



Metastases and primary tumors around dental implants: A literature review and case report of peri-implant pulmonary metastasis

Chantal Pfammatter, DDS, Dr Med Dent¹/
 Irène Hitz Lindenmüller, DDS, Dr Med Dent¹/
 Alessandro Lugli, MD, Prof Dr Med²/
 Andreas Filippi, DDS, Prof Dr Med Dent¹/
 Sebastian Kühn, DDS, Dr Med Dent¹

Objective: To perform a literature review on peri-implant metastases and primary malignoma and report a case of a pulmonary metastasis around dental implants of the anterior mandibular jaw that mimicked peri-implantitis. **Method and Materials:** A literature search of publications from June 1980 to June 2011 in the PubMed/Medline database was performed to collect information about the type, incidence, and localization of malignant primary tumors and metastases around dental implants and to evaluate potential risk factors. A descriptive statistic was performed based on the collected data with regard to the type and/or origin of tumor, its localization, and the patient's age and sex. **Results:** A total of 1,795 articles were considered for evaluation. Peri-implant metastases are described in three articles, and peri-implant primary tumors were found in 14 publications. Of all peri-implant metastases, no associated risk factors are mentioned. Those of the peri-implant tumors are alterations of the peri-implant mucosa (such as oral lichen planus, verrucous leukoplakia, and ulcer). Most of the primary tumors are squamous cell carcinoma. The mean age of the patients with peri-implant metastases was 68 years; for the peri-implant primary tumors, it was 71 years. **Conclusion:** Peri-implant metastases and primary tumors are rare. Every untypical or refractory reaction to the treatment of peri-implantitis is suspicious for malignancy as long as the contrary remains unproven. (*Quintessence Int* 2012;43:563–570)

Key words: dental implant, numb chin syndrome, peri-implantitis, primary tumor, pulmonary metastasis, risk factors

Oral cancer represents 2% of all malignant tumors. Approximately 90% of oral cancers are squamous cell carcinoma arising from the oral epithelium. The remaining 10% are malignant intraoral salivary gland tumors, melanomas, sarcomas of the soft tissues and jaw bones, non-Hodgkin lymphomas, and the exceedingly rare malignant odontogenic tumors and metastatic tumors of primary cancers located elsewhere in the body.¹ Only 1% of oral cancers are

metastases.² There is a higher incidence of hard tissue metastases in the maxillofacial region than of soft tissue metastases.^{3–7} The relationship between hard and soft tissue metastases in the oral cavity is 2:1.⁸

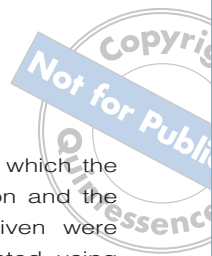
The origin of metastases differs between the sexes. Breast cancer is the most frequent metastatic oral cancer for hard tissue in females, whereas lung cancer (followed by prostate cancer) represents the most frequent metastatic tumor in males.⁸ The most commonly affected bone in the maxillofacial region is the posterior mandible.^{2–4,7–9}

Metastases and primary tumors can appear around dental implants, thus representing an even more rare event.^{10–12} Diagnosis at an early stage is challenging, since the clinical appearance of metastases and primary tumors around dental implants

¹School of Dental Medicine, Department of Oral Surgery, Oral Radiology, and Oral Medicine, University of Basel, Basel, Switzerland.

²Institut of Pathology, University of Bern, Bern, Switzerland, and University Hospital of Basel, Basel, Switzerland.

Correspondence: Dr Chantal Pfammatter, Hebelstrasse 3, 4056 Basel, Switzerland. Email: chantal.pfammatter@unibas.ch



shows typical elements of unspecific peri-implant infections such as swelling, bleeding on probing (BoP), and pain. In addition, radiographic findings in the form of peri-implant osteolysis are similar and not clearly distinguishable from peri-implant infections (conventional peri-implantitis). Peri-implant tissues are refractory to local disinfection and debridement, which is one of the first signs of malignancy besides anesthesia.

To date, the incidence and etiology of peri-implant metastasis and primary tumors remain widely unclear. Only scarce information about peri-implant metastases and primary tumors are available, which is presented most frequently in single case reports. The aim of this study was to perform a literature review of peri-implant primary tumors and metastases and to report a case of a pulmonary tumor metastasis, initially misinterpreted as peri-implantitis.

