Case report

Primary acinic cell carcinoma of mandible, report of a case and literature review

Neda Kardouni Khozestani a, c, Ata Garajei b, c, Nazanin Mahdavi a, Ali Abdolrahmani d, *

a Oral and maxillofacial pathology Department, School of Dentistry and Cancer Institute, Tehran University of Medical Sciences, Tehran Iran
b Head and Neck Surgical Oncology and Reconstructive Surgery Department, School of Medicine and Department of Oral and Maxillofacial Surgery, Tehran, Iran
c Cancer Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
d School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Keywords:
Acinic cell carcinoma
Mandible
Salivary gland tumor
Head and neck

ABSTRACT

Introduction and importance: Acinic cell carcinoma (ACC) is a rare low-grade salivary gland malignancy that accounts for approximately 17% of all salivary gland malignancies. The most common site affected by ACC is the parotid gland followed by the submandibular glands, minor salivary glands, and sublingual glands. Also, it could hardly be observed in unusual sites such as the jaw bones.

Case presentation: This case is an example of a central acinic cell carcinoma in a 73-year-old man who came up with a painless gradual swelling for 15 months. Based on clinico-radio-pathologic findings, the diagnosis of a solid variant Intraosseous Acinic Cell Carcinoma was established. Subsequently, the patient underwent hemimandibulectomy and modified radical neck dissection, followed by postoperative radiotherapy. Within a six-month follow-up period, no evidence of residual tumor was found.

Clinical discussion: Central salivary gland carcinoma is a rare entity and intraosseous ACC is more scarcely observed. Based on our findings, a total of 17 cases of primary intraosseous ACC have been reported so far. Etiology and clinical presentations of this tumor are still vague due to its rarity.

Conclusion: Dentists and oral surgeons must be aware of such a rare malignant lesion when encountering a radiolucent lesion within the jaws. The early diagnosis and a complete surgical excision to achieve tumor-free surgical margins and a long-term follow-up could result in significantly improved survival rates.

1. Introduction

Malignant Salivary gland tumors (SGTs) account for less than 3% of all head and neck malignancies and approximately 0.3% of all malignant tumors [1]. Adenoid cystic carcinoma and mucoepidermoid carcinoma are the most prevalent salivary gland carcinoma followed by acinic cell carcinoma. The prevalence of these three tumors differs across the world [2]. Acinic cell carcinoma is a rare low-grade salivary gland malignancy, which was first diagnosed by Nasse. It accounts for approximately 17% of all salivary gland malignancies. This tumor frequently involved adults in the 5th and 6th decades of life with a female predilection [3,4]. ACC is a tumor with predominant differentiation in serous acinar cells, which most frequently occurs in the parotid gland (83%) followed by submandibular glands, minor salivary glands, and sublingual glands. Furthermore, some unusual regions including the palate, mandible, nose, and paranasal sinuses could be affected [4,5]. The tumor is mainly composed of serous acinar cells variably admixed with clear, vacuolated, and intercalated ductal cells characterized by four variable patterns; solid, microcystic, papillary cystic (associated with hemorrhage), and follicular. Microcystic and solid growth patterns are the two most common patterns. Primary acinic cell carcinoma (ACC) arising in the mandible is an infrequent neoplasm and the following case has been brought up for your attention. This work has been reported in compliance with the SCARE 2020 criteria [6].

2. Case presentation

A 73-year-old man with a history of slow-growing left mandibular mass over 15 months was referred to Imam Khomeini hospital complex. His past medical history revealed controlled hypertension.

Intraoral examination illustrated painless bony expansion in the buccal aspect of the left posterior area of the mandible. No tooth...
mobility was evident. After a thorough general examination, no enlarged lymph node was detected. Paraclinical evaluations including panoramic imaging revealed a 6 cm × 3.5 cm multilocular radiolucent lesion involving the left posterior area of the mandible which was extended from the ascending ramus to the periapical area of the left mandibular canine tooth. Also in the supero-inferior dimension, it was extended from the superior alveolar ridge to the inferior border of the mandible. Moreover, the inferior alveolar canal was invaded by the tumor (Fig. 1). Necessary endodontic treatments were preceded to eliminate infectious sources prior to any surgical and adjuvant treatments. Additionally, axial and coronal CT scans of the mandible showed a large expansile lytic lesion in the left mandibular body with cortical destruction (Fig. 2). In ultrasound imaging, reactive lymph nodes on the left side of the neck were evident. Also, contrast-enhanced CT evaluation of chest-abdomen-pelvis was performed for metastatic workup.

