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Treatment of mandibular osteoradionecrosis by periosteal free flaps

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Abstract

Mandibular osteoradionecrosis (ORN) is one of the most serious complications of radiotherapy of the head and neck, and is characterised by hypoxia, hypovascularisation, and hypocellularity. Periosteal free flaps have intrinsic osteogenic, and extrinsic neoangiogenic, properties that are related to the periosteum. Our objective was to present our experience with the use of periosteal free flaps in the treatment of ORN (Notani class I or II) that are refractory to conservative management or have a large area of bone (≥2 cm) exposed. We organised a single-centre, retrospective study between 2003 and 2013 and describe the management of 11 patients (4 women and 7 men) who were being treated for refractory mandibular ORN. Thirteen periosteal free flaps were used: inner femoral condylar periosteum (n = 4), iliac crest (n = 1), external brachial with humeral periosteum (n = 1), and forearm with radial periosteum (n = 7). During follow-up we found three acute complications (haematoma, partial necrosis, and total vascular necrosis) that required immediate construction of a second periosteal free flap. There were also two chronic complications (fistula and post-traumatic fracture). With only one progressive lesion identified, the ORN was stopped in 11/12 patients. Two examples of osteoconduction were identified on postoperative images at six months and two years. Because of its osteoconductive and neoangiogenic capacities, the periosteal free flap seems to offer a real biological dimension to the treatment of ORN, and its efficiency favours its early revascularisation.

Keywords: osteoradionecrosis; free flap; management; Periosteal free flap; jaw

Introduction

Mandibular osteoradionecrosis (ORN) is a serious complication of irradiation of the head and neck, which is characterised histologically by hypoxia, hypocellularity, and hypovascularisation.[1] Prophylactic measures include identifying any risk factors,[2] controlling traumatic factors,[3] and developing prophylactic dentistry and topical treatment with

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fluoride. [4] These measures, together with technical advances such as the development of intensity modulated radiotherapy, have reduced the incidence of ORN from 38% to less than 10% within the last 40 years. [5] Despite these developments, methods of managing ORN have become increasingly controversial.

In a meta-analysis published in 2015, Rice et al[6] differentiated between ORN lesions with damage to bone above the mandibular canal from those with damage below it, and recommended conservative management for lesions classified as Notani classes I–II (above the inferior alveolar canal), and radical management with immediate reconstruction by free flap for those classified as Notani class III (below the inferior alveolar canal). However, in the case of Notani class I or II lesions with extensive exposure of bone, or those that were refractory to conservative treatment, the lack of consensus remains problematic because of the evolutionary potential of these lesions. Indeed, considering that the more complex the reconstruction, the higher the complication rate,[7] in 1997, Beauvillain de Montreuil et al[8] were the first to propose early surgical management of ORN. They recommended the use of periosteal free flaps, thereby bringing bony growth factors and progenitor cells that could trigger increased osteogenic[9] and neoangiogenic[10] responses to the ORN process.

The objective of this study was to report our experience of the use of periosteal flaps for ORN (Notani classes I or II) with a large exposed area of bone or that were refractory to conservative treatment, and to evaluate their therapeutic effectiveness on ORN.

Patients and methods

The records of 11 patients (four women and seven men), mean age 55 (range 34–69) years, were analysed in a retrospective, single-centre study. They had had revascularisation and reconstruction with periosteal free flaps between January 2003 and December 2013.

For each patient, the data collected were grouped into four distinct categories. The first included characterisation of the ORN, the time that had elapsed between the end of irradiation and the onset of symptoms, and between the diagnosis of ORN and revascularisation, the mode of occurrence (Wong classification),[11] the topography of the lesion (Urken classification)[12], the conservative management before revascularisation, and the depth of the osteolytic injury (Notani classification)[13] (Table 1). The second category concerned the surgical technique, the duration of operation, the choice of recipient vessels and anastomoses, and the type of periosteal free flap. The third category involved the complementary assessments, whether there had been a complete, doubtful, or incomplete resection of bone as evaluated on the postoperative radiograph (dental panoramic radiograph or computed tomographic (CT) scan, or both), and the histopathological confirmation of the lesions. In the fourth and last category we recorded the postoperative radiological and clinical monitoring, the duration of hospital stay, and existing acute (within 30 days) or chronic (30 days or longer) complications.