METHOD AND MATERIALS

An electronic literature search of sources published between June 1980 and June 2011 on the PubMed/Medline databases was performed to collect information about the type, incidence, and localization of malignant primary tumors and metastases around dental implants and to evaluate potential risk factors. The search was limited to studies in English, German, Italian, or French using the following terms: *peri-implant metastasis*, *peri-implant tumor*, *peri-implant carcinoma*, *peri-implant malignancy*, *oral metastasis jaw bone*, *jaw bone metastasis*, *oral cancer*, *oral squamous cell carcinoma*, *pulmonary metastasis jaw bone*, *malignancy*, *tumor recurrence*, *pulmonary metastasis*, *dental implants*, *breast metastasis*, *prostatic metastasis*, *skin metastasis*, *multiple myeloma*, *plasmacytoma*, *gastro-intestinal metastasis*, *colon metastasis*, *rectum metastasis*, *ileum metastasis*, *stomach metastasis*, *renal metastasis*, *kidney metastasis*, *thyroid gland metastasis*, and *liver metastasis*.

Any article reporting on dental metastases or primary malignant tumors around dental implants (case reports with histologic

proof) were included. Articles in which the age of patients or the localization and the type of the tumor were not given were excluded. The data were extracted using tables prepared beforehand. Two reviewers evaluated the literature, and disagreements were critically revised and discussed. A descriptive statistic was performed based on the collected data with regard to the type and/or origin of tumor, localization, age, and sex. Tables were created using a spreadsheet (Microsoft Excel 2008).

CASE REPORT

A 55-year-old woman with a history of pancreatic carcinoma and histologically proven nonsmall cell lung cancer (NSCLC) was referred by her private dentist during chemotherapy in our department because of a painful swelling of the peri-implant mucosa of the right anterior mandible. The mucosa had a smooth surface, and at this stage, it showed typical signs of inflammation in the form of pain, swelling, redness, and a probing depth of 7 mm with immediate BoP (Fig 1). The patient showed good oral hygiene. A panoramic radiograph was taken, showing vertical peri-implant bone loss of 2 to 3 mm (Fig 2) mesial and distal of the implants in the right anterior mandible. Local submarginal irrigation under local anesthesia (Septanest 2%, 1:200,000; Specialites Septodont) was initially and weekly performed by mechanical debridement and chemical disinfection with chlorhexidine (Dentohexin 0.2%, Streuli Pharma). Additionally, metronidazole gel (Colgate Elyzol 25% Dental Gel; Colgate-Palmolive) was applied locally. The clinical signs of infections decreased within the first 2 weeks. Three weeks after successful initial therapy, the swelling had increased again (Fig 3) and a slight anesthesia of the right lower lip occurred. A cone beam computed tomograph (CBCT) of the right anterior mandible was performed, showing an osteolytic process (Fig 4). Biopsies of the buccal and lingual peri-implant regions were taken for histologic evaluation. The patient died 4 weeks after diagnosis.



Fig 1 Clinical manifestations of an assumed peri-implantitis. The buccal mucosa around the mandibular right lateral incisor implant showed a smooth surface with typical signs of inflammation in the form of pain, swelling, redness, and a probing depth of 7 mm, with immediate BoP.

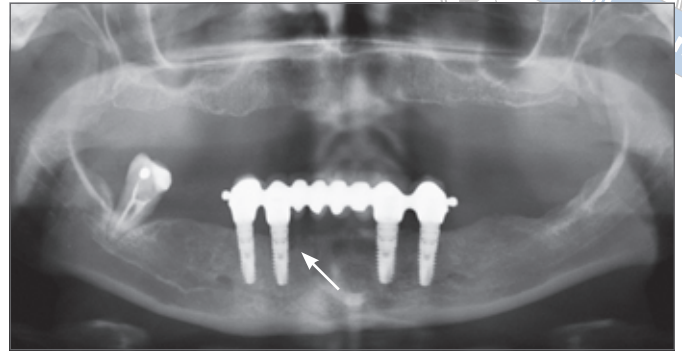


Fig 2 The panoramic radiograph shows a vertical bone loss of 2 to 3 mm around the implants (white arrow).



Fig 3 (above) Clinical manifestations: An increased swollen buccal mucosa around the mandibular right lateral incisor implant. The surface of the mucosa was more smooth and did not attach at the implant. The surrounding region was sensitive.