The patient underwent incisional biopsy and the specimen referred to our pathology lab consisted of multiple fragments of grey-tan tissue totally measuring 2 × 2 × 0.3 cm with a soft consistency. Microscopic examinations demonstrated sheets and clusters of large polygonal malignant cells with densely abundant granular basophilic cytoplasm and a majority of eccentric, round, and slightly pleomorphic nuclei and inconspicuous nucleoli (Fig. 3). Additionally, infiltrative borders presented as small nests and cords at the periphery of the tumor were noticed. Immunohistochemical studies were performed. The tumor cells were strong membranous positive for EMA and CK8/18. However, immunoreactivity was detected neither for Pan-CK, S100 protein nor for CEA. Furthermore, IHC findings for the Anoctamin-1 (DOG1) marker, a marker of intercalated ductal differentiation, were strongly positive as expected (Fig. 4). In conclusion, the lesion was preliminarily diagnosed as a solid variant of “Intraosseous Acinic Cell Carcinoma”. Finally, the patient underwent surgery which included wide mandibular segmental resection. Since no obvious cervical lymphadenopathy on ultrasonic examination was found, Selective Neck Dissection (level I-III) was performed. The submandibular gland and lingual mandibular cortex were intact. Therefore, the intraosseous source of this lesion was confirmed. To reconstruct the mandibular defect, reconstruction plate and submental flap with revers flow technique were applied. The tumor was defined as Stage IV (T4N0M0) according to the TNM criteria. Histological examination of the whole excised tumor confirmed the initial diagnosis (Fig. 5). All surgical margins except the posterior lingual soft tissue margin were free from tumor. Considering the surgical margin involvement, and the patient’s refusal to reoperation, consequently the patient received radiotherapy. The patient was followed and within the six-month follow-up period, no evidence of residual tumor was found.

3. Literature search

A systematic search was carried out in Medline (through PubMed), Scopus, Embase, and Web of Science databases up to March 1, 2021. The search was performed without restrictions on language or publication year. Medical Subject Headings (MeSh) were used to find search terms. After finalizing the search syntax for PubMed, it was adapted to other databases. (see full search strategy in supplementary table). Reference lists of included articles were manually screened.

The study flow diagram is presented in Fig. 6. Initially, the search strategy retrieved 513 references. After removing duplicates, 429 publications remained. After screening the titles and abstracts, 396 articles were excluded. The full texts of the remaining 33 articles were assessed and 15 articles met the inclusion criteria and therefore included in this study. The clinicopathological data of ACC cases reported in the literature were summarized in Table 1.
lesions which involves the transformation of the mucus-secreting cells in
the epithelial linings of developmental odontogenic cysts. Malignant
transformation also could be instigated by epithelial rests of Malassez
and epithelial components of existing odontogenic tumors [11]. The last
reason is related to the entrapment of salivary gland tissue in the jaw
during mandibular bone development [8]. In General, ACC can be more
prevalent in females in both intra and extra-osseous types. However, in
our case, the case was a 73-year-old man. Same as our case the posterior
site of the mandible and ascending ramus are the most common site of
intraosseous involvement in the head and neck region. Due to diagnostic
challenges, a precise diagnostic workup is mandatory to rule out the
possibility of this tumor in dealing with radiolucent lesions of the jaws
[12]. The diagnosis of ACCs is extremely challenging due to its great
paraclinical similarities in both radiological and cytological aspects.
Considering the radiological appearance of this lesion, it could be in
differential diagnosis with odontogenic jaw neoplasms, particularly
ameloblastoma. Therefore, pre-treatment incisional biopsy with a suf-
ficient amount of specimens from jaw lesions is essential to make a
definite diagnosis. The key point in the diagnosis of ACC is to identify
serious acinar differentiation [13]. From microscopic differential diag-
nosis perspectives, ACC can be mainly in differential with secretory
carcinoma due to microcystic or papillary-cystic and solid appearance.
However, the existence of typical serous acinar cells with numerous
basophilic granular cytoplasm comprising PAS-positive/diastase-
resistant zymogen granules could lead to the diagnosis of ACC [14].
Moreover, these tumors can be distinguished based on immunohisto-
chemical profiles. ACC cases entirely show diffuse intense membranous
and cytoplasmic immunostaining for DOG1 and negative immuno-
reaction for Vimentin, mammaglobin, S100, and Adipophilin [15–17].
Other monomorphic oncocytic neoplasms that cause difficulty in diag-
nosis include High grade mucopidermoid carcinoma with oncocytic
differentiation as well as monotonous oncocyctic cell proliferation
including oncocytoma and oncocyctic carcinoma.