We then assessed the effectiveness of revascularisation by the absence of either progression or local recurrence of the ORN. Lesions distant from the initial surgical site or recurrence after a period of healing were considered to be new, and independent of the primary lesion.

Results

Characteristics of management of ORN

The mean time between the end of irradiation and the first symptoms of ORN was 48.5 (40) months. Objective analysis of the patients' history showed a triggering factor in eight. Revascularisation had been proposed because conservative management had failed (n = 7) or because more than 2 cm of bone were exposed (n = 5). The mean (SD) time between the diagnosis of ORN and reconstruction was 7.5 (6.5) months (9.5 (4) months for the group who had initial conservative management, compared with 2.2 (0.9) months for the group who had had immediate revascularisation) (Table 1).

Surgical technique: distribution and types of flaps

We used 13 periosteal free flaps: five were "true" periosteal free flaps of internal femoral condyle (n = 4) or iliac crest (n = 1), and eight were periosteal free flaps with accompanying soft tissue – external brachial free flap with humeral periosteum (n = 1) and forearm free flaps with radial periosteum (n = 7).

The mean (range) duration of revascularisation was 414 (246–612) minutes. We preferred an end-to-end arterial anastomosis in 12 cases: on the facial artery (n = 7), the lingual artery (n = 1), and the superior thyroid artery (n = 4). In one case we did an end-to-side anastomosis on the external carotid artery. For the venous anastomosis, we made one end-to-side anastomosis (on the retromandibular vein), and 12 end-to-end anastomoses: on the thyrolinguofacial trunk (n = 8), and the external (n = 2) and the internal jugular (n = 3) veins. In all patients, the arterial anastomosis was made after permeability had been assured, and an immediate and frank venous return was apparent.

All reconstructions were made after resection (segmental mandibulectomy) of the pathological bone until healthy bleeding bone was reached. No revascularisation was attempted after simple curettage or debridement. The histological examinations of the resected bones showed infiltration into the connective tissue with no osteocytes, osteoclasts, or osteoblasts, and no signs of recurrent tumour in any sample. It did not allow the clinician to judge whether the osteoradionecrotic bone had been completely excised, despite operative bony bleeding.

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Table 1
Characteristics of the group studied and methods of revascularisation.

Case No.	Sex	Site of tumour	Dose of DXR (Gy)	Trigger factors[1]	Topography of the ORN [2]	Depth of osteolytic damage [3]	Conservative management before revascularisation	Delays between diagnosis of ORN and treatment (days)	Type of periosteal free flap	Postoperative morbidity	Treatment of morbidity	Duration of follow up (days)	Efficacy of revascularisation
1	M	Lower lip	NK	4	S	I	Curettage (n = 2) Pentoclo regimen (1 cure)	293	Internal femoral condylar periosteum	–	–	1297	Healing
2	F	Base of tongue	75	3	R + B	I	Curettage (n = 3) Surgical debridement (n = 2) Pentoclo regimen (1 cure)	628	Internal femoral condylar periosteum	Complete necrosis (<7 days)	Immediate reconstruction by a second forearm free flap with radial periosteum	2175	Healing
3	F	Mobile tongue	70	3	S + S	II	Curettage (n = 3) Long term antibiotics (1 cure) Hyperbaric oxygen (30 sessions)	325	Forearm free flap with radial periosteum	Post traumatic mandibular fracture	–	1375	Healing
4	M	Oropharynx	60	4	B	II	Curettage (n = 2) Pentoclo regimen (1 cure)	192	Forearm free flap with radial periosteum	Partial necrosis with bone exposure	Local care	1088	Progressive continuation of the ORN injury
5	F	Oropharynx	NK	1	S + B	I	Curettage (n = 3) Long-term antibiotics (1 cure)	193	Forearm free flap with radial periosteum	Development of skin fistula with intolerance to a vascular clip	Fistula cured with vascular clip resection	4964	Healing
6	M	Base of tongue	50	3	B	II	–	31	Forearm free flap with radial periosteum		–	4056	Healing
7	M	Mobile tongue	NK	4	B	II	–	68	Iliac crest periosteum	–	–	2089	Healing
8	M	Oropharynx	50	3	R	II	Hyperbaric oxygen (30 sessions)	43	External brachial free flap with humeral periosteum	–	–	1242	Healing
9	M	Oropharynx + larynx	50	3	R	II	–	39	Internal femoral condylar periosteum	Haematoma	Surgical drainage of haematoma	352	Healing
10	M	Larynx	65	3	B + R	I	Curettage (n = 4)	514	Internal femoral condylar periosteum	–	–	3869	Healing
10	M	Larynx	65	3	B	I	–	58	Forearm free flap with radial periosteum	–	–	3046	Healing
11	M	Tongue base	80	4	B	I	–	131	Forearm free flap with radial periosteum	–	–	4439	Healing