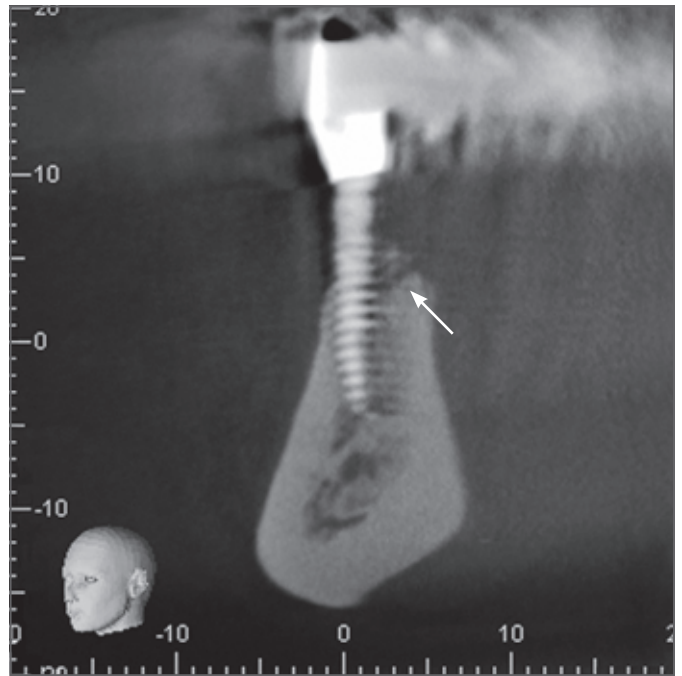


Fig 4 (right) The CBCT showed an osteolytic process, affecting the anterior region of the mandibular jaw. The arrow points to the building of the sequestrum.

RESULTS

A total of 1,795 articles were considered for evaluation. Of these, 17 publications matching the inclusion criteria (excluding the current case) could be identified. The results are summarized in Tables 1 and 2.

Metastases

Peri-implant metastases are described in three case reports (the current case not

included), including seven implants (see Table 1). The metastases had different origins: in two cases (six implants affected), the primary tumor was identified as mamma carcinoma.^{10,11} One case presented peri-implant bronchus metastasis.¹² Four implants were localized in the anterior mandible. Two implants, which were affected by a metastasis of mamma carcinoma, were localized in the anterior maxilla. The mean age of the patients with peri-implant metastases was 68 years. The only reported risk



Table 1 Summary of reported cases of peri-implant metastases around dental implants

Article	Type of article	No. of cases	Mean age	Sex	Localization
Orhan et al ¹⁰	Case report	1	69	Female	Anterior mandible/posterior mandible
Dib et al ¹¹	Case report	1	67	Female	2 anterior mandible/2 anterior maxilla
Verhoeven et al ¹²	Case report	1	67	Female	Anterior mandible
Current case	Case report	1	(55)	Female	Anterior mandible
Total	4 case reports	4	68 (65)	(4) Female	5 anterior mandible/2 anterior maxilla/ 1 posterior mandible

Table 2 Summary of reported cases of primary tumors around dental implants

Article	Type of article	No. of cases	Mean age	Sex	Localization
Friedman et al ¹³	Case report	1	65	1 male	Anterior mandible
Clapp et al ¹⁴	Case report	3	78	2 male/1 female	Mandible ¹
Moxley et al ¹⁵	Case report	1	74	1 female	Anterior mandible
Block et al ¹⁶	Case report	1	72	1 male	2 anterior mandible
Shaw et al ¹⁷	Case report	2	68	1 male/1 female	2 anterior mandible
Czerninski et al ¹⁸	Case report/ review	8 ² /2	66	4 ² /1 male/ 4 ² /1 female	Posterior mandible/2 anterior mandible
Poggio ¹⁹	Case report	1	75	1 male	Anterior mandible
Abu El-Naaj et al ²⁰	Case report	2	71	1 male/1 female	Anterior mandible
Kwok et al ²¹	Case report	3	67	2 male/1 female	2 anterior mandible
Gallego et al ²²	Case report	1	81	1 female	3 anterior mandible
Schache et al ²³	Case report	1	77	1 male	Anterior mandible/posterior mandible
Eguia del Valle et al ²⁴	Case report	1	76	1 male	Posterior mandible
Gulati et al ²⁵	Case report	1	62	1 female	Anterior mandible/posterior mandible
Meijer et al ²⁶	Case report	1	65	1 female	Anterior mandible
Total	13 case reports/ 1 review	21	71	12 male/9 female	18 anterior mandible/4 posterior mandible

¹No information about the exact localization, not included in the total; ²Six of them were also described in other publications.

factor was an amelanotic tumor in the eye.¹¹ The ratio between females and males for the peri-implant metastasis was 3:0.

