Int. J. Oral Maxillofac. Surg. 2006; 35: 1001–1004
doi:10.1016/j.ijom.2006.08.006, available online at http://www.sciencedirect.com

International Journal of
Oral & Maxillofacial Surgery

Clinical Paper
Head and Neck Oncology

Infected osteoradionecrosis of the mandible: follow-up study suggests deterioration in outcome for patients with *Actinomyces*-positive bone biopsies

T. Hansen[1], W. Wagner[2], C. J. Kirkpatrick[1], M. Kunkel[2]
[1]Institute of Pathology, Johannes Gutenberg-University of Mainz, Langenbeckstr. 1, D-55101 Mainz, Germany; [2]Clinic of Maxillofacial Surgery, Johannes Gutenberg-University of Mainz, Augustusplatz 2, D-55131 Mainz, Germany

T. Hansen, W. Wagner, C. J. Kirkpatrick, M. Kunkel: Infected osteoradionecrosis of the mandible: follow-up study suggests deterioration in outcome for patients with Actinomyces-positive bone biopsies. Int. J. Oral Maxillofac. Surg. 2006; 35: 1001–1004.

Abstract. Infected osteoradionecrosis (IORN) is one of the major complications of oral cancer radiotherapy. Recent studies showed a high prevalence of *Actinomyces* in IORN. In this study, the clinical follow up of IORN patients ($n = 25$; 20 male, 5 female) with regard to *Actinomyces* detection in the mandible was analyzed. Within 1.6–119 months of follow up, disease control was achieved in almost 90% of the patients with *Actinomyces*-negative bone biopsies, but only in 25% of the *Actinomyces*-positive group. The presence of *Actinomyces* was associated with a significantly higher risk of treatment failure ($P = 0.004$; Fisher's exact test). This held true when the data were controlled for 'extent of bone destruction', 'type of surgery' and 'soft-tissue closure' in a logistic regression analysis ($P = 0.018$; Wald test). Since *Actinomyces* was detected in a significant number of patients with non-healing mucosal defects, this microbe may promote the persistence of chronic non-healing inflammatory processes. *Actinomyces* positivity defines a subpopulation with a clinically deteriorated course of mandibular IORN.

Key words: infected osteoradionecrosis; *Actinomyces*; follow-up; outcome; mucosal healing.

Accepted for publication 24 August 2006

Osteoradionecrosis is one of the most feared complications of head and neck cancer treatment. Due to an incidence of between 3% and 35%, it can be considered as a calculated risk of the radiotherapy. The pathogenesis of osteoradionecrosis is still under discussion, but devitalization of bone and the disruption of vascular supply by irradiation play a central role[1,2,12]. A serious complication of this devitalized bone is infection. Infected osteoradionecrosis (IORN) is associated with an increased risk of bone fracture, thus causing severe impairment of quality of life. Several mechanisms independent of bone

0901-5027/111001 + 04 $30.00/0

damage contribute to the development of IORN. Ionizing radiation commonly leads to salivary gland dysfunction, also called radiation xerostomia. The distorted glands are not able to produce sufficient saliva, which plays a crucial role in the oral clearance, physiological bacterial microenvironment and thus maintenance of mucosal integrity. These conditions finally result in an increased predisposition to infections[2]. Several studies showed particularly high numbers of IORN cases positive for *Actinomyces* spp.[5,7,8,10], but the clinical significance of these findings remains largely unexplored. The aim of the present study was to determine the impact of *Actinomyces* on the clinical course of IORN patients by relating occurrence of *Actinomyces* in the mandibular bone tissue to clinical outcome.

Materials and methods

Patients and treatment

The study population consisted of 25 patients (20 males, 5 females). Inclusion criteria were as follows: irradiation due to head and neck neoplasms, IORN of the mandible proven by histology, biopsy material for the detection/exclusion of *Actinomyces*, follow-up data available. Median age was 57.6 years. The clinical variables and the outcome data are summarized in Table 1. Patients presented with the typical clinical symptoms of IORN[6] such as bone exposition and sequestration, fistula formation and inflammatory infiltration. Bone involvement was additionally confirmed by radiography and/or computed tomography. Radiographically measured bone damage was divided into two groups, the first group showing less than 50% of the mandibular height involved, and the second group revealing more than 50% of the mandibular height affected (summarized in Table 1).