NK = not known; Gy = Gray; ORN = osteoradionecrosis; DXR = radiotherapy; Pentoclo = pentoxifylline, alpha tocopherol, and clodronate.
(1) *Wong classification*: Stage 1 = exposure of bone resulting from necrosis of the tumour where death of the tumour results in a loss of soft tissue coverage. Stage 2 = exposure of bone as a consequence of recurrence of the tumour. Stage 3 = Exposure of bone as a result of oral surgical (surgical salvage) or other dental interventions including prosthetic dental treatment. Stage 4 = de novo exposure of bone with no apparent cause apart from exposure to radiation.
(2) *Urken classification*: S = symphisis; B = body of the mandible; R = ramus of the mandible; and C = condyle.
(3) *Notani classification*: Class I = ORN confined to the dentoalveolar bone. Class II = ORN limited to the dentoalveolar bone or mandible above the inferior canal, or both. Class III = ORN involving the mandible below the inferior dental canal, or pathological fracture, or fistula through skin.

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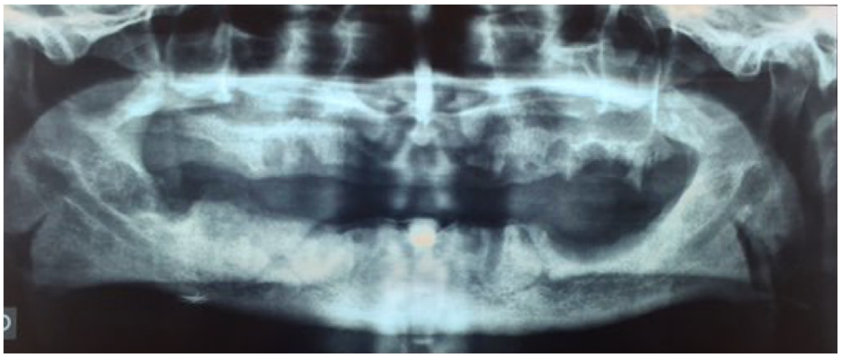

Fig. 1. Dental panoramic view of case 9 with a Notabi class II ORN of the right mandibular angle before revascularisation.

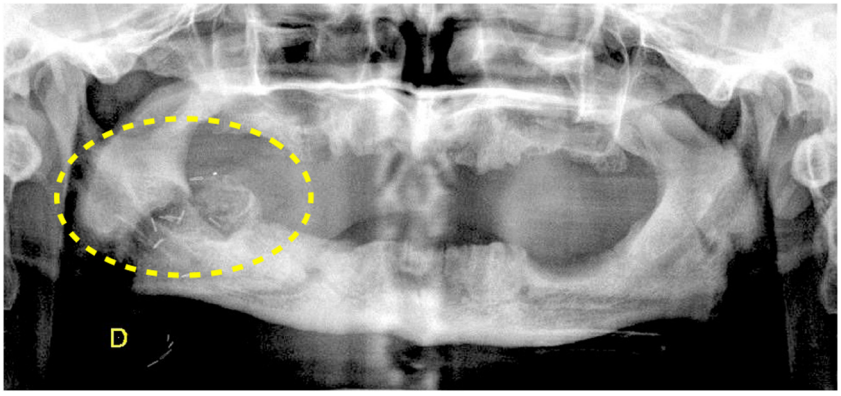

Fig. 2. Dental panoramic view of case 9 taken one year after revascularisation (yellow circle) by an internal femoral condylar periosteal free flap with osteoconduction from the periosteal free flap reconstruction.

