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Case report

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

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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 hemi-mandibulectomy 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

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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.

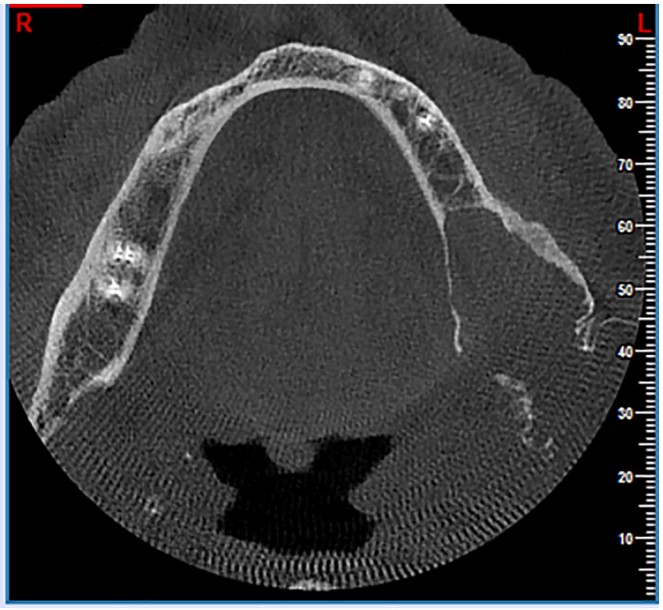

Fig. 2. Axial CT scan of mandible shows a large lytic expansile mass lesion in left mandibular body with cortical destruction.

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.

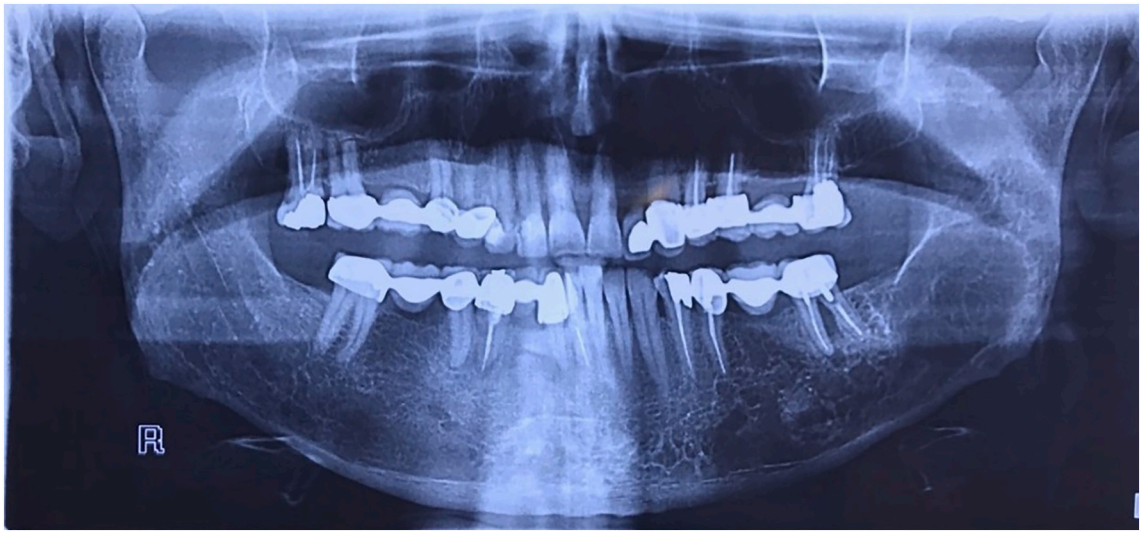

Fig. 1. Multilocular radiolucent lesion extending from the ascending ramus to periapical area of left mandibular canine. Mandibular canal involvement was clear.

