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Case Report

Ameloblastic carcinoma, secondary type, with prominent squamous differentiation: a case report and literature review

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In this case report, we describe a 55-year-old male diagnosed with ameloblastic carcinoma. The tumor arose from an intraosseous cystic ameloblastoma with prominent squamous differentiation and frank invasion of the gingiva. It is challenging to diagnose ameloblastic carcinoma based only on superficial biopsy specimen, due to prominent squamous differentiation and overlying involvement of the squamous epithelium. Radiographic images and immunohistochemical studies may be helpful for accurate diagnosis.

Keywords: ameloblastic carcinoma, ameloblastoma, squamous cell carcinoma, biopsy

1. Introduction:

Ameloblastic carcinoma is a rare but aggressive malignant epithelial odontogenic tumor [1] with characteristic histopathological and clinical features, which requires aggressive surgical treatment and surveillance [2]. Primary ameloblastic carcinoma is de novo or originates from a pre-existing ameloblastoma or odontogenic cyst [3, 4]. If there is malignant transformation of ameloblastoma or transformation after repeated postsurgical recurrences, it is of secondary type [5]. There is no consensus on the treatment of ameloblastic carcinoma. However, wide surgical excision with or without radiotherapy is the most common treatment modality [6].

We report a case of secondary type ameloblastic carcinoma of mandible arising from an intraosseous cystic ameloblastoma with prominent squamous differentiation and frank invasion of the gingiva upwards to gingival squamous epithelium. It is important to differentiate ameloblastic carcinoma of bone from squamous cell carcinoma of gingiva as they require different treatment modalities and have different outcomes. This is diagnostically challenging based on superficial biopsy specimen alone, due to prominent squamous differentiation and overlying involvement of the squamous epithelium. Clinical information, such as radiological images and immunohistochemical studies, may be helpful for accurate diagnosis.

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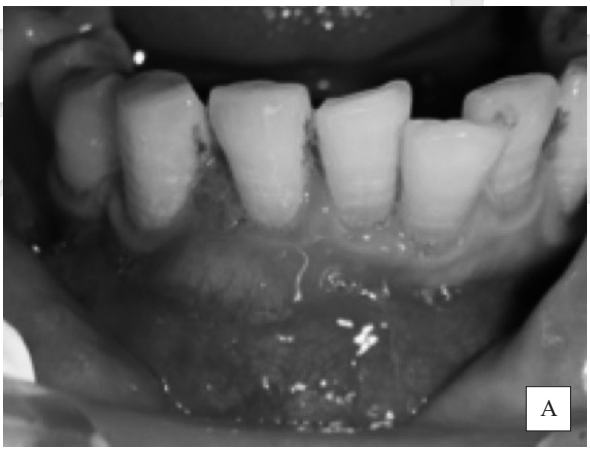
2. Case presentation:

A 55-year-old male presented with a painless tumor over the lower anterior lingual area for 3 years, with gradual labial gingival swelling over a period of months. He denied any systemic disease or trauma history. On physical examination, asymmetric swelling in the chin area, especially on the right side, was noted with painless expansion of lower anterior labial alveolar bone plate and shallow



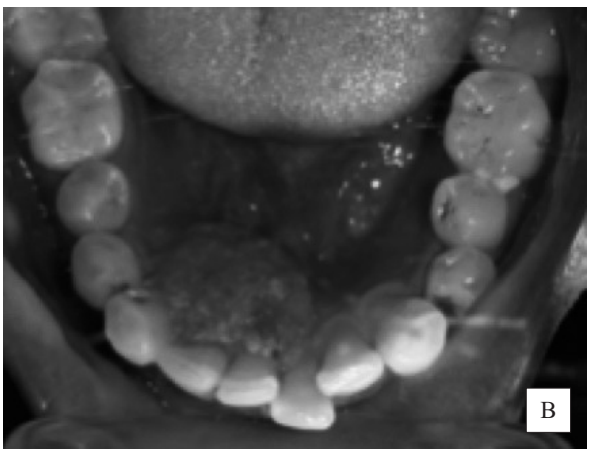


Fig 1. A. Asymmetric swelling in the chin area, especially on the right side.
B. Exophytic mass (2.0×1.5 cm) in the lingual area of teeth #31 to #43.