Postoperative outcome and follow-up

The postoperative period (within seven days of operation) was marked by three acute complications: haematoma, partial necrosis, and ischaemic vascular necrosis that required immediate replacement with a new forearm free flap with radial periosteum. In two further cases (more than seven days postoperatively), we encountered two chronic complications: a skin fistula caused by intolerance to a vascular clip, and a traumatic mandibular fracture.

Within a mean (range) follow-up time of 83 (11.7–165.5) months we found only one patient whose ORN had progressed as result of exposure of the bone and, despite complete resection, this means that the treatment was effective in only 11/12. Two patients showed evidence of new bone formation on the follow-up radiographs (Figs. 1 and 2).

Dental rehabilitation for all patients was begun six months postoperatively in the absence of recurrence or progression of ORN. Among them, three patients had dental implants inserted without activating any new ORN.

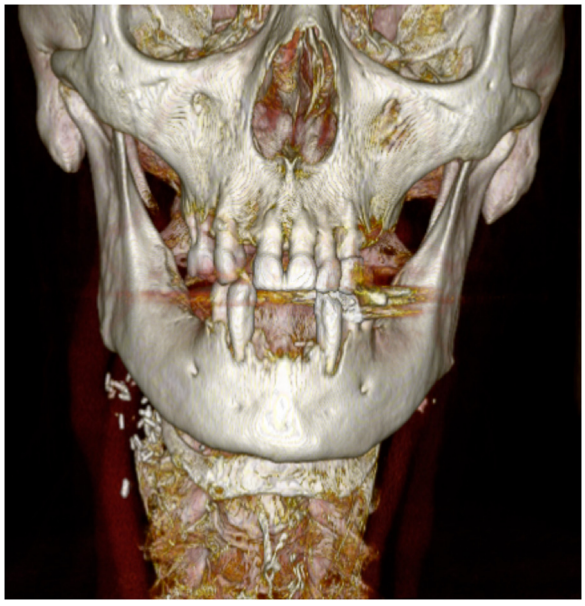

Fig. 3. Three-dimensional reconstruction of the preoperative computed tomographic scan showing a symphyseal osteolytic lesion.

Case Reports

Revascularisation by a forearm free flap with radial periosteum[14]

A 64-year-old patient had a squamous cell carcinoma of the tongue resected, followed by bilateral neck dissection, reconstruction with a forearm free flap, and postoperative radiotherapy (65 Gy). Five years later, he developed ORN of the mandibular symphysis (Wong stage 4) (Fig. 3).

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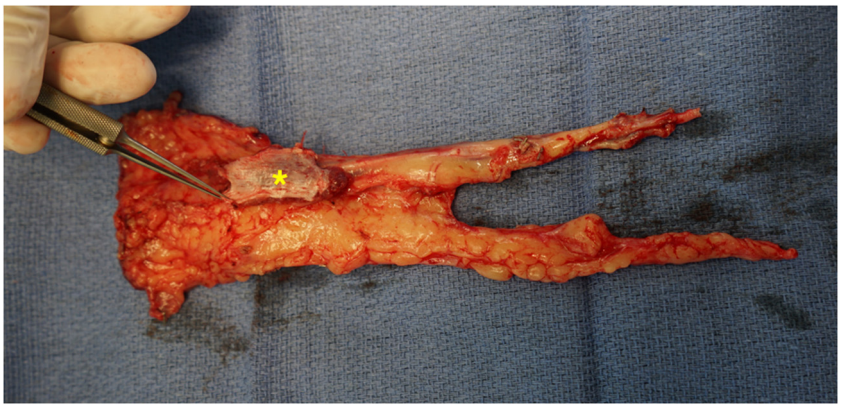

Fig. 4. Intraoperative photograph of the forearm free flap with radial periosteum (yellow star).

