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Combined reconstruction plate fixation and submandibular gland translocation for the management of medication-related osteonecrosis of the mandible

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Abstract. The aim of this study was to summarize the clinical outcomes of patients with stage 3 mandibular medication-related osteonecrosis of the jaw (MRONJ) treated using reconstruction plate fixation and ipsilateral submandibular gland translocation after mandibulectomy. The medical records of patients with stage 3 mandibular MRONJ treated using the above surgical method between September 2014 and July 2019 were reviewed. Of a total of 27 patients included in this study, 23 (85.2%) experienced primary wound healing. The remaining four patients developed wound dehiscence and infection within 1 week after the operation. Three of these patients recovered after the plate was removed, and one patient died of the primary cancer. The follow-up period ranged from 3 months to 5 years, with an average of 12.7 months. The 23 patients with primary wound healing had a symmetrical facial appearance, with normal mouth opening and occlusion. Plate fracture occurred in two patients at 1 year and 3 years after the operation. Radioisotope scanning in 10 patients showed that the function of the translocated submandibular gland was normal at 6 months after the operation. In summary, for patients with stage 3 MRONJ involving the mandibular angle and/or body, reconstruction plate fixation and submandibular gland translocation after segmental mandibulectomy is an effective treatment method.

Key words: bisphosphonates; osteonecrosis; surgical treatment; reconstruction plate; submandibular gland.

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Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is an adverse effect of treatment with bisphosphonates (BPs). In 2003, Marx[1] first reported osteonecrosis of the jaw following treatment with intravenous BPs, and concluded that the jaw disease was related to BPs. In 2009, the American Association of Oral and Maxillofacial Surgeons (AAOMS) issued guidelines covering the diagnostic criteria, staging, and treatment principles for BRONJ[2]. As other bone resorption inhibitors (such as denosumab) and anti-angiogenic drugs (such as sunitinib) can also cause osteonecrosis of the jaw, the AAOMS in 2014 recommended renaming this condition as medication-related osteonecrosis of the jaw (MRONJ)[3].

As the clinical application of BPs has increased, their remarkable effects in the treatment of bone metabolic diseases have become apparent; however, the numbers of cases of MRONJ have also gradually increased. While the AAOMS criteria for the diagnosis and staging of MRONJ have been widely accepted, no consensus has yet been reached on the principles of treatment of MRONJ. The AAOMS recommends conservative treatment for patients in the early stages of MRONJ (stages 1 and 2), and limits surgical treatment to patients with stage 3 disease or stage 2 disease with a poor prognosis after conservative treatment[3]. Recently, however, an increasing number of researchers have been recommending early active surgical treatment, and limiting conservative treatment to patients with a poor general condition and those who are unwilling to undergo surgical treatment[4,5].

The main purpose of the surgical treatment of MRONJ is to relieve pain and delay the development of lesions. The surgical treatment of mandibular MRONJ involves the following: soft tissue debridement, sequestrectomy, block mandibulectomy, and segmental mandibulectomy. The necessity of surgical repair can be determined after segmental mandibulectomy, according to the condition of the patient. For patients with stage 3 mandibular MRONJ, we perform a segmental mandibulectomy and reconstruction with titanium plate fixation along with translocation of the submandibular gland to the defect area. The aim of this study was to summarize and analyse the outcomes of this treatment for mandibular MRONJ.

Materials and methods

Patients

The medical data of patients with stage 3 mandibular MRONJ treated using segmental mandibulectomy followed by reconstruction with plate fixation and ipsilateral submandibular gland translocation in the Department of Oral and Maxillofacial Surgery, Peking University School and Hospital of Stomatology, between September 2014 and July 2019, were analysed retrospectively. The exclusion criteria were as follows: (1) poor general condition leading to an inability to tolerate general anaesthesia, and (2) large lesions that were not limited to the mandibular body and angle, but rather extended to the ramus posteriorly or the symphysis anteriorly or even to the contralateral mandible.

The healing of the intra- and extraoral wounds and the complications occurring after the operation and during the follow-up period were evaluated.

At 6 months after the operation, technetium 99m (^{99m}Tc) scintigraphy ($Na^{99m}TcO_4$, 185 MBq) of the bilateral submandibular glands was performed in some patients to evaluate the function of the transposed submandibular glands.

