Primary intraosseous ACC of mandible of possible salivary origin: 
A rare clinical entity

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ABSTRACT

INTRODUCTION: Adenoid cystic carcinoma (ACC) is a malignant tumor mainly of salivary origin which is well known for its deceptively benign histologic appearance characterized by indolent, locally invasive growth with high propensity for local recurrence and distant metastasis. 

PRESENTATION OF CASE: An unusual case of a 23-year-old woman was reported in our hospital. After investigations, it showed that it is a second primary intraosseous lesion of mandible that occurred subsequently after ACC of parotid gland. After diagnosis was established, resection of tumor and reconstruction with a free fibula flap was performed. Ten months follow-up showed no signs of recurrence or metastasis. 

DISCUSSION: Among the salivary neoplasms, adenoid cystic carcinoma is very rare and intraosseous lesions are even rarer. We found a total of 26 cases of primary ACC of the mandible reported in the literature. Pain and swelling were the most frequent symptoms. 

CONCLUSION: This case illustrates two key facts. First, not all cystic lesions are necessarily metastatic or recurrence. Second is, even though the exact origin of this tumor is unknown, central salivary gland tumors should be considered in the differential diagnosis of cystic lytic lesions in the mandible.

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1. Introduction

ACC is a malignant neoplasm that accounts for 1–2% of all head and neck malignancies.1 In the parotid gland it is rare and centrally arising intraosseous ACC are even rarer. To our knowledge, till date only about 26 cases of central ACC arising in the mandible were reported.2 Loco-regional lymphatic spread is rare but late distant metastases are relatively frequent.3 Although it presents a widespread age distribution, peak incidence occurs predominantly among women, between the 5th and 6th decades of life.4 It is clinically deceptive by virtue of its small size and slow growth, which belies its extensive subclinical invasion relentlessly into adjacent structures.5 However, tumor grade, stage, lymph node metastasis, invasion of major nerves, and margin status remain the most consistent predictors of prognosis.6 The treatment of choice is total resection with a wide margin, although in some cases it has been coupled with X-rays. We hereby present a rare case of intraosseous ACC of right mandible, which arises subsequently after a primary ACC of the left parotid gland.

2. Case presentation

A 23-year-old, systematically healthy female patient presented in our oral and maxillofacial department of Second Xiangya Hospital of Central South University with a chief complaint of pain and swelling in the right posterior mandibular region. The patient reported a rapid increase in size of the lesion over the past 6 months. Past history revealed that about 1 month ago, the patient had undergone parotidectomy of the left parotid gland due to similar symptoms which presented 4 years ago. The left parotid gland tumor resection was conducted in a local hospital where the histopathology impression was that of an ACC of cribriform pattern.

On initial physical assessment a tender, hard fixed swelling measuring 2 cm × 4 cm was evident on palpation of the right mandible. The overlying skin was intact and no ulceration was noted. A 10-cm surgical scar was noted on the left parotid region. Regional lymphadenopathy was not evident. Intraoral examination was unremarkable, with intact overlying mucosa, normal in color with no signs of inflammation, ulceration or pus discharge. Hematological tests were requested which rendered a normal complete blood count, erythrocyte sedimentation rate, and blood chemistry. Based on the patient’s history and clinical examination associated with a rapid growth of the observed lesion, a provisional diagnosis of intraosseous ACC was hypothesized and further investigations were carried out. Subsequently,
radiographic investigations consisting of computed tomography (CT) and orthopantomogram (OPG) were performed.

OPG showed irregular radiolucency extending from mandibular right first premolar to mandibular right first molar with poorly defined border giving "floating teeth appearance" and apical root resorption (Fig. 1). CT revealed a well-demarcated osteolytic lesion and root resorption in the involved teeth. The lesion was confined within the mandible without erosion of the cortical bone (Fig. 2).

Radiologically, focal sclerosing osteitis, cementoblastoma, cementifying and ossifying fibroma, periapical cemental dysplasia, complex odontoma, and calcifying epithelial odontogenic tumor should be considered in the differential diagnosis.

Since, clinically and radiographically, they may mimic odontogenic cysts and tumors, a final diagnosis can be obtained only after histological examination.²

Incisional biopsy was carried out and histopathologic analysis demonstrated cribriform growth pattern displaying several prominent pseudocysts surrounded by basaloïd cells with hyperchromatic angulated nuclei. The lumina of few ductal structures contained a mucinous substance that was faintly eosinophilic. The hyalinized eosinophilic product was also seen surrounding these cribriform islands. At the periphery, epithelial cells were arranged as single ductal structures formed by layers of isomorphic cells. However, the cribriform pattern appeared to dominate, giving the entire structure a typical "swiss cheese" appearance. The histologic features were consistent with a cribriform variant of ACC of possible salivary gland origin (Fig. 3a–c).