Histomorphologic features which may help differentiate these tu-
ors from each other are as follows: in MEC cases, the presence of
unique MEC foci consisting of mucous, intermediate, and epidermoid
cells could assist. In oncocytoma cases, the presence of prominent
monotonous oncocyctic cell proliferation could be helpful. Furthermore,
in oncocytic carcinoma increased Atypia, mitotic activity, and
perineural-vascular-soft tissue invasion could facilitate the diagnosis
[18,19].

In addition, the use of immunohistochemical studies to confirm the
diagnosis is helpful in this regard. DOG1 positivity is detected in salivary
gland tumors that show the differentiation of acinar and intercalated
ducts, especially in AcCCA, while DOG-1 negativity is noticed in
oncocytoma and oncocytic carcinoma [18,19].

ACC has 4 histological variants; solid, microcystic, papillary-cystic,
and follicular variants. Based on a few case reports the solid variant
seems to be the most common type of central ACC. Clinical factors such
as aging, large tumor size, involved surgical margins, and the presence
of distant metastasis could lead to poor prognosis. But in contrast to
clinical factors, histopathological staging is not a reliable predictive
factor [5,20]. Surgical excision is the predominant treatment modality
for salivary gland malignancies including ACC. Radiotherapy may be
useful in cases of perineural invasion, positive margins, advanced tu-
mors with cervical lymph node involvement, and large tumors with a
local spread. However, adjuvant radiotherapy may not provide better
survival outcomes [5,21]. ACC has a high recurrence potential of
approximately 35% and the potential of late local recurrence even 30
years after its first emergence. Therefore, long-term follow-up is highly
mandatory [4].

4. Discussion and conclusion

Primary intraosseous malignancies are a heterogeneous group of
neoplasms that could provide significant diagnostic challenges. Primary
intraosseous malignancies of the jaws consisted of three major histologic
malignancies; salivary gland carcinomas, odontogenic carcinomas, and
squamous cell carcinomas [7]. Among primary intra-osseous salivary
gland carcinomas occurring in jaws, mucoepidermoid carcinoma seems
to be the most common (68.5%) neoplasm followed by adenoid cystic
carcinoma (16.2%) and adenocarcinoma not otherwise specified (5%)
[8,9]. Central ACC is an extremely rare lesion with insidious and gradual
progression reported in only a few cases in the literature. Central ACC
has occurred in a wide range of ages (19–84 years) similar to the extra-
osseous salivary gland ACC [10].

The incidence of salivary gland tumors in the jaws could be clarified
from different perspectives. The first one pertains to the pathogenesis of

Fig. 3. H&E staining shows sheets of large acinar cells with basophilic to
amphophilic cytoplasm with numerous dark-staining granules and round small
eccentrically located nuclei.

Fig. 4. Acinic cell carcinoma with abundant acinar cells and intense mem-
branous and variable cytoplasmic staining with DOG1.
Fig. 5. (a) left hemimandibulectomy and modified radical neck dissection were performed. (b) reconstruction plate and submental flap with revers flow technique were used to rehabilitate mandibular defect.
Records identified through database searching (n=513):
- PubMed via MEDLINE (n=360)
- Scopus (n=411)
- Web of Science (n=27)
- Embase (n=45)

Additional records identified through other sources and hand search (n=2):
- Google scholar (n=1)
- References of included studies (n=1)

Records after duplicates removed (n=429)

Records screened by title and abstract (n=429)

Records excluded (n=396)

Full-text articles assessed for eligibility (n=33)

Full-text articles excluded, with reasons (n=18):
- extra-ossceous (n=12)
- Other histologic entity (n=4)
- Review (n=2)

Studies included in qualitative synthesis (n=15):