After one year of unsuccessful medical management including three episodes of curettage, long-term antibiotic treatment, and 30 sessions of hyperbaric oxygen, it was decided to revascularise the area with a radial forearm periosteal flap (Fig. 4). First, we did a marginal mandibulectomy, and then we reconstructed it with a radial forearm free flap with radial periosteum, without separating the vascular pedicle from the radial periosteal membrane. To facilitate the harvest, we find it preferable to dissect the sensitive branches of the radial nerve, and start the periosteal incision from the radial side.

In the second step, we position the flap with sutures from the radial periosteum to the mandibular periosteum, and the skin paddle is sutured to the oral mucosa without tension. Finally, end-to-end vascular anastomoses were made between the radial artery and the right superior thyroid artery, and between the cephalic vein and the thyrolinguofacial venous trunk.

Oral feeding was allowed seven days postoperatively and the patient was discharged on the 13th postoperative day. At six months' follow-up clinical examination showed complete integration of the flap (Fig. 5), with no recurrence of the ORN on CT.

Revascularisation by a internal femoral condylar periosteal free flap[15]

A 55-year-old patient was treated for a squamous cell carcinoma of the base of the tongue. He was initially given radiochemotherapy (three curative doses of cisplatin and 60 Gy radiation). Four years later he developed mandibular ORN after extraction of a molar. After 17 months of ineffective medical management including three episodes of curettage, two surgical debridements, and one episode of the Pentoclo regimen, revascularisation was chosen (Supplemental data 1, online only), using an internal femoral condylar periosteal free flap harvested after marginal mandibulectomy. After careful dissection of the medial genicular artery (Supplemental data 2), a femoral condylar periosteal membrane was harvested (Supplemental data 3). The flap was then positioned in the oral cavity, allowing a tight bony cover

Fig. 5. Photograph 14 days postoperatively showing the integration of the flap.

and sutured to the mucosa without tension with interrupted absorbable sutures. End-to-end vascular anastomoses were made to the facial vessels. The postoperative follow-up was uneventful, the patient started oral feeding on the fifth postoperative day and was discharged from hospital on the ninth day (Supplemental data 4).

At the one year follow-up, radiological (Supplemental data 5) and clinical monitoring showed complete integration of the flap, with no recurrence of ORN.

Discussion

With an incidence between 5% and 10%, mandibular ORN is a serious public health problem.[4] Recently, the questioning of the effectiveness of the main conservative treatments (hyperbaric oxygen,[16] long term antibiotics,[17] and the Pentoclo regimen[18]) has made it difficult to establish a consensus about how to manage such lesions. However, it seems to be accepted that pathological fractures or advanced lesions (Notani class III) are dependent on surgical treatment with

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reconstruction by a microanastomosed free flap. The management of refractory lesions above the mandibular canal (Notani classes I or II) may be problematic. We propose to extend the use of free flaps in the management of ORN, the efficiency of which is from 86% to 100%,[19] to lesions above the mandibular canal that are refractory to conservative management or (according to the conclusion of Delanian et al[20]) with more than 20 mm of exposed bone. In this way we hope to stop the development of ORN by providing periosteal bony vascular supplementation before the bony infrastructure weakens enough to require the use of a free flap of bone, which would increase the risk of complications.[7] Indeed, revascularisation for Notani class I or II lesions that are accessible to a soft-tissue free flap, resection of the pathological bone, and cover of a bleeding bone without tension, seem to stop the ORN.

Our hypothesis is that the supply of healthy vascularised tissue without irradiated cells is a biological response to the hypoxia, hypocellularity, and hypovascularisation of the ORN.[1] The reconstruction with restoration of bony tightness alone also avoids the use of inert osteosynthesis material, which in an irradiated area causes 6.5% to 57.7% of chronic complications[19] and generally requires one or more complementary interventions with the risk of reactivating the ORN.

