

# Histopathological Features of Secondary Squamous Cell Carcinoma Around a Dental Implant in the Mandible After Chemoradiotherapy: A Case Report With a Clinicopathological Review

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Oral squamous cell carcinoma (OSCC) around a dental implant is a rare pathologic condition. This report describes a case of recurrent OSCC surrounding a dental implant, histopathologic findings, and a literature review of this condition. A 58-year-old Japanese woman underwent chemoradiotherapy for OSCC in the right lower gingiva, resulting in a complete response. Nine years after primary chemoradiotherapy, a dental implant was placed in her atrophic mandible. Three years later, an OSCC developed around the dental implant in the right lower premolar region. Marginal mandibulectomy was performed. Microscopic examination showed medullary invasion around the implant surface, suggesting that tumor infiltration of the bone was through the interface between the implant and bone. However, no downward invasion through the interface was evident. OSCC can develop around dental implants that are placed for oral rehabilitation after ablative surgery. Staging of OSCC and planning of surgical management should be carried out carefully, because implants placed adjacent to the OSCC can influence tumor invasion. A high degree of vigilance for OSCC is required during follow-up of patients with dental implants who have OSCC risk factors such as premalignant lesions. Detailed evaluation, including biopsy examination, is essential for distinguishing peri-implantitis from OSCC.

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The treatment of head and neck malignancies has become increasingly successful, with improvements in survival rate and functional outcome.<sup>1-3</sup> Therapy for oral malignancies usually involves surgical excision followed by radiotherapy with or without chemotherapy.<sup>4</sup> Ablative surgery of the oral cavity leads to orofacial anatomic alterations even if reconstruction by a pedicled or free flap is carried out. Further, patients who receive radiotherapy have xerostomia and mucosal atrophy. The use of conventional removable dentures is difficult for patients who have such post-treatment conditions of the oral cavity.

Prosthetic rehabilitation using dental implants has become routine practice and has a high success rate.<sup>5</sup> The safety and effectiveness of dental implants have been extensively shown. Thus, dental implants are a feasible option for oral rehabilitation after ablative surgery of oral malignancies.<sup>6,7</sup>

Peri-implantitis is a condition characterized by inflammation and loss of supporting tissue around dental implants.<sup>8</sup> A common cause of peri-implantitis is dental plaque, which initiates gingivitis that progresses to pocketing and then bone loss. The clinical and radiologic appearance of peri-implantitis, namely

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hyperplasia, ulceration, and bone absorption around implants, can resemble that of malignancy. It is especially important to consider the differential diagnosis of malignancy for sudden onset and rapid progression of the lesion without response to therapy. In such cases, an exhaustive and detailed evaluation must be performed, and biopsy examination must be carried out to distinguish the inflammatory lesion from a soft tissue neoplasm.<sup>9,10</sup>

Inflammatory responses play decisive roles at different stages of tumor development, including initiation, promotion, malignant conversion, invasion, and metastasis.<sup>11</sup> Under normal circumstances, the acute inflammatory response is self-limiting. However, abnormal cellular alterations accompanying persistent inflammation, such as oxidative stress, gene mutations, epigenetic changes, and inflammatory cytokine-induced cell proliferation, are proposed to be carcinogenic factors.<sup>12</sup> The area between the gingiva and the implant develops constant inflammation, which can affect the stability of the mucosa; this inflammation might act as an initiating or promoting agent in the development of cancer in the mucosa. Dental implants per se have no known malignant potential and have been categorized as group 3 (not classifiable as to their carcinogenicity to humans) in an evaluation of carcinogenic risks associated with surgical implants.<sup>13</sup>

The occurrence of oral squamous cell carcinoma (OSCC) around dental implants is rare. This report describes a case of OSCC around a dental implant for which pathologic examination was performed to assess invasion around the implant. In addition, previous reports of OSCC around dental implants are reviewed.

## Report of Case

In 2000, a 58-year-old Japanese woman was referred by her dental practitioner to the Department of Oral and Maxillofacial Surgery, Shimane University Hospital (Izumo, Japan) because of tumor formation in the right lower gingiva. Her medical history was unremarkable except for alcohol and tobacco use. A 25 × 18 mm lesion extended from the premolar to the molar region and had a cauliflower-like surface with induration. The regional lymph nodes were not swollen. Radiography and enhanced computed tomography (CT) did not show any obvious marginal bony erosion under the lesion and swelling of the cervical lymph nodes. The incisional biopsy specimen showed histologic features of well-differentiated SCC. The clinical diagnosis was SCC in the lower gingiva (T2N0M0, stage II) and surgical resection was planned. However, the patient refused surgery and chemoradiotherapy was scheduled. The patient received a total of

69.2 Gy of irradiation and continuous subcutaneous injection of peplomycin 25 mg and 2 doses of superselective arterial infusion of carboplatin (500 + 300 mg). Concurrent chemoradiotherapy resulted in a complete response.

At that time, the patient wore a lower partial denture; however, she lost all her residual teeth in 2002. The difficulties in wearing a full denture increased gradually because of chemoradiotherapy-induced atrophy of the alveolar bone and xerostomia. However, no precancerous lesions or conditions, such as leukoplakia or lichen planus, appeared.

Because of the difficulties in wearing dentures, the patient desired to receive implant treatment. Accordingly, dental implant treatment was planned for the mandible after informing the patient of the risk of implant failure in the irradiated jaw and obtaining informed consent from her. In January 2009, the dental implant was inserted into the mandible. The postoperative course was uneventful. Subsequently, a patient-attachable denture supported by 4 dental implants was fabricated (Fig 1).

At 12 years after treatment of the primary lesion, a mass with a superficial white lesion around the implant in the right premolar region was noted at the same site as the primary lesion. The placed implant showed no mobility. An incisional biopsy specimen showed SCC. Radiography and enhanced CT depicted destruction of the cortical bone at the buccal and distal aspects of the implant (Fig 2). However, no enlargement of the regional lymph nodes was detected. In June 2012, marginal resection of the mandible and reconstructive surgery using a pedicled buccal fat pad graft were performed under general anesthesia. Moreover, reconstruction plate placement was performed to prevent pathologic fracture of the mandible. The grafted buccal fat pad was epithelized by postoperative day 14. A lower denture supported by the 3 remaining implants could be worn by 4 months postoperatively. At 2 years after resection of the second tumor, the patient remained free of disease with good oral function.

## PATHOLOGIC EXAMINATION

A sagittal section of the resected specimen was examined to assess microscopic invasion around the implant. The specimen showed tumor invasion from the crest of the ridge with subsequent tracking to the interface between the implant and bone, and the remaining bone was integrated with the dental implant at the implant neck. This established that the entry point was not between the gingiva and the implant, but from the adjacent crest of the ridge. Because the tumor invaded the implant surface, downward invasion along the interface between the implant

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