

# The Role of Endotracheal Tube in Medication-Related Osteonecrosis of the Jaw - A Case Report

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## Abstract

**Rationale:** Various traumatic risk factors have been correlated to the development of medication-related osteonecrosis of the jaw (MRONJ), with long-term use of antiresorptive or antiangiogenic medications. No previous cases of MRONJ secondary to endotracheal intubation have been reported in the oral and maxillofacial surgery literature. **Patient Concerns:** This case report describes a patient on long-term oral bisphosphonate therapy who presented with a nonhealing ulcer and exposed bony island along her right mandibular torus after undergoing general anaesthesia. **Diagnosis:** The lesion was diagnosed to be MRONJ secondary to pressure necrosis from postendotracheal intubation. These findings are suggested to be the result of poor control of the endotracheal tube while managing the airway. **Treatment and Outcomes:** After treatment with antibiotics and mouth rinses, the necrotic bone spontaneously dislodged with complete mucosalisation of the exposed site within 2 weeks. **Take-away Lessons:** Given the severe impact of MRONJ, it is imperative to recognise and minimise all controllable risk factors associated with its development.

**Keywords:** Bisphosphonate, endotracheal tube, general anaesthesia, medication-related osteonecrosis of the jaw, osteonecrosis

## INTRODUCTION

Numerous studies have reported the debilitating outcomes in patients with medication-related osteonecrosis of the jaw (MRONJ), a rare adverse event associated with the prolonged use of antiresorptive or antiangiogenic drugs. The pathogenesis of MRONJ is often attributed to the imbalance between bone formation and resorption.<sup>[1]</sup> Trauma to the alveolar bone caused by dental extraction, periodontal surgery, or implant placement is considered the main precipitating factor for MRONJ in majority of the cases. There is limited information on the impact of less common sources of trauma, such as endotracheal intubation. Here, we describe a rare case of jaw osteonecrosis suspected to be rooted in traumatic endotracheal intubation. Understanding this relationship further may prove useful for preventing adverse events in patients undergoing general anaesthetic procedures.

## CASE REPORT

In September 2020, a 63-year-old female (height: 64 inches; weight: 52 kg) underwent a complete hysterectomy for ovarian malignancy. She had a history of osteoporosis and had been

treated with oral alendronic acid (70 mg) weekly for the last 4 years (August 2016–August 2020). The preoperative airway assessment revealed a Mallampati score of 2 with normal mouth opening and range of neck motion. Following general anaesthetic induction, intubation was completed using a size 3 Macintosh blade and an 8-mm endotracheal tube (ETT) to a depth of 22 cm with a grade I Cormack–Lehane view of the larynx. The patient was kept in the supine position for the duration of the procedure with the ETT secured to the right side of her mouth. After the eight hour long surgical procedure, she was extubated without any documented trauma. During the surgery, she received six hours of continuous infusion of several vasoconstrictors for a total of 5085 µg phenylephrine and 409 µg norepinephrine. She also received 14 boluses to

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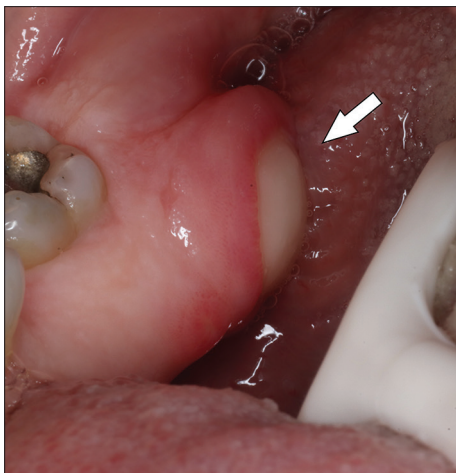
include phenylephrine: 11 bolus doses for a total of 950 µg and norepinephrine: 3 bolus doses for a total of 12 µg.

One week after the surgery, the patient noted an area of exposed bone along her right mandibular torus, which measured 5 mm × 6 mm in dimension [Figure 1]. The exposed bone was nonmobile and was delineated by tender erythematous bulbous gingival mucosa. Maxillofacial cone-beam computed tomography identified a wavy, irregular pattern of the cortical borders of the right tori without any osteolytic lesions or bony sequestrum [Figure 2]. Thus, the American Association of Oral and Maxillofacial Surgeons staging system was used to classify the lesion as stage 2.<sup>[1]</sup> The patient was treated with chlorhexidine mouth rinse and 14-day course of antibiotic therapy. At 1-month follow-up visit, a bony sequestrum was noted to have spontaneously dislodged [Figure 3]. Full mucosalisation and complete healing of the site were noted within 2 weeks [Figure 4].

## DISCUSSION

Prolonged use of antiresorptive medications has been implicated in the development of MRONJ, especially

