Clinicopathologic evaluation of malignancy adjacent to dental implants

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Objective. The aim of this study was to describe a new case series of peri-implant malignancy, review the literature, and discuss the implications of malignancies resembling peri-implantitis.
Study Design. This study was a retrospective analysis of cases from 2000 to 2016.
Results. Seven patients (two males and five females), aged 44 to 89 years, were included, representing 1.5% of oral malignancy cases. Five cases were squamous carcinoma, one of basal cell carcinoma, and one of carcinoma of metastatic origin. Six cases presented with nonulcerated overgrowth, with bone loss in three and massive osteolysis in one. Misinterpretation as peri-implantitis delayed diagnosis in six cases. Risk factors included previous oral malignancy (2), potentially malignant conditions (2), and smoking (1). Of the 47 cases in the English language literature, 85% were squamous cell carcinoma and 8.5% had distant metastasis. Most cases had one or more risk factors.
Conclusions. Peri-implant malignancy may represent up to 1.5% of oral malignancy cases. Clinical features imitating peri-implantitis may delay diagnosis. Lesions failing to respond to treatment, especially in patients with pre-existing risk factors, should significantly increase suspicion. Histopathology is crucial for diagnosis. (Oral Surg Oral Med Oral Pathol Oral Radiol 2017;123:103-112)

Peri-implantitis (PI) is a common disease involving the mucosa and alveolar bone surrounding dental implants. The clinical presentation includes erythema, swelling, suppuration, pocket formation, and bone loss.[1] It is considered a multifactorial condition, attributed to bacterial infections, poor oral hygiene, surgical trauma, genetic predisposition, implant surface characteristics, faulty or incorrect prosthetic design, occlusal overload, or improper surgical placement. There are no universally accepted protocols for the treatment of PI. In the majority of cases, peri-implant tissue removed during treatment is not submitted for histopathologic examination. Thus, there is only sparse information in the literature regarding the microscopic findings in PI. A review of several small case series, which included analyses of biopsy material from PI, reported hyperplasia and ulceration of pocket epithelium and the presence of a mixed population of inflammatory cells.[2] A study of 117 biopsies from PI cases reported that close to 50% of cases did not exhibit simple inflammatory changes. Instead, other potentially aggressive lesions, such as pyogenic granuloma, giant cell granuloma, or *Actinomyces*-related inflammation were diagnosed.[3] These entities exhibit clinical and radiographic characteristics that imitate PI but fail to respond to conventional treatment modalities. Rarely, primary as well as metastatic tumors have been described around or adjacent to dental implants, some of which also clinically imitate PI.[4-29]

The objectives of the present study were to describe a new case series of malignancy around dental implants, investigate the spectrum of clinicopathologic characteristics, and discuss the implications of clinical features overlapping with those of conventional PI.

Guiding the present study were two propositions: (1) Malignancy in conjunction with dental implants may not be as rare as previously believed and is possibly underdiagnosed because it imitates PI; (2) patients presenting with malignancies in conjunction with dental implants may have recognizable predisposing factors for oral cancer unrelated to the dental implant procedure.

MATERIALS AND METHODS

We performed a retrospective clinicopathologic analysis of all cases diagnosed with implant-related malignancy collected from our archives between 2000 and 2016. Data collected from patients' files and pathology reports included age, gender, location of the tumor,

Statement of Clinical Relevance

Clinicoradiographic presentation of peri-implant malignancy may mimic peri-implantitis and lead to delayed diagnosis. Peri-implant malignancy most frequently occurs in patients with recognized risk factors for oral cancer. Increased awareness of the possibility of primary or metastatic malignancy imitating peri-implantitis and biopsy are recommended in patients at risk.

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clinical presentation, duration between the first report of signs and symptoms and actual diagnosis of cancer, risk factors or predisposing factors, treatment, and follow-up.

Literature review (using PubMed and Google Scholar) was performed on data published between 2000 and 2016 in English (or with an abstract in English). All types of articles, including reviews and case reports, were retrieved. The key words included "gingiva," "mandible," "maxilla," "dental implant," "cancer," "malignant," and "malignancy"; both human and animal studies were retrieved. The information of interest included age, gender, location of the tumor, clinical presentation, duration between the first report of signs and symptoms and actual diagnosis of cancer, risk factors or predisposing factors, treatment, and follow-up.