As far as the choice of soft-tissue free flaps in the treatment of ORN is concerned, we know of no studies that have evaluated the superiority of periosteal composite free flaps compared with fasciocutaneous free flaps in the treatment of early ORN. Nevertheless, the effectiveness of periosteal free flaps in the treatment of degenerative osteoarthritis[21] seems to offer a real biological dimension in the treatment of defects of bony consolidation, which benefits from secondary remodelling of the periosteal flap. In 2007, our team had already decided to use this approach to ORN with a high risk of progression.[21] However, the association of severity factors with risk factors for ORN limits its analysis.[22,23]

Between 1992 and 2002, D'Hauthuille et al[24] reported eight patients with ORN treated by periosteal free flaps that healed completely, including two secondary radiological osteoconductions, and one histological proof of the osteoconductive capacity of the periosteal free flap. In addition to its neoangiogenic capacity and potential for recruiting cells, therefore, the integration of a free flap with periosteal osteoconductivity is an obvious advantage in the physiological therapeutic approach to osteoradionecrotic injuries.

It is remarkable to see how our use of composite periosteal free flaps has increased since 1992 (2/8 patients compared with 8/13 with ORN).[24] This evolution is explained by the many advantages attached to the additional fasciocutaneous interface with the periosteal membrane. Indeed, the skin paddle offers easy monitoring of tissue viability and an additional interface, which optimises bony tightness and facilitates the placement of the periosteal flap (which requires a bony anchor to avoid non-union and exposure of the surgical site). The presence of a skin paddle, in addition to covering ORN, also allows us to correct oral scars, either with surgical flanges or post-radiation retraction. Despite limited complications at the donor site, the periosteal flaps (iliac crest or internal femoral condyle) have short vascular pedicles and these, together with their tendency to retract postoperatively, are their main limitations. Our experience has led us to favour the use of the forearm free flap with a radial periosteal component, mainly because the cutaneous paddle and its long vascular pedicle are so thin. This allows us to adapt to vascular constraints encountered in irradiated or multioperated areas (depleted vessels in the neck or reactive arteriosclerosis). Nevertheless, it is interesting to note that all cases of osteoconduction in our department (four between 1992 and 2013) were secondary to reconstruction by an internal femoral condylar free flap. This suggests that the "true" periosteal free flap has an osteoconductive potential superior to that of the composite periosteal free flap.

We are aware that proposing revascularisation for the management of Notani class I or II lesions may seem disproportionate. However, it is important to consider the effectiveness of different treatments and the progression of the lesions. If we consider the conclusions of Delanian et al[20] and Rice et al,[6] it is possible to accept that a conservative approach can be proposed in case of ORN located above the mandibular canal and when less than 2 cm of bone are exposed but, in the case of ineffectiveness or aggravation during conservative treatment, the diagnosis of refractory lesion must be considered as reason enough to suggest that potentially the initial strategy should be modified.

Under these conditions, the periosteal flap is a reliable and curative alternative for the osteolytic lesions above the mandibular canal, as it allows both control of the ORN and restoration of oral function. Nevertheless, it is necessary to validate this therapeutic approach in a large prospective study with several expert centres to define a common strategy for dealing with ORN of the jaw, because with its high complication rate at any stage (18%–75%)[19] the failure of the initial reconstruction may aggravate the initial lesion. Irradiation and further operations on the neck will only complicate the management further.

Conclusion

The periosteal free flap is an effective way to treat Notani class I or II ORN that is refractory to conservative management or has more than 2 cm of bone exposed. Because of their neoangiogenic and osteoconductive properties, periosteal free flaps can be considered to be the first step in a cellular approach to the treatment of mandibular ORN. However, our experience needs to be confirmed by a larger prospective study to confirm the importance of reconstruction in the management of ORN, and to identify the limits of medical treatments so that we offer patients the best risk:benefit ratio between efficacy and complications.

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Ethics statement/confirmation of patients' permission

This study adhered to the principles of the Declaration of Helsinki in terms of medical protocols and ethics. Consent for publication was obtained from all patients.

Conflict of interest

We have no conflicts of interest.

Financial disclosure

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.bjoms.2019.01.028.

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