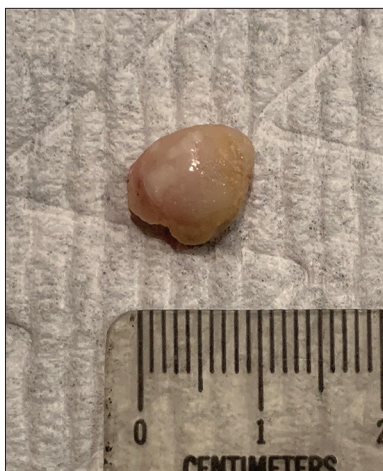
parenteral bisphosphonates, such as zoledronate and pamidronate. Bisphosphonates inhibit osteoclast differentiation and function, which is vital in bone healing and remodeling after trauma.<sup>[1]</sup> The first documented case report describing osteonecrosis after laryngoscopy and ETT placement was published in August 2010. A total of four cases were reported in which patients developed an exposed area of the bone near the mylohyoid ridge within weeks of undergoing endotracheal intubation.<sup>[2]</sup> In this case report, our patient reported a 4-year history of bisphosphonate use followed by oral trauma in the form of pressure necrosis by ETT while undergoing general anaesthetic. A disproportionately large ETT was used for intubation. Furthermore, the tube was secured at the oral commissure, which positioned the ETT firmly against the thin mucosa overlying the bony prominence of the mandibular torus. This resulted in the development of dehiscence of the distal portion of her prominent mandibular tori along with radiographic bony changes after only one week. Such clinical abnormalities are often a result of iatrogenic trauma associated with dentoalveolar surgical procedures. The loss of soft tissue and periosteum subsequently led to avascular necrosis of the exposed bone. Noticeably, bony lesions in patients with a history of bisphosphonate use exhibit poorer demarcation and irregular pattern.



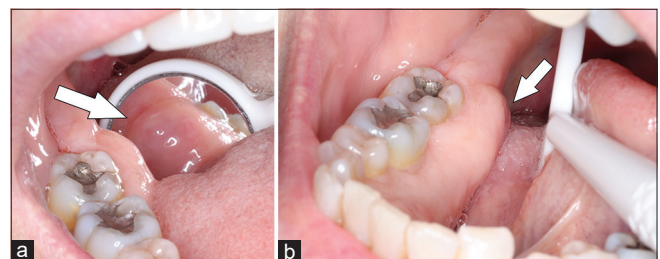
**Figure 1:** Right mandibular torus demonstrating exposed bone (white arrow)



**Figure 2:** Axial view CBCT demonstrating cortical irregularity along medial aspect of the right mandibular torus (black arrow)



**Figure 3:** Dislodged bony sequestrum



**Figure 4:** (a) Fully mucosalised right posterior lingual mandibular mucosa 2 weeks after dislodgement of the bony sequestrum (white arrow), (b) Additional view of fully mucosalised right posterior lingual mandibular mucosa (white arrow)

Bisphosphonate toxicity to oral mucosa is well established. As bisphosphonate accumulates in high concentration within the bones of the oral cavity and is locally released at the onset of trauma, the overlying oral mucosa becomes susceptible to injury from even subclinical trauma.<sup>[3]</sup> In addition, local toxicity of bisphosphonates further impedes cellular proliferation of the oral mucosa and delays normal wound healing.<sup>[4]</sup> This significantly prolongs the continuous exposure of the underlying bone to oral microflora and the subsequent risk of development of MRONJ. In our patient, continuous exposure of the mandibular torus to the oral microflora creates a setting for biofilm formation. In addition, the development of MRONJ is often preceded by local inflammatory changes such as those seen in pressure necrosis caused by ETT. These localised inflammatory or infectious processes cause acidification, which in turn increases dissociation of bisphosphonate from the hydroxyapatite within the bony lacunas. This increase in the level of bisphosphonate exerts an inhibitory effect on the osteoclasts, soft tissue, and vascularity, thus making the area susceptible to the development of MRONJ.<sup>[5]</sup>

An additional proposed etiology of MRONJ is the inhibition of angiogenesis.<sup>[1]</sup> Bisphosphonate use has an inhibitory effect on endothelial progenitor cells and vascular endothelial growth factor, both of which play a key role in neovascularisation.<sup>[4]</sup> Many of the current treatment modalities of MRONJ include vasodilatory medications such as pentoxifylline.<sup>[6]</sup> Our case demonstrates a confounding factor which is pressure from an ill-positioned ETT against the bony protuberance in the oral cavity. In addition, the patient was hypotensive during the surgery and treated with large doses of vasoconstricting medications. Periods of increased vasoconstriction in the setting of pressure from ETT may have led to mucosal ischaemia and inflammation. In patients with a known history of long-term bisphosphonate use, it may be beneficial to consider limiting vasoconstrictor use.

The sample size of this case report is an obvious limitation as this case report only highlights one case of MRONJ in the setting of oral trauma from ETT placement. As clinicians become more cognizant of these potential complications, there is greater opportunity to document such findings and increase understanding of different contributing factors in the future. This will allow all providers to take the necessary precautions to minimize the risk of MRONJ development.

## CONCLUSION

The development of MRONJ is likely multifactorial to include oversuppression of bone turnover, antiangiogenic effect, soft

tissue toxicity, role of bacteria, and inflammation, all of which work in synergy to present a unique clinical picture. Patients with significant bisphosphonate use can be susceptible to the development of MRONJ secondary to intubation trauma and ETT placement. This risk further increases in patients with bony outgrowths such as mandibular tori or prominent mylohyoid ridges, which are more susceptible to oral trauma. Any manipulation of the airway in patients with a history of bisphosphonate use should be performed with additional care and interventions such as use of bougie, red rubber catheter, or fiberoptic devices. Furthermore, an appropriately sized or smaller ETT should be selected and secured in the middle of the mouth, such as near the philtrum, to minimise further trauma.

## Informed consent

Verbal consent has been obtained and recorded in the medical case record of the patient and has been signed by witness regarding publication of the case report and photographs for the case. Written consent can be obtained if needed.

The views expressed in this case report are those of the author and do not reflect the official policy of the Department of the Army/Navy/Air Force, Department of Defense, or US Government.

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## Conflicts of interest

There are no conflicts of interest.

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