Surgical method

The operation was performed under general anaesthesia via a combined intra- and extraoral approach. The intraoral incision was made along the fistula and gingival margin, and the submandibular incision was made to adequately expose the mandibular lesion and the normal bone on either side of the lesion (Fig. 1A). A

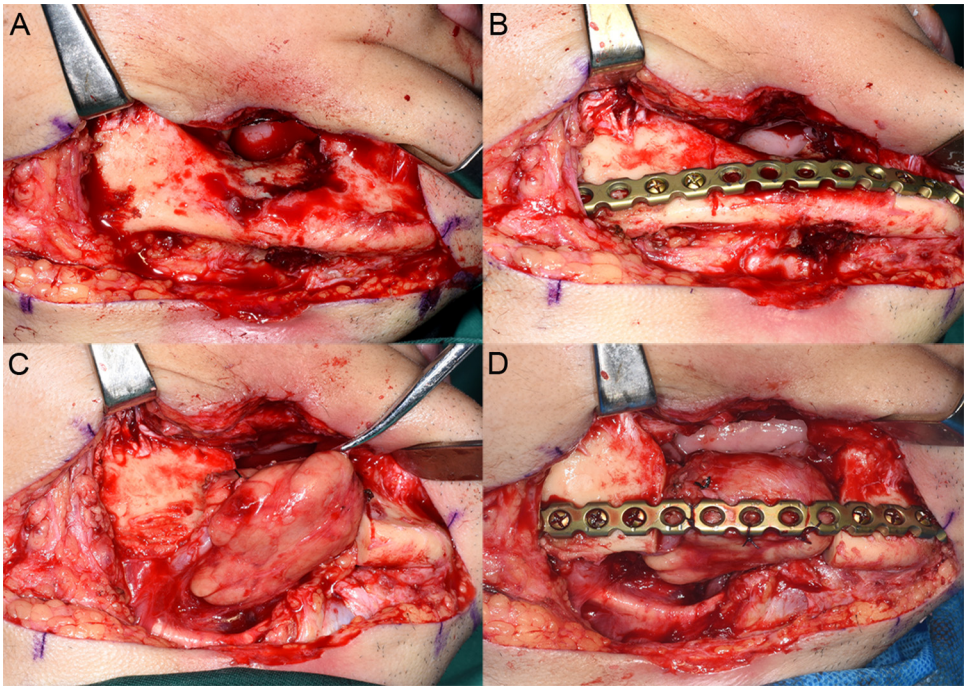

Fig. 1. Surgical procedure. (A) Exposure of the area to be resected through intraoral and extraoral incisions. (B) Bending the reconstruction plate to fit the mandible before the osteotomy. (C) Segmental osteotomy of the mandible and release of the submandibular gland. (D) Fixation of the mandible with the reconstruction plate and transposition and suturing of the submandibular gland to the defect area.

2.4-mm titanium reconstruction plate of an appropriate length was bent across the area to be resected so that it conformed to the shape of the mandible. The plate and the buccal surface of the mandible were closely fitted, and at least three holes were made on the surface of the normal bone on either side of the area to be resected to enable subsequent plate fixation (Fig. 1B). Then the plate was removed and a segmental mandibulectomy was performed to completely resect the lesion in the mandible.

The submandibular gland was dissected outside the capsule, and the submandibular gland duct and the submandibular ganglion were protected. The proximal end of the facial artery was preserved, and the submandibular gland was fully released (Fig. 1C). Next, the gland was transposed to the mandibular defect area below the reconstruction plate and sutured to the plate (Fig. 1D). The affected teeth were extracted. The wound margin of the alveolar mucosa was repaired and closely sutured. The external surgical wound was also closely sutured, and complete haemostasis was achieved. A rubber drainage tube was placed in the wound and removed 3–4 days after the surgery. A nasogastric tube was inserted postoperatively, and nasal feeding was performed for 2 weeks.

Results

General information

Between September 2014 and July 2019, a total of 27 patients (28 lesions) with stage 3 mandibular MRONJ underwent surgical treatment in the study hospital. There were 13 male patients and 14 female patients. They ranged in age from 47 to 84 years (average 64.5 years). The primary diseases in these patients were as follows: breast cancer in 10 patients, renal cancer in three, prostate cancer in three, lung cancer in three, multiple myeloma in two, rectal cancer in one, vaginal cancer in one, and osteoporosis in four.

All 23 cancer patients had osseous metastases and had been administered zoledronic acid 4 mg intravenously once a month, for 6 months to 10 years. For two patients, this drug had been replaced with disodium pamidronate. The four patients with osteoporosis had been treated with oral alendronate 70 mg/week, for 1 year 4 months to 4 years.

Among these 27 patients, 13 had undergone a sequestrectomy or block resection in the study hospital or another hospital. The incisions had not healed and the disease had recurred.

