard care to standard care augmented with hyperbaric oxygen treatment. It found that the latter did not significantly improve healing of MRONJ.³

The incidence of MRONJ has been quoted as approximately 1% by Cooney *et al.*² However, anecdotally the incidence appears to be higher. It is possible that the condition is under-reported as it falls between many stools: dentists, dental specialists, doctors and oncologists.

An enquiry to the Health Products Regulatory Authority (HPRA) revealed that the authority had listed six suspected adverse reactions of MRONJ for the period January 1, 2014 to October 31, 2019. The use of HPRA listings comes with their caveat that “the information comes from a variety of sources; an inclusion of an event does not necessarily mean that it has been caused by the medicine in question and that the information does not represent the opinion of the HPRA”.

Dentists who come across MRONJ should report the adverse reaction to the HPRA. In this regard it is also advisable to open a channel of communication with the patient’s oncologist or care team.

MRONJ has been divided into four stages. Stage 0 is an unexposed variant. Stage 1 displays bone exposure. Stage 2 has bone exposure with infection present and a pathological fracture or fistula. Stage 3 has evidence of osteolysis extending to the inferior border of the mandible or the sinus floor.³

This case was monitored closely and was managed in general practice. Any progression would warrant a referral to specialist services.

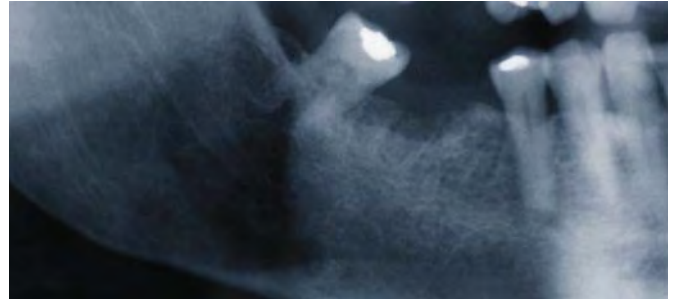


FIGURE 8: Sectional panoramic, December 2019.

Conclusion

This case of a spontaneous occurrence of MRONJ was managed conservatively in general practice. Care was comprised of monthly hygiene visits combined with daily chlorhexidine mouthwash. The patient was at high risk of developing MRONJ – he had had intravenous treatment with zoledronate, a bisphosphonate, to control hypercalcaemia, along with concurrent use of corticosteroids and previous use of immunotherapy.

There may be an under-reporting of MRONJ as an adverse reaction to bisphosphonates and anti-cancer drugs. Dentists who encounter this type of event are encouraged to open a channel of communication with the patient’s care team. The occurrence should also be reported to the HPRA.

Acknowledgements

I would like to acknowledge the contribution of the HPRA in providing the listing of suspected MRONJ.

References

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CPD questions



To claim CPD points, go to the MEMBERS’ SECTION of www.dentist.ie and answer the following questions:

1. MRONJ is a lesion that may occur following:

- ☐ A: treatment with specific drugs
☐ B: radiation therapy

2. Standard care in a case of MRONJ includes which mouthwash:

- ☐ A: Warm salt water
☐ B: Chlorhexidine
☐ C: Hydrogen peroxide

3. An adverse drug reaction should be reported to which body?

- ☐ A: Irish Dental Association
☐ B: Dental Council of Ireland
☐ C: Health Products Regulatory Authority