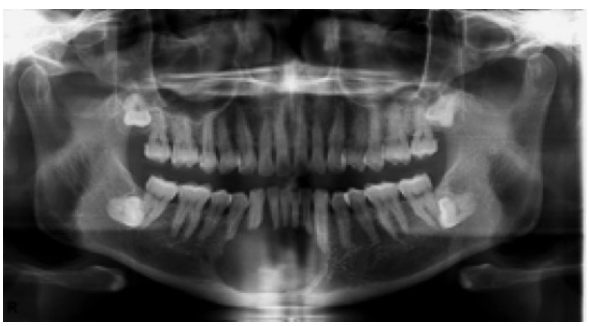


Fig 2. Panoramic radiograph shows well-defined radiolucent lesion in the anterior mandible with root end resorption.

anterior vestibule (Fig. 1A). There was neither local heat nor paresthesia. There was an exophytic mass in the oral cavity with slight induration. It measured 2.0×1.5 cm and was located in the lingual area of teeth #31 to #43 (Fig. 1B). The overlying gingival epithelium showed irregular surface. Tooth mobility over #32 to #43, grade III, was also noted. There was no palpable lymphadenopathy or mass in the neck. Panoramic radiograph revealed a well-defined radiolucent lesion in the anterior mandible extending from teeth #44 to #33, with root end resorption (Fig. 2). Incisional biopsies taken from two sites, one from lower anterior mandible and one from #41 lingual region, led to the diagnosis of squamous cell carcinoma. The anterior mandible with tumor lesion was widely resected.

The histopathological features of the tumor revealed an intraosseous cystic ameloblastoma with de-differentiated component of ameloblastic carcinoma formation (Fig 3A). Nests of basaloid or columnar tumor cells arranged in reticular or solid pattern with peripheral nuclear palisading, nuclear atypia, and focal cellular change were seen (Fig. 3B). The tumor invaded the mandible and the peripheral soft tissue, upwards to the overlying gingival squamous epithelium. Erosion and pseudoepitheliomatous hyperplasia in the gingival squamous epithelium were also noted. There was marked squamous differentiation both in the benign cystic epithelium and the malignant component. Immunohistochemical analysis demonstrated higher percentage of cells with Ki-67(+) in the component of ameloblastic carcinoma (Fig 3C) and higher immunoexpression of high molecular weight cytokeratin (34βE12) (Fig 3D) than of low molecular weight cytokeratin (CK8) in the ameloblastic carcinoma (Fig 3E). After the main specimen was analyzed, the biopsy specimens were re-examined and the final diagnosis was ameloblastic carcinoma, secondary type, with squamous differentiation.

The postoperative course was smooth. The patient did not receive radiotherapy. After 15 months of follow-up, there was no evidence of tumor recurrence or metastasis.

3. Discussion:

Ameloblastic carcinoma represents an entity of malignant transformation of histological ameloblastoma that was first identified by William Shafer in 1983. As a rare malignant epithelial odontogenic tumor, characteristic histopathological