**Table 1**
Clinicopathological data of ACC cases reported in literature.

| Author          | Year | Sex  | Age | Site                  | Left/right | variant  | Treatment                                           | outcome                   |
|-----------------|------|------|-----|-----------------------|------------|----------|----------------------------------------------------|---------------------------|
| Ito et al       | 1970 | Female | 25  | Ascending ramus       | Left       | Solid    | Block resection                                    | Tumor free (3 years)      |
| Abrams et al    | 1978 | Female | 19  | Third molar area      | Left       | Micro-cystic | En bloc resection                                 | Tumor free (3.5 years)    |
| Spiro et al     | 1978 | –     | –   | Lower molar area      | –          | –        | Unroofing and curettage                            | Unknown                   |
| Chaudhury et al | 1986 | –     | –   | Mandible             | –          | –        | –                                                  | –                         |
| Bondi et al     | 1989 | Female | 79  | Lower molar area      | Left       | –        | En bloc resection                                 | Tumor free (1 years)      |
| Flood et al.    | 1991 | Female | 22  | Body of mandible      | Left       | Papillary-cystic | Wide excision with neck dissection | Died from other disease |
| Nakazawa et al  | 1998 | Female | 84  | Ascending ramus       | Left       | Follicular | None                                               | Alive with tumor (1 year) |
| Martinez-Madrigal et al | 2000 | Female | 48  | Angle                 | –          | Solid    | Marginal mandibulectomy with radiotherapy          | Tumor free (12 month)     |
| Hara et al.     | 2003 | Male  | 76  | Body                  | –          | Solid    | Wide excision with neck dissection                 | Tumor free (2 months)     |
| Li et al        | 2008 | Female | 39  | Mandibular ramus      | Left       | –        | Transfer treatment                                 | –                         |
| Hiremath et al  | 2013 | Female | 65  | Ramus and body of mandible | Left   | Follicular | –                                                  | –                         |
| Lakshmana et al | 2017 | Female | 35  | Mandible             | Left       | Solid    | Complete surgical removal                          | Tumor free (more than 1 year) |
| Rajpaul et al   | 2018 | Female | 31  | Mandible             | Left       | Micro-cystic | Segmental resection | –                         |
| Kim et al       | 2018 | Male  | 47  | Mandible             | Left       | Solid    | Segmental resection                                | –                         |
| Munjal et al    | 2020 | Male  | 77  | Ascending ramus       | Right      | –        | Wide excision with neck dissection                 | –                         |
| Present study   | 2021 | Male  | 73  | Posterior Mandible    | Left       | Solid    | Wide excision with neck dissection                 | Under treatment procedure |

**Fig. 6.** PRISMA flow chart.
Primary acinic cell carcinoma (ACC) observed in the mandible is an extremely rare neoplasm. The literature review illustrates that the present case is the 17th case of central mandibular ACC. Despite its rarity, dental and medical healthcare providers dealing with jaw issues should be aware of such a slow-growing malignant tumor when encountering radiolucent lesions of the jaws. Early diagnosis, complete excision to achieve tumor free margins and long term follow up could result in significant survival rates improvement. This study mainly focuses on the diagnostic challenges of central ACC; Consequently, further studies with a longer follow-up period is essential to find out more about the prognosis of this rare tumor.

Supplementary data to this article can be found online at [https://doi.org/10.1016/j.ijscr.2021.106065](https://doi.org/10.1016/j.ijscr.2021.106065).

**Abbreviation**

| Abbreviation | Full Form |
|--------------|-----------|
| ACC           | Acinic cell carcinoma                      |
| EMA          | Epithelial membrane antigen                |
| CK           | Cytokeratin                                  |
| Pan-CK      | Pan cytokeratin                             |
| IHC         | Immunohistochemistry                        |
| CEA         | Carcinoembryonic Antigen                    |
| PAS         | Periodic acid–Schiff                        |

**Sources of funding**

None to declare by all authors.

**Ethics approval**

Ethics approval not applicable.

**Consent**

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

**Research registration**

This is not a ‘First in Man’ study, and thus we did not register this case report.

**Guarantor**

Ali Abdolrahmani.

**Provenance and peer review**

Not commissioned, externally peer-reviewed.

**CRediT authorship contribution statement**

Dr. Kardouni analyzed and interpreted the patient data and IHC studies. Dr. Garajei conducted the clinical examination and participated in the surgery carried out in this case. Dr. Mahdavi performed the literature review and revised manuscript. Dr. Abdolrahmani prepared the major part of the manuscript. All authors read and approved the final manuscript.

**Declaration of competing interest**

The authors declare that they have no competing interests.

**References**

[1] Del Signore AG, Megewala UC. The rising incidence of major salivary gland cancer in the United States. Ear Nose Throat J. 2017;96(3):E13-E6.

[2] T. Galdiris, M. Kappler, W. Reich, A. Eckert. Current aspects of salivary gland tumors - a systematic review of the literature, GMS Interdisciplinary Plastic and Reconstructive Surgery DGPW 8 (2019) (Doc12).

[3] L.R. Oliveira, D.F. Soave, J.P. Oliveira da Costa, A. Ribeiro-Silva, Acinic cell carcinoma of parotid gland: report of three cases and literature review, Rev. Port. Estomatol. Med. Dentaria Cir. Maxilofacial 51 (1) (2010) 5–11.