Surgical treatment for IORN involved careful resection of the necrotic bone, extirpation of the fistula and meticulous soft-tissue closure. Due to the nature of the disease, the specific amount of bone removal was highly variable (depending on the extent of involved bone, the height and stability of the residual mandible, the soft tissue available for coverage etc.) and thus far from standardized. For descriptive purposes, two principal therapeutic approaches are specified in our study:

(a) Conservative debridgement solely of the involved bone primarily by curettage of the lesion (defined as 'minor resection' in Table 1).
(b) Resection beyond the borders of the involved bone resulting in typical resection patterns (box-shaped, segmental etc.; defined as 'major resection' in Table 1).

Except for the direct access to the necrotic bone, periostal integrity at the adjacent bone was preserved and wound closure was performed after epiperiostal mobilization of the mucosa. In the retromolar area, larger resection defects were covered by (epiperiostal) transposition of the masseter muscle, the mylohyoid muscle or the buccal fat pad. Microvascular free flaps were not used in the context of IORN treatment in this cohort. In general, patients received postoperatively antibiotic therapy using either amoxicillin/clavulan acid for at least 3 days or, in the case of allergy, clindamycin for at least 3 days.

Table 1. Patient data and results of histology and clinical outcome

No.	Sex	Age	Carcinoma	Radiation dose (Gy)	Cause	Localization	Extent of damage	Resection	Act	Duration time (months)	Outcome
1	M	75.03	SCC	60	Tooth extraction	Md	+	Minor	Yes	42.66	Su
2*	M	59.95	SCC	60	Tooth extraction	Md	+	Minor	Yes*	26.25	Fa
3	M	55.48	SCC	70	Spontaneous bone exposure	Md	+	Minor	Yes	18.45	Su
4	M	49.32	SCC	60	Infected osteoplasty	Md	++	Major	Yes	44.41	Fa
5	M	46.24	SCC	60	Dental implants	Md	+	Minor	Yes	29.3	Fa
6	M	43.82	SCC	60	Osteosynthesis	Md	++	Minor	No	27.96	Su
7	M	66.05	SCC	60	Tooth extraction	Md	++	Major	Yes	34.67	Fa
8	M	72.21	SCC	60	Tooth extraction	Md	+	Minor, MF	Yes	25.49	Su
9	M	70.13	SCC	70	Spontaneous bone exposure	Md	+	Minor	Yes*	51.81	Fa
10†	M	64.59	SCC	70	Spontaneous bone exposure	Md	+	Major, MF	Yes*	9.24	Fa
11†	M	45.21	ACC	70	Tooth extraction	Md	+	Major	Yes	101.58	Fa
12	F	63.3	SCC	60	Apical osteitis	Md	+	Minor, MF	No	63.78	Su
13	M	46.28	SCC	ND	Spontaneous bone exposure	Md	+	Minor	No	35.56	Fa
14	M	74.85	SCC	60	Spontaneous bone exposure	Md	+	Minor	No	1.55	Su
15	M	53.88	SCC	72	Osteosynthesis	Md	++	Minor	No	29.57	Su
16	F	59.92	SCC	60	HA for alveolar ridge augmentation	Md	+	Minor	No	75.76	Su
17	M	56.91	ACC	40	Tooth extraction	Md	+	Minor	Yes*	103.45	Fa
18	M	63.93	SCC	60	Dental implants	Md	++	Minor	Yes	89.47	Fa
19	F	65.16	SCC	60	Osteosynthesis	Md	++	Minor	No	118.42	Su
20	M	62.44	SCC	60	Tooth extraction	Md	++	Major	Yes*	68.45	Fa
21†	F	55.66	SCC	48	Tooth extraction	Md	+	Minor	No	3.91	Su
22‡	F	49.77	SCC	60	Spontaneous bone exposure	Md	+	Major, MF	No	37.73	Su
23	M	48.03	SCC	60	Apical osteitis	Md	+	Minor, MF	Yes*	9.41	Fa
24	M	50.1	SCC	58	Tissue ulceration due to prosthesis	Md	+	Minor	Yes	7.63	Su
25	M	42.05	SCC	60	Radix relicta	Md	++	Major	Yes	75.69	Fa

ACC, adenoid cystic carcinoma; Act, *Actinomyces*; F, female; Fa, failure; HA, hydroxylapatite; M, male; Md, mandible; MF, muscle flap; ND, no data; SCC, squamous cell carcinoma; Su, success (+, less than 50% of mandibular body height; ++, more than 50% of mandibular body height).

* *Actinomyces* detected twice.

† Tumor-related death.

‡ Died not because of tumor.