The treatment suggested was surgical excision without neck dissection. Surgical treatment consisted of hemi-mandibulectomy, followed by mandibular reconstruction using titanium plates and free fibular flap (Fig. 4). The excised lesion was again sent for histopathological investigations. Histopathological analysis of the resected specimen showed similar features of the incisional biopsy, and the assessment of the surgical margins did not show evidences of residual tumor (Figs. 5–7). No metastatic nodes were seen. Patient was advised for post-surgical radiotherapy. The patient is still being monitored, and after 10 months of follow-up she is alive with no evidences of local recurrence or metastasis.
reported in the literature. The most common site was the posterior body or angle of the mandible. Pain and swelling were the most frequent symptoms. The age of affected patients under 24 years is more rare.

CT and MR imaging are a good guide to better surgical planning, especially with regard to the submucosal extent and perineural spread, which can be difficult to assess clinically. The lesions are generally poorly defined and have infiltrative margins. The center of the lesion, as was the case with our patient, is usually low density on the CT scan and radiograph, a characteristic that help us to differentiate it from a primary squamous cell carcinoma. Due to the exceedingly rare occurrence of primary intraosseous ACC, the diagnosis of such neoplasms is vexatious and, in spite of the histology, should rely on the application of strict diagnostic criteria, including: (1) radiographic evidence of osteolysis; (2) presence of intact cortical plates; (3) absence of any primary tumor within the major or minor salivary glands; and (4) histologic confirmation of the typical architectural and morphologic features of ACC.

All these diagnostic criteria were satisfied in the case reported here except the presence of a similar but not primary tumor in the parotid gland which got treated about 1 month ago. Currently the parotid gland is free of tumor. However since both appear simultaneously, metastasis was ruled out since metastasis is usually late in occurrence and no clear pathway of metastasis were found histologically arising from the left parotid gland to the right mandible. Histologically, it gives evidence of possible salivary gland origin due to its similar cribriform pattern. Perineural spread from the previous tumor was not evident in this present case. It is probable that both tumor originated consecutively, however due to its indolent nature, its presence in the mandible was later diagnosed.

The pathogenesis of central salivary gland neoplasms is unknown, but several theories have been proposed. Some theories propose that the pathogenesis most likely involves a neoplastic transformation of the mucus-secreting cells commonly found in the epithelial linings of dentigerous cysts. It is thought that ectopic entrainment of retromolar mucous glands or developmentally included embryonic remnants of submandibular glands within recesses or lacunae of the mandible could explain the intraosseous origin of a tumor. Recently, Mahomed et al. reported a case of central ACC of the mandible, which showed areas of cribriform and tubular growth patterns merged with cystic spaces. Some of the latter were lined by epithelium that resembled the reduced enamel epithelium or showed corrugated luminal surface reminiscent of odontogenic keratocyst, besides the formation of aberrant dental

3. Discussion

The World Health Organization defines ACC as a “basaloid tumor consisting of epithelial and myoepithelial cells in various morphological configurations, including tubular, cribriform and solid patterns. It has a relentless clinical course and usually fatal outcome.” Primary ACC of the mandible is an extremely rare occurrence. We found a total of 26 cases of primary ACC of the mandible
hard tissue. In fact, as suggested by Mahomed et al.,\textsuperscript{13} epithelial rests derived from the oral ectoderm within the jaws possibly have the capacity to differentiate along both odontogenic and salivary tissues which may have been possible in the present case.

In some circumstances, ACC may undergo dedifferentiation to a high-grade tumor with necrosis, a high mitotic rate and loss of the distinction between ductal and myoepithelial cells. In such situation, immunohistochemical markers like CD43, which are diagnostic for ACC, can be an adjuvant.\textsuperscript{14} In our case, histological evaluation was diagnostic of cribriform pattern of ACC, which excludes the need for immunohistochemistry. The differential diagnosis of ACC includes tumors that also exhibit tubular and cribriform structures such as polymorphous low-grade adenocarcinoma, tumors with basaloïd cellular morphology such as basal cell adenoma and basal cell adenocarcinoma, and tumors with a dual population of ductal and myoepithelial cells such as pleomorphic adenoma.

The cornerstone of treatment is surgery, while radiotherapy has been considered for advanced stages and as adjuvant in the presence of positive microscopic margins. Hemi-mandibulectomy, followed by mandibular reconstruction using titanium plates and free fibular flap is advocated for ACC in mandible. Our case was an intraosseous ACC of mandible. The patient underwent wide surgical excision of the tumor, with an en-bloc partial resection of the mandible. Perineural infiltration was not evident, and the surgical margins were tumor free. The morphologic features of the tumor were consistent with the diagnosis of ACC of possible salivary gland origin. As metastasis to regional lymph nodes is uncommon, neck dissection is typically not indicated.\textsuperscript{15} Similar treatment protocol was followed. In this present case the reconstruction was performed by using osteocutaneous fibular flap which is the most commonly used flap for oromandibular reconstruction because of its similar bony architecture, long vascular pedicle and low donor site morbidity.\textsuperscript{16} The patient is alive and well, with no evidence of recurrence or distant metastases. However, long-term follow-up is essential regardless of the site because of the tumor’s propensity for late recurrence and metastasis.