Primary tumors

Peri-implant primary tumors are described in 14 articles, revealing a total of 28 implants from 21 single case descriptions (see Table 2).¹³⁻²⁶ Most of the implants (n = 18) were localized in the anterior mandible, except for four implants, which were situated in the molar region. Squamous cell carcinoma (n = 13) and plasmacytoma (n = 1)

are the only primary peri-implant tumors described.¹⁹ Eight of the cases with a peri-implant primary tumor such as the squamous cell carcinoma had previously had squamous cell carcinoma. The mean age of the patients with primary peri-implant tumors was 71 years. The ratio between male and females was 4:3.

Risk factors and medical history

The 21 peri-implant primary tumors showed various associated risk factors. The most





Origin
Breast
Breast
Bronchus
Bronchus
2 breast, 2 bronchus

Origin
Squamous cell carcinoma
Squamous cell carcinoma
Squamous cell carcinoma
Squamous cell carcinoma
Squamous cell carcinoma
Squamous cell carcinoma
Plasmacytoma
Squamous cell carcinoma
Squamous cell carcinoma
Squamous cell carcinoma
Squamous cell carcinoma
Squamous cell carcinoma
Squamous cell carcinoma
Squamous cell carcinoma
13 squamous cell carcinoma, 1 plasmacytoma

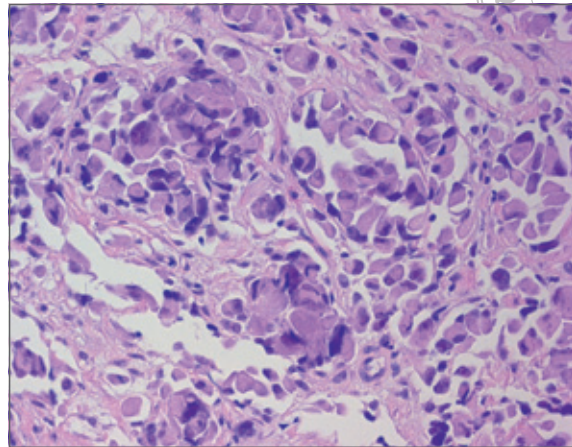


Fig 5 Histology of the mandibular right lateral incisor region: a poorly differentiated carcinoma, histomorphologically consistent with a metastasis of NSCLC (hematoxylin-eosin, original magnification $\times 40$).

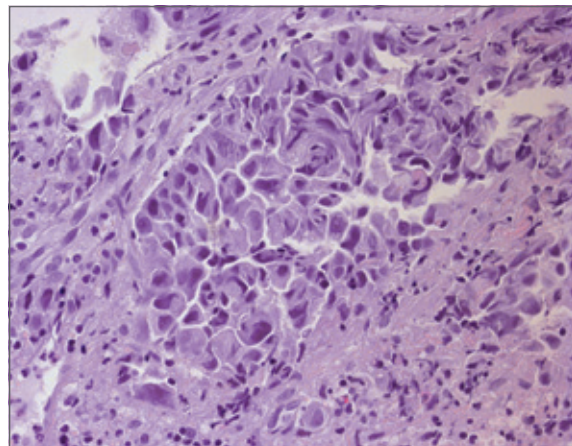


Fig 6 Histology of the lung. Biopsy of the lung with an infiltration of NSCLC (hematoxylin-eosin, original magnification $\times 40$).

common risk factors were the alterations of the peri-implant mucosa such as oral lichen planus,^{18,20,22} verrucous leukoplakia,^{16,17} verrucous carcinoma,¹⁶ or a preceding squamous cell carcinoma.^{15,17,18,21,22,25} Systemic changes were reported as ventricular arrhythmia, hyperuricemia, and arterial hypertension.²⁴ Also, cigarette and alcohol use were reported as risk factors.^{13,14,16,18,20,21,25} No information about associated risk factors for peri-implant metastases could be extracted.