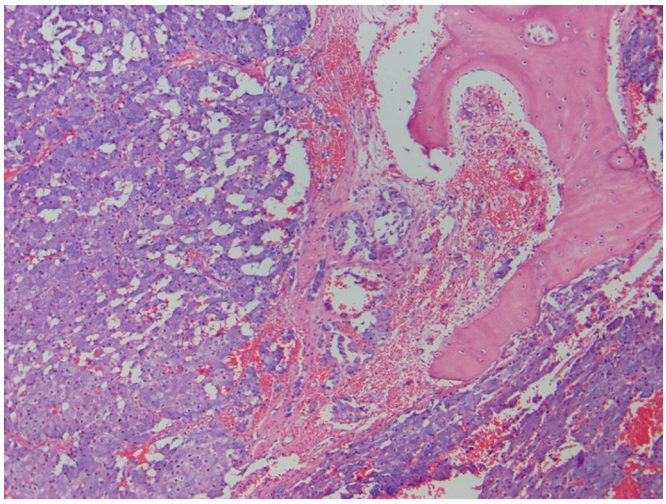

Fig. 3. H&E staining shows sheets of large acinar cells with basophilic to amphophilic cytoplasm with numerous dark-staining granules and round small eccentrically located nuclei.

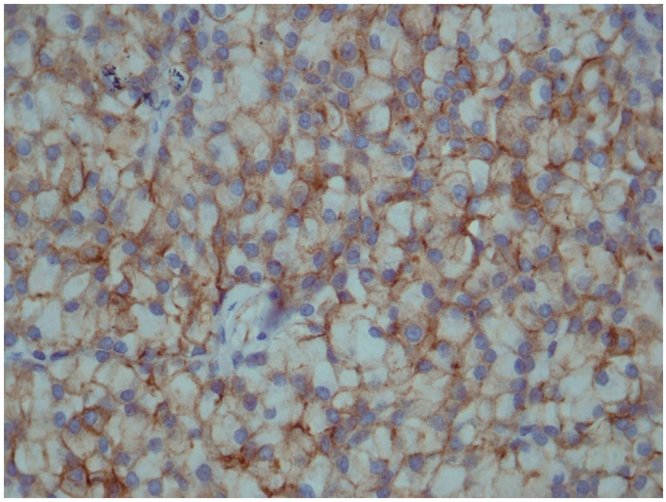

Fig. 4. Acinic cell carcinoma with abundant acinar cells and intense membranous and variable cytoplasmic staining with DOG1.

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 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 sufficient amount of specimens from jaw lesions is essential to make a definite diagnosis. The key point in the diagnosis of ACC is to identify serous acinar differentiation [13]. From microscopic differential diagnosis 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 immunohistochemical profiles. ACC cases entirely show diffuse intense membranous and cytoplasmic immunostaining for DOG1 and negative immunoreaction for Vimentin, mammaglobin, S100, and Adipophilin [15–17]. Other monomorphic oncocytic neoplasms that cause difficulty in diagnosis include High grade mucoepidermoid carcinoma with oncocytic differentiation as well as monotonous oncocytic cell proliferation including oncocytoma and oncocytic carcinoma.

Histomorphologic features which may help differentiate these tumors 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 oncocytic 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 AciCCA, 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 tumors 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].