4. Conclusion

ACC represents a special diagnostic and therapeutic challenge due to its extraordinary nature. Though it is believed that there are some general tendencies, such as the propensity for it to spread into surrounding nerve tissue or metastasize to other areas of the body, yet each patient have their own diverse patterns and experiences. This present case illustrates two key facts about the diverse pattern of ACC. First, is not all cystic lytic lesions are necessary metastatic or recurrence and at the same time even though two tumors exhibit similar histologic features, they may have originated separately. The second fact is even though the exact origin of this tumor is unknown, central salivary gland tumors should be considered in the differential diagnosis of cystic lytic lesions in the mandible. Moreover, oromandibular reconstruction is recommended as it can meet the patient’s enhanced expectations and demands with an ambitious esthetic and functional results.

Conflict of interest statement

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Ethical approval

Written consent form was obtained from patient, and can be provided upon editor’s request.

Author contributions

Dr. Ren collected all data and photographs to draft the manuscript. Dr. Chickooere wrote the manuscript for submission. Both authors contributed equally for the article and thereby both are co-first authors.

References

1. Dodd RL, Slevin NJ. Salivary gland adenoid cystic carcinoma: a review of chemotherapy and molecular. Oral Oncol 2006 Sep;42(8):759–69.
2. Brookstone MS, Huvos AG. Central salivary gland tumors of the maxilla and mandible: a clinicopathologic study of 11 cases with an analysis of the literature. J Oral Maxillofac Surg 1992;50:229–36.
3. Langdon JD, Henk JM. Malignant tumours of the mouth, jaws and salivary glands. 2nd ed. London, Boston, Melbourne, Auckland: Edward Arnold; 1995. p. 209–10.
4. Waldron CA, El-Mofty SK, Gneppe DR. Tumors of the intraoral minor salivary glands: a demographic and histologic study of 426 cases. Oral Surg Oral Med Oral Pathol 1988;66:323–33.
5. Huang MX, Ma DQ, Sun KH, Yu GY, Guo CB, Gao F. Factors influencing survival rate in adenoid cystic carcinoma of the salivary glands. Int J Oral Maxillofac Surg 1997;26:435–9.
6. Jesse Jaso, Reenu Malhotra. Adenoid cystic carcinoma. Arch Pathol Lab Med 2011;135(April (4)):511–5.
7. Martinez-Madrigal F, Pineda-Daboin K, Casiraghi O. Salivary gland tumors of the mandible. Am J Diagn Pathol 2000;4:347–53.
8. Barrett AW, Speight PM. Perineural invasion in adenoid cystic carcinoma of the salivary glands: a valid prognostic indicator? Oral Oncol 2000;35:316–40.
9. Al-Sukhun J, Lindqvist C, Hietanen J, Levoo I, Penttila H. Central adenoid cystic carcinoma of the mandible: case report and literature review of 16 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101(3):304–8.
10. de Kerviler E, Bely N, Laccourreye O, Clement O, Halimi P, Frija G. The arypepiglotic fold as a rare location of adenoid cystic carcinoma. AJNR Am J Neuroradiol 1995;16:1375–7.
11. Schafer WG, Hine MK, Levy BM. Textbook of oral pathology. Philadelphia: Saunders; 1974.
12. Jafek BW, Strife JL. Accessory lobe of the submandibular gland. Diagn Radiol 1973;75–7.
13. Mahomed F, Altini M, Meer S, Nikhotso E, Pearl C. Central adenoid cystic carcinoma of the mandible with odontogenic features: report of a case. Head Neck 2009;31(February (2)):975–80.
14. Hotte SJ, Winquist EW, Lamont E, MacKenzie M, Vokes E, Chen EX, et al. Imatinib mesylate in patients with adenoid cystic cancers of the salivary glands expressing c-kit: a Princess Margaret Hospital phase II consortium study. J Clin Oncol 2005;23(January (2)):585–90.
15. Neville BW, Darnall DD, Allen CM, Bouquot JE. Oral and maxillofacial pathology. 2nd ed. Philadelphia: W.B. Saunders Company; 2002. p. 95–106.
16. Hidalgo DA. Fibula free flap: a new method of mandible reconstruction. Plast Reconstr Surg 1989;84:71–9.