Histologic results

The hematoxylin-eosin biopsy showed an infiltration of a poorly differentiated carcinoma (Fig 5). The biopsy was compared with the morphology of the independently retrieved lung biopsy specimen, which showed NSCLC (Fig 6). The morphologies of the carcinoma of the peri-implant biopsies and the primary pulmonary carcinoma were comparable. Thereby, the neoplastic infiltration in the right peri-implant anterior mandible was consistent with pulmonary cancer metastasis.



DISCUSSION

Only three cases of peri-implant metastasis have been reported to date. In contrast, the number of described peri-implant primary tumors is much higher. Nevertheless, both primary peri-implant tumors and metastasis represent rare events. The small number of detected reports does not allow for statistical analysis in this study, thus explaining the rather short descriptive statistic. The low incidence may cause difficulties in correct and quick diagnostics of peri-implant metastasis or primary tumors. Pulmonary metastases of the gingiva are reported in 13 cases,²⁷ whereas the appearance around dental implants has been described only once until now.¹² Concerning our case, the authors presumed it was peri-implantitis related to the immunosuppression caused by the chemotherapy to which the patient was exposed. Additionally, the typical clinical signs of peri-implantitis with BoP, increased probing depth, loss of bony support, and sudden reaction on local scaling and debriding procedure could initially be observed in our case.¹² Besides clinical appearance, the radiographic findings with vertical peri-implant bone loss showed diagnostic characteristics similar to the bone loss related to conventional peri-implant infection. Only the beginning anesthesia of the lower lip in combination with a refractive reaction to local hygiene treatment 2 weeks after initial success led to the suspicion of a malignant process in our case. Anesthesia or even paraesthesia and hypesthesia as well as the numb chin syndrome, also called mental neuropathy, are well known to represent first symptoms of either primary or metastatic malignant tumors and have been described as first symptoms in other cases as well.^{10,28-34}

The localization of metastases in the jawbones, like in most of the cases evaluated in this review, affects the anterior part of the mandible, despite the fact that Hirshberg et al⁸ and Lim et al³⁵ described a predominant appearance of metastases in the posterior mandible.

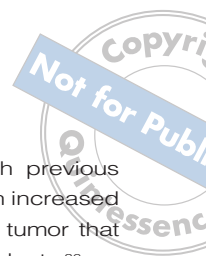
Eight of the cases with a peri-implant primary tumor had previously had squamous cell carcinoma. We assume that the previous eight cases are recrudescences. It is generally

well established that patients with previous squamous cell carcinoma are at an increased risk of developing a new primary tumor that can occur in bone treated with implants.³⁶

It is remarkable that the pathogenesis of the metastatic process in the jawbones is not clear. One theory explaining the metastatic pathogenesis is the vascular theory of the jaw. The mandibular premolar and molar region represent a region with rich bone marrow. In this situation, the blood flow slows and causes a change of blood circulation. A result may be a higher entrapment of metastatic cells.³⁷ Considerations have also been given to the Batson plexus, which leads the arterial blood from the skull to the sacrum and makes an anastomosis at the circle of Willis with the internal carotid.³⁸ This might explain how metastases can reach the oral cavity by passing filtration through the lungs, but without requiring any previous pulmonary participation.³⁹ The high bone turnover in this region involves the jaws in cases of advanced disease. Raubenheimer and Noffke described the process of metastases in bones based on a cascade that includes detachment of tumor cells from the primary site, invasion into the surrounding tissue, intravasation, transport to the site of metastasis, extravasation, and bone degradation or bone formation.⁴⁰

Primary malignancy is undetected in about two-thirds of all cases.⁴¹ Other authors reported that in about one-third to one-fifth of all cases, the primary cancer is not found until the oral metastases were diagnosed.^{5,7,9,35} Hirshberg et al stated that the lung and breast are the most common primary sites in women and men,⁹ respectively, whereas a review of the Japanese literature identifies the uterus as a primary tumor location for women.⁴² An analysis of 41 Korean patients suggest the liver as the most common primary site for tumors, but the lung remains the primary site for metastases to jawbones (23 cases).³⁵

In the current case, the peri-implantitis could act as an initiating agent for malignancy, because the mucosa was already damaged.⁴³ Shaw et al¹⁷ discussed the possibility that the presence of implants and fixed protheses inhibit complete examination of oral mucosa at recalls and delay definitive diagnosis.





Our observations and descriptions were based on data from case reports, which are defined to be level 4 research.⁴⁴ More evidence-based literature (level 1 to 3) about the incidence of peri-implant metastases and primary tumors around dental implants and the possible risk factors would be necessary to yield reliable results.