The osteonecrosis occurred on the right side in 17 patients, on the left side in nine patients, and on both sides in one patient.

Immediate postoperative outcomes

Among the 27 patients, 23 (85.2%) experienced primary wound healing, with no complications such as wound dehiscence and infection. In the remaining four patients, wound infection and dehiscence occurred within 1 week after the operation and did not heal with regular wound dressings. For three of these patients, the plate was removed, and the wound healed after the second operation. One female patient died of primary breast cancer after 3 months of continuous dressings.

Outcomes during follow-up

The follow-up period ranged from 3 months to 5 years, with an average of 12.7 months. The 23 patients with primary wound healing had a symmetrical facial appearance, with normal mouth opening and occlusion. Bilateral radioisotope scanning of the salivary glands was performed in 10 patients at 6 months after the operation. The results showed that the uptake and excretion functions of the translocated submandibular gland were not affected (Fig. 2).

Among the 23 patients with primary wound healing after plate implantation, two male patients developed plate fracture. One of these patients developed a plate fracture at 3 years after the treatment. The fractured plate was replaced with two reconstruction plates during a second operation, and the wound healed well eventually. In the other patient, plate fracture occurred at 1 year after the operation. A new reconstruction plate was placed for this patient, and the wound healed without complications.

Discussion

With the widespread clinical application of BPs and other drugs for the treatment of metabolic bone diseases, MRONJ caused by these drugs has attracted more and more attention. The treatment of MRONJ includes non-surgical treatments, such as medical treatment and hyperbaric oxygen therapy, as well as surgical treatments, such as sequestrectomy, block resection, and segmental resection. Thus far, there is no consensus on the optimal treatment of MRONJ; however, several studies have

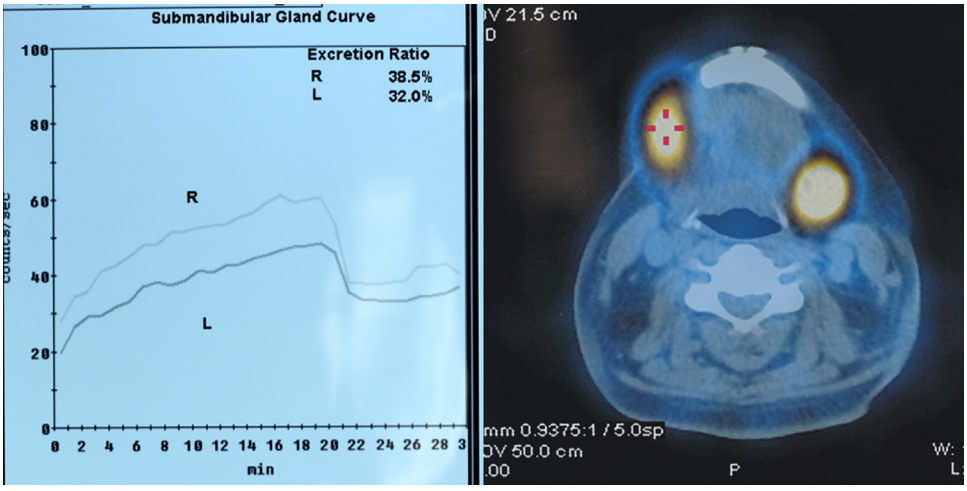

Fig. 2. Radioisotope scanning at 6 months after the operation showed that the right submandibular gland was located in the defect area in the mandible. The uptake and excretion functions of the gland were normal.

shown that the overall success rate of MRONJ treatment is higher for surgical methods than for non-surgical methods[6]. In terms of mucosal healing, extensive surgery is better than conservative surgery, and conservative surgery is better than non-surgical treatment[7].

For patients with stage 2 or stage 3 mandibular MRONJ, we have found that sequestrectomy or block resection do not yield good outcomes, and wound dehiscence and infection often occur even before the patient is discharged. In the present series, 13 of the 27 patients had undergone sequestrectomy or block mandibulectomy, and all of them had developed disease recurrence after the surgery.