[4] N. Al-Zaher, A. Obeid, S. Al-Salam, B.S. Al-Kayyal, Acinic cell carcinoma of the salivary glands: a literature review, Hematol. Oncol. Stem Cell Ther. 2 (1) (2009) 259–264.

[5] K. Triantafillidou, F. Iordanidis, K. Psomaderis, E. Kalimeras, Acinic cell carcinoma of minor salivary glands: a clinical and immunohistochemical study, J. Oral Maxillofac. Surg. 68 (10) (2010) 2489–2496.

[6] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, The SCARE 2020 guideline: updating consensus surgical Case Report (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.

[7] Morais E, Carlan L, Gil de Farias Morais H, Pinheiro J, Martins H, Barboza C, et al. Primary intraosseous squamous cell carcinoma involving the jaw bones: a systematic review and update. Head Neck Pathol. 2020.

[8] Y. Li, L.J. Li, J. Huang, B. Han, J. Pan, Central malignant salivary gland tumors of the jaw: retrospective clinical analysis of 22 cases, J. Oral Maxillofac. Surg. 66 (11) (2008) 2247–2253.

[9] S.I. Park, W. Park, S. Choi, Y. Jang, H. Kim, S.-H. Kim, et al., Clinical outcome of minor salivary gland cancers in the oral cavity: a comparative analysis with squamous cell carcinomas of the oral cavity, Front. Oncol. 10 (2020) (881-).

[10] Cha W, Kim M-S, Ahn J-C, Cho S-W, Sunwoo W, Song CM, et al. Clinical analysis of acinic cell carcinoma in parotid gland. Clin. Exp. Otorhinolaryngol.. 2011;4(3): 188-92.

[11] H.Y. Hu, Y.Y. Liu, H. Wang, M. Jiang, Primary intraosseous adenoid cystic carcinoma of the mandible: a comprehensive review with analysis of 2 additional cases, J. Oral Maxillofac. Surg. 75 (8) (2017) 1685–1701.

[12] S.I. Chiouea, R. Peol, E.L. Barnes, R.R. Seartha, Salivary type tumors seen in consultation, Virchows Arch. 454 (4) (2009) 457–466.

[13] B.C. Namboodiripad, A review: immunological markers for malignant salivary gland tumors, J. Oral Biol. Craniofacial Res. 4 (2) (2014) 127-134.

[14] E. Luquin, M. Jorissen, M. Delbec-Rychter, R. Hermans, E. Hauben, Mammary analogue secretory carcinoma of the sinus ethmoidalis, Histopathology 67 (5) (2015) 749–751.

[15] Montalvo N, Galarza D, Redroban L. Secretory carcinoma of the parotid: making the correct diagnosis of a rare salivary gland carcinoma when molecular biology testing is not available. Case Rep. Pathol. 2019;2019:5103496.

[16] S.A. Khurram, P.M. Speight, Characterisation of DOG-1 expression in salivary gland tumours and comparison with myoepithelial markers, Head Neck Pathol. 13 (2) (2019) 140–149.

[17] V. Vander Poorten, A. Triantafyllou, L.D. Thompson, J. Bishop, E. Hauben, J. Hunt, et al., Salivary acinic cell carcinoma: reappraisal and update, Eur. Arch. Otorhinolaryngol. 273 (11) (2016) 3531–3531.

[18] C.C. Griffith, A.C. Schmitt, J.L. Little, K.R. Magliocca, New developments in salivary gland pathology: clinically useful ancillary testing and new potentially targetable molecular alterations, Arch. Pathol. Lab. Med. 141 (3) (2017) 381–395.

[19] C. Özcan, D. Talas, K. Gözür, O. Aydin, Incidental deep lobe parotid gland oncocyteic neoplasms in an operated larynx cancer patient, Oral Oncol. Extra 42 (6) (2006) 235–240.

[20] Neskey DM, Klein JD, Hicks S, Garden AS, Bell DM, El-Naggar AK, et al. Prognostic factors associated with decreased survival in patients with acinic cell carcinoma. JAMA Otolaryngol. Head Neck Surg.. 2015;141(11):1195–202.

[21] Andreoli MT, Andreoli SM, shrine MG, Devaliah AK. Radiotherapy in parotid acinic cell carcinoma: does it have an impact on survival? Arch. Otolaryngol. Head Neck Surg.. 2012;138(5):663–6.