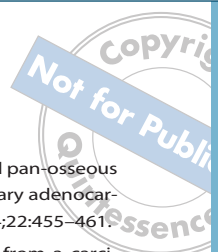
Clinical and histologic diagnosis of a peri-implant metastasis can cause difficulties. Every atypical or refractory reaction on treatment is suspicious for malignancy until the contrary is proven.

Second primary malignancy or metastases can masquerade as benign peri-implant complications, so a high degree of vigilance is required in the follow-up of these patients.

REFERENCES

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; 127:2893–2917.
2. Valdivieso M, Ostria J, Lobos N. Oral and maxillofacial metastases of neoplasms from other sites of the body. *Med Oral* 1999;4:583–587.
3. Hirshberg A, Buchner A. Metastatic tumours to the oral region. An overview. *Eur J Cancer B Oral Oncol* 1995;31B:355–360.
4. Morishita M, Fukuda J. Hepatocellular carcinoma metastatic to the maxillary incisal gingiva. *J Oral Maxillofac Surg* 1984;42:812–815.
5. Zachariades N, Koumoura F, Vairaktaris E, Mezitis M. Metastatic tumors to the jaws: A report of seven cases. *J Oral Maxillofac Surg* 1989;47:991–996.
6. Piattelli A, Fioroni M, Rubini C. Gingival metastasis from a prostate adenocarcinoma: Report of a case. *J Periodontol* 1999;70:441–444.
7. van der Waal RI, Buter J, van der Waal I. Oral metastases: Report of 24 cases. *Br J Oral Maxillofac Surg* 2003;41:3–6.
8. Hirshberg A, Shnaiderman-Shapiro A, Kaplan I, Berger R. Metastatic tumours to the oral cavity—pathogenesis and analysis of 673 cases. *Oral Oncol* 2008;44:743–752.
9. Hirshberg A, Leibovich P, Buchner A. Metastatic tumors to the jawbones: Analysis of 390 cases. *J Oral Pathol Med* 1994;23:337–341.
10. Orhan K, Bayndr H, Aksoy S, Seker BK, Berberoglu A, Ozan O. Numb chin syndrome as a manifestation of possible breast cancer metastasis around dental implants. *J Craniofac Surg* 2011;22:942–945.
11. Dib LL, Soares AL, Sandoval RL, Nannmark U. Breast metastasis around dental implants: A case report. *Clin Implant Dent Relat Res* 2007;9:112–115.
12. Verhoeven JW, Cune MS, van Es RJ. An unusual case of implant failure. *Int J Prosthodont* 2007;20:51–54.
13. Friedman KE, Vernon SE. Squamous cell carcinoma developing in conjunction with a mandibular staple bone plate. *J Oral Maxillofac Surg* 1983;41:265–266.
14. Clapp C, Wheeler JC, Martof AB, Levine PA. Oral squamous cell carcinoma in association with dental osseointegrated implants. An unusual occurrence. *Arch Otolaryngol Head Neck Surg* 1996;122:1402–1403.
15. Moxley JE, Stoelinga PJ, Blijdorp PA. Squamous cell carcinoma associated with a mandibular staple implant. *J Oral Maxillofac Surg* 1997;55:1020–1022.
16. Block MS, Scheufler E. Squamous cell carcinoma appearing as peri-implant bone loss: A case report. *J Oral Maxillofac Surg* 2001;59:1349–1352.
17. Shaw R, Sutton D, Brown J, Cawood J. Further malignancy in field change adjacent to osseointegrated implants. *Int J Oral Maxillofac Surg* 2004;33:353–355.
18. Czerninski R, Kaplan I, Almozino G, Maly A, Regev E. Oral squamous cell carcinoma around dental implants. *Quintessence Int* 2006;37:707–711.
19. Poggio CE. Plasmacytoma of the mandible associated with a dental implant failure: A clinical report. *Clin Oral Implants Res* 2007;18:540–543.
20. Abu El-Naaj I, Trost O, Tagger-Green N, et al. Peri-implantitis or squamous cell carcinoma [in French]? *Rev Stomatol Chir Maxillofac* 2007;108:458–460.
21. Kwok J, Eyeson J, Thompson I, McGurk M. Dental implants and squamous cell carcinoma in the at risk patient—Report of three cases. *Br Dent J* 2008;205:543–545.
22. Gallego L, Junquera L, Baladron J, Villarreal P. Oral squamous cell carcinoma associated with symphyseal dental implants: An unusual case report. *J Am Dent Assoc* 2008;139:1061–1065.
23. Schache A, Thavaraj S, Kalavrezos N. Osseointegrated implants: A potential route of entry for squamous cell carcinoma of the mandible. *Br J Oral Maxillofac Surg* 2008;46:397–399.
24. Eguia del Valle A, Martinez-Conde Llamosas R, Lopez Vicente J, Uribarri Etxebarria A, Aguirre Urizar JM. Primary oral squamous cell carcinoma arising around dental osseointegrated implants mimicking peri-implantitis. *Med Oral Patol Oral Cir Bucal* 2008;13:e489–e491.
25. Gulati A, Puthussery FJ, Downie IP, Flood TR. Squamous cell carcinoma presenting as peri-implantitis: A case report. *Ann R Coll Surg Engl* 2009;91:W8–10.
26. Meijer GJ, Dieleman FJ, Berge SJ, Merckx MA. Removal of an oral squamous cell carcinoma including parts of osseointegrated implants in the marginal mandibulectomy. A case report. *Oral Maxillofac Surg* 2010;14:253–256.