The present study was written in accordance with the ethical requirements (both Israeli and Good Clinical Practice/Pharmaceuticals for Human Use standards) for clinical trials.

RESULTS

Literature review

A search of the literature published between 2000 and 2016 yielded 25 articles, describing 47 cases of oral malignancy involving dental implants.[4-29] We noticed a sharp increase in the number of reported cases in the last 10 years (Table I).

Cases in the literature showed a female predominance, with a male/female ratio of 1:1.5. The mean age of patients was 67.2 years. The mandible was involved in 42 cases (89.4%) and the maxilla in five cases (10.6%). Forty cases (85.1%) were squamous cell carcinoma (SCC), four (8.5%) were metastatic spread from lung or breast cancer, and one case each (2.1%) were osteosarcoma, plasmacytoma, and lymphoma. Peri-implant malignancies were primary tumors in 29 cases (61.7%), recurrent or second primary in 11 cases (23.4%), and metastasis from distant tumors in 4 cases (8.5%). Recognized risk factors for oral cancer included potentially malignant conditions (erythroplakia, leukoplakia, oral lichen planus [OLP] or proliferative verrucous leukoplakia [PVL]) in 21 cases (44.7%). Previous oral malignancy was reported in 22 cases (46.8%), primary extra-oral malignancy in eight cases (17%), past or present smoking in 15 cases (31.9%), and alcohol abuse in eight cases (17%), with co-existing risk factors in several cases. Detailed information on history of smoking (e.g., pack-years) was not given in the majority of cases. Information on alcohol use (or abuse) was also unsatisfactory; in most cases, it was only mentioned as a potential risk factor, without any quantitative information.

The initial clinical appearance imitated PI in 17 cases (36.2%) and presented as a mass or swelling in 18 cases (38.3%) and as an ulcer or ulcerated mass in nine cases (19.1%). In one case (2.1%), numb chin syndrome as a metastatic lesion was described.

New cases

The study included seven patients, two males and five females (M:F = 1:2.5). The age range was 44 to 89 years (mean 69 years). The number of cases of oral malignancy (primary tumors and metastases from extraoral sites) in the archives of pathology was found to range between 30 and 35 new cases per year during the period 2000-2016. Peri-implant malignancy was thus calculated to represent between 1% and 1.5 % of all oral malignancies.

In five cases (71.4%), the diagnosis was SCC (Figures 1 and 2); in the remaining cases, one case (14.3%) each was of basal cell carcinoma (BCC) (Figure 3) and metastatic carcinoma, most probably from the lungs (Figures 4A and 4B). Five cases (71.4%) occurred in the mandibular alveolar mucosa and two cases (28.6%) in the maxillary alveolar mucosa (Table II).

Clinical presentation was variable and included erythematous nonulcerated overgrowth in six cases (85.7%) and ulcerated erythematous mass in one (14.3%). Peri-implant bone loss was documented in three cases (47.8%) and massive osteolysis with expansion in one (14.3%).

Predisposing or risk factors were identified in five cases. Case 1 had a diagnosis of lower lip BCC of cutaneous origin, extending onto the mandibular alveolar mucosa, 3 years before implantation. A first local recurrence was resected 2 years after the diagnosis. One year after implantation, an overgrowth around a mandibular implant was removed and a biopsy performed, resulting in the diagnosis of BCC. It was considered a recurrence by extension from the original tumor because of the tumor's proximity to the margin of the previous resection. The patient had not received radiation therapy. Case 2 was a heavy smoker for approximately 40 years; case 4 had linear white lesions on the adjacent buccal mucosa, clinically suspicious for OLP or leukoplakia (no biopsy was performed before the discovery of the malignancy); case 6 presented a red-white lesion on the buccal mucosa, which was clinically consistent with OLP or erythroleukoplakia, (no biopsy was performed before the discovery of the malignancy); case 7 had been diagnosed with PVL that had been present for 6 years, during which time the patient presented with two existing SCC lesions in two different locations, 4 years and 1 year before peri-implant involvement. She had been treated by surgery alone for the first tumor of the right buccal mucosa, developed a peri-implant malignancy approximately 4 year later on the left buccal mucosa and mandibular