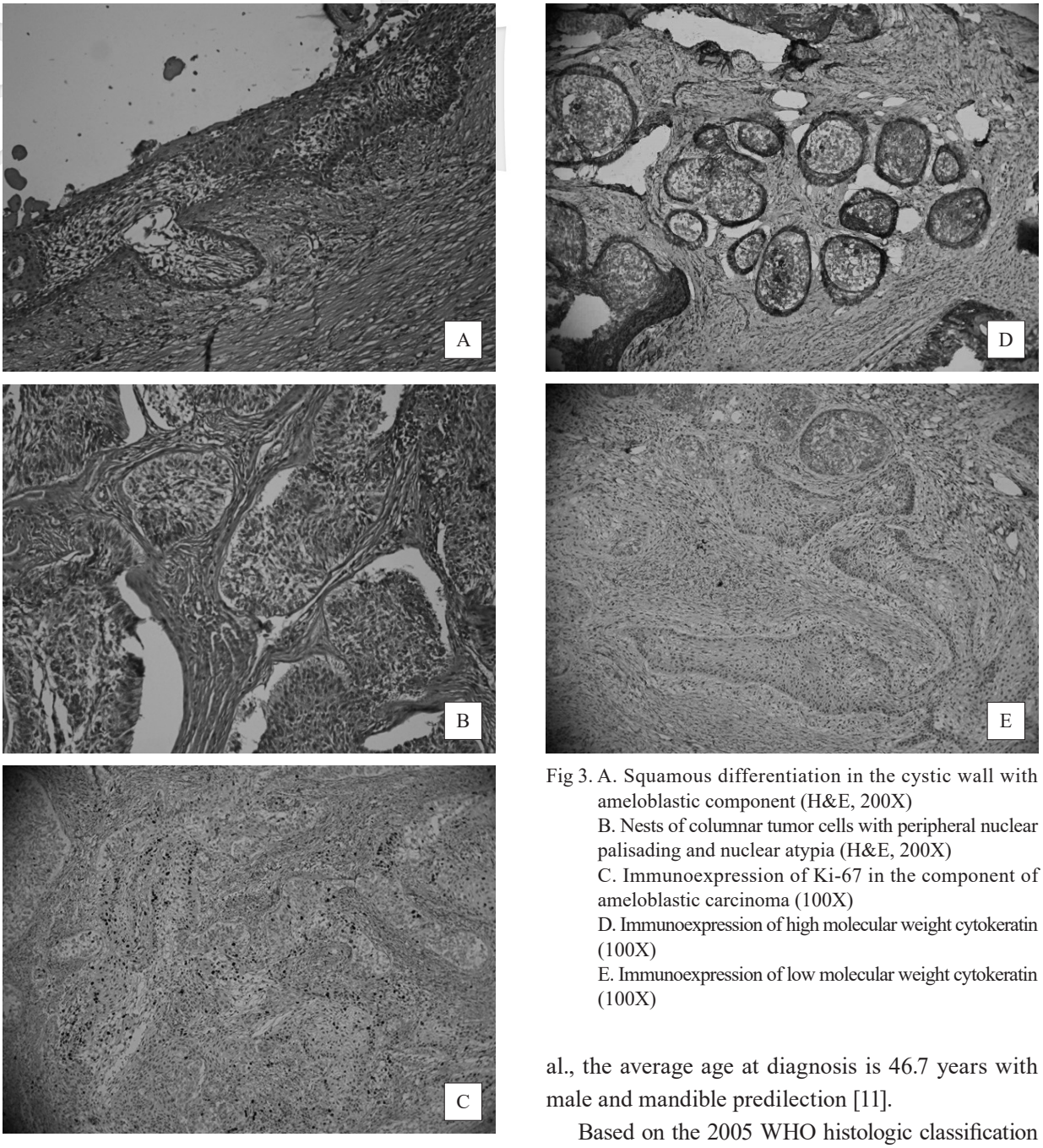


Fig 3. A. Squamous differentiation in the cystic wall with ameloblastic component (H&E, 200X)
B. Nests of columnar tumor cells with peripheral nuclear palisading and nuclear atypia (H&E, 200X)
C. Immunoexpression of Ki-67 in the component of ameloblastic carcinoma (100X)
D. Immunoexpression of high molecular weight cytokeratin (100X)
E. Immunoexpression of low molecular weight cytokeratin (100X)

and clinical features are helpful for diagnosis. Even though definite metastasis is not a required clinical course, aggressive treatment and follow up are necessary [1, 2][7]. This differentiates malignant ameloblastoma from metastasizing ameloblastoma which more commonly represents benign histological picture in both primary and metastatic tumors [3, 8-10]. According to a review of 18 cases by Deng et al., the average age at diagnosis is 46.7 years with male and mandible predilection [11].

Based on the 2005 WHO histologic classification of odontogenic tumors, ameloblastic carcinomas can be divided into primary and secondary types. The primary type is accompanied by histologic features of ameloblastoma with cytologic atypia and the secondary type is defined as a malignant transformation of a preexisting benign ameloblastoma, regardless of the presence or absence of metastasis [12]. Occasionally, an ameloblastoma may present with poorly defined histopathological features or if

left untreated the entire lesion may be replaced by malignant cells [5].

The differential diagnoses of ameloblastoma and ameloblastic carcinoma depend on the integration of histological changes with demographic features and biologic behavior. The diagnostic criteria of ameloblastic carcinoma include cytologic atypia and increased mitotic index [13] and are based on certain histopathological features, such as higher mitotic activity and higher proliferating index (such as higher Ki-67). Cellular features representing malignancy such as nuclear atypia, nuclear pleomorphism, basilar hyperplasia, and hyperchromatism are usually present. In addition, occasional perineural or perivascular invasion or invasion to surrounding tissues may be observed [14]. In our case, frank invasion of bone and gingiva was observed, with no definite evidence of perineural or perivascular invasion.

The histologic features that distinguish ameloblastic carcinoma from squamous cell carcinoma include the presence of stellate reticulum and distinctive cystic formation and the absence of frank keratinization [1]. Immunoreaction to CK19 may be useful for identifying odontogenic origin of odontogenic carcinoma and distinguishing intraosseous squamous cell carcinoma from gingival squamous cell carcinoma [15]. In our case, squamous component in the tumor, either malignant or benign, was immunoreactive to CK19 but not gingival epithelium. Additional consideration in making a differential diagnosis is that squamous cell carcinoma arises in the lining of an odontogenic cyst [16]. Histologically, this lesion tends to more closely resemble oral squamous cell carcinoma that lacks stellate reticulum-like zones and peripheral palisading [17].

The clinical presentation of ameloblastic carcinoma varies from cystic changes with benign clinical features to large tumor mass with ulceration and bone resorption or tooth mobility [18]. Swelling is the chief complaint with or without discomfort, in addition to toothache, tooth mobility, non-healing extraction site, ulcer or fistula, facial asymmetry, and trismus [19]. Radiographically, there are no pathognomonic features of ameloblastic carcinoma, only common changes associated with malignancy such as radiolucency with ill-defined margins [20]. It is believed that “moth-eaten” or ill-defined lesion is a result of advanced gingival invasion with underlying bone destruction [21].