27. Yoshii T, Muraoka S, Sano N, Furudoi S, Komori T. Large cell carcinoma of the lung metastatic to the mandibular gingiva. *J Periodontol* 2002;73:571–574.
28. Lossos A, Siegal T. Numb chin syndrome in cancer patients: Etiology, response to treatment, and prognostic significance. *Neurology* 1992;42:1181–1184.
29. Marinella MA. Metastatic large cell lung cancer presenting with numb chin syndrome. *Respir Med* 1997;91:235–236.
30. Marinella MA. Ophthalmoplegia: An unusual manifestation of hypocalcemia. *Am J Emerg Med* 1999;17:105–106.
31. Bar-Ziv J, Slasky BS. CT imaging of mental nerve neuropathy: The numb chin syndrome. *AJR Am J Roentgenol* 1997;168:371–376.
32. Simpson JF. Numb-chin syndrome. *Lancet* 1970; 2:1366.
33. Burt RK, Sharfman WH, Karp BI, Wilson WH. Mental neuropathy (numb chin syndrome). A harbinger of tumor progression or relapse. *Cancer* 1992;70: 877–881.
34. Lossos A, Siegal T. Case 27-1994: The numb chin syndrome. *N Engl J Med* 1994;331:1460.
35. Lim SY, Kim SA, Ahn SG, et al. Metastatic tumours to the jaws and oral soft tissues: A retrospective analysis of 41 Korean patients. *Int J Oral Maxillofac Surg* 2006;35:412–415.
36. Jovanovic A, van der Tol IG, Kostense PJ, et al. Second respiratory and upper digestive tract cancer following oral squamous cell carcinoma. *Eur J Cancer B Oral Oncol* 1994;30B:225–229.
37. Shankar S. Dental pulp metastases and pan-osseous mandibular involvement with mammary adenocarcinoma. *Br J Oral Maxillofac Surg* 1984;22:455–461.
38. Wolujewicz MA. Condylar metastasis from a carcinoma of the prostate gland. *Br J Oral Surg* 1980;18: 175–182.
39. Zachariades N, Papanicolaou S. Breast cancer metastatic to the mandible. *J Oral Maxillofac Surg* 1982; 40:813–818.
40. Raubenheimer EJ, Noffke CE. Pathogenesis of bone metastasis: A review. *J Oral Pathol Med* 2006;35: 129–135.
41. D’Silva NJ, Summerlin DJ, Cordell KG, et al. Metastatic tumors in the jaws: A retrospective study of 114 cases. *J Am Dent Assoc* 2006;137:1667–1672.
42. Nishimura Y, Yakata H, Kawasaki T, Nakajima T. Metastatic tumours of the mouth and jaws. A review of the Japanese literature. *J Maxillofac Surg* 1982; 10:253–258.
43. Esposito M, Worthington HV, Coulthard P. Interventions for replacing missing teeth: Treatment of perimplantitis. *Cochrane Database Syst Rev* 2004: CD004970.
44. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence-based medicine: What it is and what it isn’t. *Clin Orthop Relat Res* 2007;455:3–5.