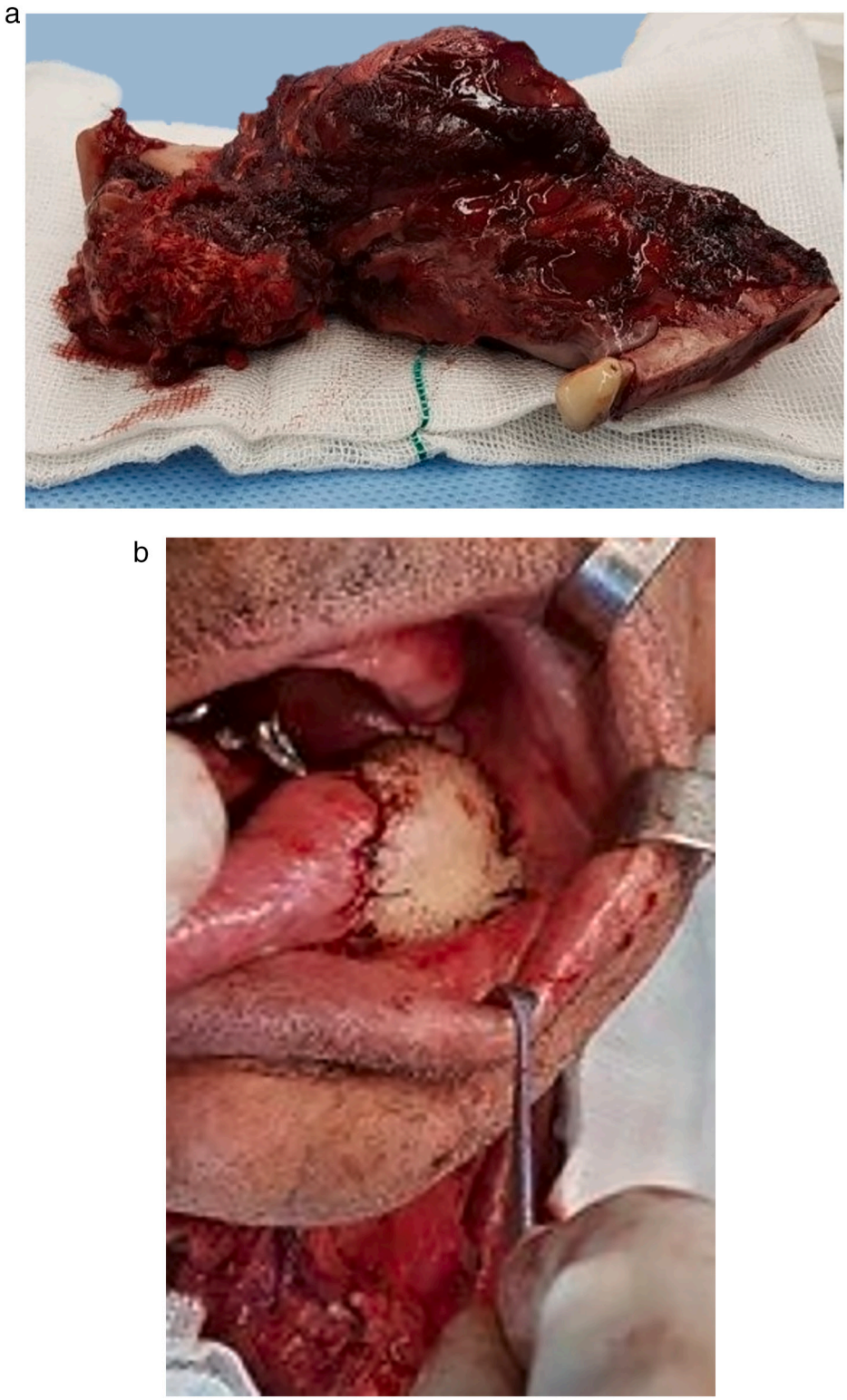

Fig. 5. (a) left hemimandibulectomy and modified radical neck dissection were performed. (b) reconstruction plate and submental flap with revers flow technique were used to rehabilitate mandibular defect.