To promote soft tissue healing and eliminate dead space, many authors have used a variety of local flaps. Mücke et al.[8] reported the cases of 26 patients with mandibular MRONJ for whom a mylohyoid muscle flap was used after the surgical removal of the dead bone. Compared with a local mucoperiosteal flap, the mylohyoid muscle flap significantly decreased the recurrence rate. Ristow et al.[9] assessed the outcomes of MRONJ patients for whom both a mylohyoid muscle flap and a mucoperiosteal flap had been used to close the wound after the surgical removal of the dead bone. After 8 months of follow-up, mucosal healing was observed in 88.0% of the patients. Some authors have used a nasolabial flap to close the wound, and have reported significantly higher recovery rates than those obtained with a local mucoperiosteal flap[10]. However, thus far, there has been no report of the use of submandibular gland translocation to eliminate the dead space caused by mandibulectomy and close the intraoral wound in MRONJ patients. Dissection of the submandibular gland, ligation of the distal ends of the facial artery and vein, and transposition of the gland to the defect area effectively eliminates the dead space left after mandibular resection. Additionally, suturing the submandibular gland with the intraoral mucosa effectively promotes wound closure and healing of the soft tissues. Finally, the function of the translocated submandibular gland is not affected.

For patients with stage 3 mandibular MRONJ, there is no consensus on whether to repair the mandibular defect after the removal of the dead bone. Marx et al.[11] suggested using a reconstruction plate to bridge the jaw defect instead of a free bone flap. Although the postoperative effect was good, there remained a risk of plate fatigue and fracture. Pautke et al.[12] reported a case of MRONJ in a transplanted ilium after partial mandibular resection and ilium bone flap reconstruction, suggesting that MRONJ may also occur in the graft bone. Pichardo et al.[13] reported 15 cases of stage 3 mandibular MRONJ. After the removal of the dead bone, no reconstruction was performed. The authors reported that 11 patients recovered after the operation, while four patients were down-staged to stage 1 MRONJ. Therefore, the authors concluded that surgical debridement should be the first choice for patients with stage 3 mandibular MRONJ and a poor general condition, and that extensive resection and reconstruction are not necessary.

Some authors have suggested that for patients with a good general condition, long life-expectancy, and extensive lesions, complete removal of the dead bone followed by microvascular free flap reconstruction should be considered to improve their quality of life; however, tumour metastasis in the transplanted bone should be excluded before the operation[14]. The following free tissue flaps have been used in the surgical treatment of MRONJ: fibula bone flap, ilium bone flap, scapula flap, forearm flap, and anterolateral thigh flap[15]. Mücke et al.[14] reported the cases of 25 patients who underwent vascularized reconstruction after MRONJ surgery. The disease recurred in only one patient after the surgery. The authors concluded that a bone flap containing muscle and skin can be used for mandibular reconstruction in MRONJ patients. Caldroney et al.[16] reported 11 cases of stage 3 mandibular MRONJ. After the resection of the lesion, vascularized bone reconstruction was performed. There was no recurrence after the operation and two of the patients successfully underwent treatment with dental implants.

In recent years, the clinical application of free composite tissue transplantation for the repair of the bone defect after mandibular resection for MRONJ has achieved good results[17]. However, many MRONJ patients have a variety of adverse factors that limit the use of vascularized bone repair, such as older age, poor general condition, and multiple bone metastases. Furthermore, patients and their families are reluctant to choose active treatments such as free bone flap transplantation.

For patients with recalcitrant stage 2 or stage 3 mandibular MRONJ, we performed lesion resection, followed by plate reconstruction and submandibular gland translocation. The reconstruction plate bridged the mandibular defect well. The translocated submandibular gland eliminated the dead space and helped to properly close the intraoral mucosal incision, which significantly improved the success rate of the operation. This method does have certain limitations. First, it is mainly suitable for the repair of defects involving the mandibular angle and/or body. Submandibular gland translocation cannot be used for lesions exceeding this extent, due to the limitations of gland volume and range of translocation; hence, the transposed gland cannot fill the dead space resulting from the removal of extensive lesions. If the defect area is too large, there is a risk of insufficient fixation strength of the plate and an increased possibility of plate exposure. Second, plate fracture can occur in the long term. In the series presented here, two male patients developed plate fracture at 1 year and 3 years after the surgery; their wounds healed well after the plate was replaced. Therefore, long-term follow-up should be conducted after this procedure, and patients should be careful when eating and avoid eating hard foods to prevent plate fracture.

In conclusion, for patients who have recalcitrant stage 2 or stage 3 mandibular MRONJ involving the mandibular angle and/or body and who are unwilling or unable to undergo free bone flap reconstruction because of a poor general condition, the surgical method presented here is a reliable alternative that can significantly improve the rate of postoperative mucosal healing, as well as patient quality of life.

Funding

None.

Competing interests

All authors declare that they have no conflict of interest.

Ethical approval

The Ethics Committee of Peking University School and Hospital of Stomatology (PKUSSIRB-201949119) approved this study.

Patient consent

All participants signed an informed consent agreement.

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