Due to local aggressiveness, radical surgical resection with clear margins has been the main treatment modality. Radiation therapy is not known to be particularly useful and is usually reserved for cases with known perineural spread or massive soft tissue invasion. As distant metastasis may develop years after initial diagnosis, long-term surveillance is imperative and is accomplished by routine physical examinations along with serial radiographic follow up [18].

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References:

1. Ozlugedik S, Ozcan M, Basturk O, Deren O, Kaptanoglu E, Adanali G, Unal A: Ameloblastic carcinoma arising from anterior skull base. Skull Base 2005; 4: 269-72.
2. Devenney-Cakir B, Dunfee B, Subramaniam R, Sundararajan D, Mehra P, Spiegel J, Sakai O: Ameloblastic carcinoma of the mandible with metastasis to the skull and lung: advanced imaging appearance including computed tomography, magnetic resonance imaging and positron emission tomography computed tomography. Dento maxillo facial radiology 2010; 39: 449-53.
3. Slootweg PMüller H: Malignant ameloblastoma or ameloblastic carcinoma. Oral surgery, oral medicine, oral pathology, oral radiology and endodontics 1984; 57: 168-76.
4. Cizmecý O, Aslan A, Onel D, Demiryont M: Ameloblastic carcinoma ex ameloblastoma of the mandible: case report. Otolaryngology--head and neck surgery 2004; 130: 633-4.
5. Karakida K, Aoki T, Sakamoto H, Takahashi M, Akamatsu T, Ogura G, Sekido Y, Ota Y: Ameloblastic carcinoma, secondary type: a case report. Oral surgery, oral medicine, oral pathology, oral radiology and endodontics 2010; 110: e33-7.
6. Dhir K, Sciubba J,Tufano R: Ameloblastic carcinoma

of the maxilla. Oral Oncology 2003; 39: 736-41.
7. Nagai N, Takeshita N, Nagatsuka H, Inoue M, K N, Nojima T, Yamasaki M, Hoh C: Ameloblastic carcinoma: case report and review. Journal of Oral Pathology and Medicine 1991; 20: 460-3.
8. Shafer W, Hine M, Levy B: *A textbook of oral pathology*. 4th ed. 1993, Philadelphia, Pennsylvania: Saunders.
9. Peter A, Philipsen H: *Odontogenic tumors and allied lesions*. 2004, London: Quintessence.
10. Lau S, Tideman H, Wu P: Ameloblastic carcinoma of the jaws. A report of two cases. Oral surgery, oral medicine, oral pathology, oral radiology and endodontics 1998; 85: 78-81.
11. Deng L, Wang R, Yang M, Li W, Zou L: Ameloblastic carcinoma: Clinicopathological analysis of 18 cases and a systematic review. Head & Neck 2019; 41: 4191-4198.
12. Mahmoud S, Amer H, Mohamed S: Primary ameloblastic carcinoma: literature review with case series. Polish journal of pathology 2018; 69: 243-253.
13. Slater L: Odontogenic malignancies. Oral and maxillofacial surgery clinics of North America. 2004; 16: 409-24.
14. Roy Chowdhury S, Ramen S, Chattopadhyay P, Moorchung N, Rajkumar K: Ameloblastic carcinoma of the mandible. Journal of maxillofacial and oral surgery 2010; 9: 198-201.
15. Kawai S, Ito E, Yamaguchi A, Eishi Y, Okada N: Immunohistochemical characteristics of odontogenic carcinomas: their use in diagnosing and elucidating histogenesis. Oral Medicine and Pathology 2009; 13: 55-63.
16. Gandy S, Keller E, Unni K: Ameloblastic carcinoma: report of two cases. Journal of Oral and Maxillofacial Surgery 1992; 50: 1097-102.
17. Gorio L, Golblatt L, Edwards P, Hartman K: Ameloblastic carcinoma: a clinicopathologic study and assessment of eight cases. Oral surgery, oral medicine, oral pathology, oral radiology and endodontics 1987; 64: 570-6.
18. Eversole L: Malignant epithelial odontigenic tumors. Seminars in diagnostic pathology 1999; 16: 317-24.
19. Akrish S, Buchner A, Shoshani Y, Vered M, Dayan D: Ameloblastic carcinoma: report of a new case, literature review, and comparison to ameloblastoma. Journal of Oral and Maxillofacial Surgery 2007; 65: 777-83.
20. Goldenberg D, Sciubba J, Koch W, Tufano R: Malignant odontogenic tumors: a 22-year experience. Laryngoscope 2004; 114: 1770-4.
21. Huang J, Luo H, Li Q, Li T: Primary intraosseous squamous cell carcinoma of the jaws. Clinicopathologic presentation and prognostic factors. Archives of pathology & laboratory medicine. 2009; 133: 1834-40.