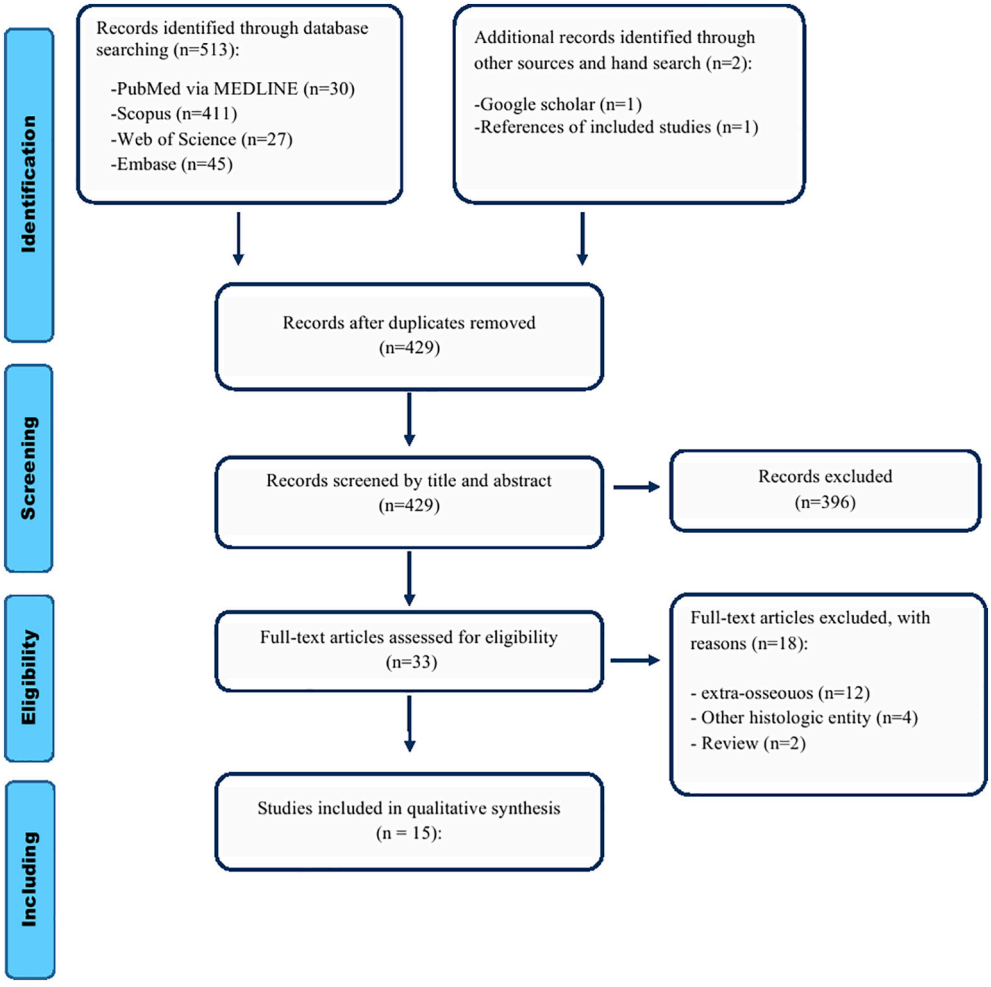

Fig. 6. PRISMA flow chart.

Table 1
Clinicopathological data of ACC cases reported in literature.

	Author	year	Sex	Age	Site	Left/ right	variant	Treatment	outcome
1	Ito et al	1970	Female	25	Ascending ramus	Left	Solid	Block resection	Tumor free (3 years)
2	Abrams et al	1978	Female	19	Third molar area	Left	Micro-cystic	*En bloc* resection	Tumor free (3.5 years)
3	Spiro et al	1978	–	–	Lower molar area	–	–	Unroofing and curettage	Unknown
4	Chaudhry et al	1986	–	–	Mandible	–	–	–	–
5	Bondi et al	1989	Female	79	Lower molar area	Left	–	*En bloc* resection	Tumor free (1 years)
6	Flood et al.	1991	Female	22	Body of mandible	Left	Papillary-cystic	Wide excision with neck dissection	Died from other disease
7	Nakazawa et al	1998	Female	84	Ascending ramus	Left	Follicular	None	Alive with tumor (1 year)
8	Martinez-Madrigal	2000	Female	48	Angle	–	Solid	Marginal mandibulectomy with	Tumor free (12 month)
9	et al		Male	76	Body	–		radiotherapy	Tumor free (2 month)
10	Hara et al.	2003	Female	67	Third molar area	Left	Solid	Wide excision with neck dissection	Tumor free (3 years)
11	Li et al	2008	Female	39	Mandibular ramus	–	–	Transfer treatment	–
12	Hiremath et al	2013	Female	65	Ramus and body of mandible	Left	Follicular	–	–
13	Lakshmana et al	2017	Female	35	Mandible	Left	Solid	–	–
14	Bajpai et al	2018	Female	31	Mandible	bilateral	Micro-cystic	Complete surgical removal	Tumor free (more than 1 year)
15	Kim et al	2018	Male	47	Mandible	Left	Solid	Segmental resection	Tumor free (7 month)
16	Munjal et al	2020	Male	77	Ascending ramus	Right	–	Wide excision with neck dissection	–
17	Present study	2021	Male	73	Posterior Mandible	Left	Solid	Wide excision with neck dissection	Under treatment procedure

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.

Abbreviation

ACC	acinic cell carcinoma
EMA	epithelial membrane antigen
CK	cytokeratin
Pan-CK	pan cytokeratin
IHC	immunohistochemistry
CEA	Carcinoembryonic Antigen
PAS	Periodic acid–Schiff

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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.

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