CASE REPORT

Intraosseous Adenoid Cystic Carcinoma of the Jaws Masquerading as a Cyst.

Latha Mary Cherian, Bhagya J, Indu M, Sudharani, Rasla P C, Krishnapriya S.

Abstract

Background: The rarity and diversity of primary intraosseous malignancies along with their innocuous clinical presentation pose a great diagnostic challenge to pathologists. Adenoid cystic carcinoma (ACC) is an uncommonand slow-growing salivary gland tumor characterized by perineural invasion, late distant metastasis, and a high recurrence rate.Primary intraosseous ACC of the jaws are furthermore few and far between with a little more than 50 cases reported.

Case Presentation: A 34-year-old male patient presented to the oral medicine and radiology department of our institution with the chief complaint of intermittent pain of moderate intensity in relation to the left lower back teeth in the past two months. On examination, no relevant findings were noted, however, OPG revealed a periapical radiolucent lesion in relation to 38. With a provisional diagnosis of an odontogenic cyst, an incisional biopsy was performed under local anesthesia andthe histopathology examination wassuggestive of adenoid cystic carcinoma. Further MRI and CT scans of the salivary glands appeared normal implying their intraosseous origin.

Conclusion: Intraosseous malignancies are often diagnosed at an advanced stage chiefly through histological examination and complete clinical-radiological workup. This case implies the importance of considering malignant salivary gland tumors in the differential diagnosis of radiolucencies of the mandible.

Keywords: Adenoid cystic, Carcinoma, Intraosseous, Jaw neoplasms, Salivary gland neoplasms

Introduction

Malignant salivary gland tumors of the jaws are extremely rare comprising <0.4% of all salivary gland carcinomas. Mucoepidermoid carcinoma is the most common intraosseous salivary gland neoplasm followed by adenoid cystic carcinoma (ACC), adenocarcinomas, and acinic cell carcinomas.[1] ACC is a slow-growing tumor characterized by perineural invasion (PNI) and late distant metastasis to lungs, bone, and soft tissue.[2] Adults between the 4th and 6th decade are most affected with high incidence in palatal minor salivary glands and a female predilection of 3:2. However, the central variant exhibits no such predilection.[3,4] Primary intraosseous adenoid cystic carcinoma (PIACC) affects the mandible more frequently than the maxilla with a typical clinical presentation of mild pain, swelling, and rarely paresthesia.[2,5] A little more than 50 cases of PIACC arising centrally within the mandible are only reported so far in the literature pointing towards its rarity.

Case Report

A 34-year-old male patient presented to the OPD with the chief complaint of intermittent pain of moderate intensity in relation to left lower back teeth for two months. The pain subsided on taking analgesics, however, recurred with the same intensity after a few days. No relevant intraoral findings were noticed, and the overlying mucosa was normal except for the pericoronitis in relation to impacted 38. (Figure 1) All associated teeth were vital. No associated paresthesia, with no obvious redness, swelling, hyperplasia or ulceration in the overlying mucosa. On palpation, mild lingual cortical expansion extending from the distal aspect of 38 was noted with no rise in local temperature. A panoramic radiograph showed a radiopaque-radiolucent lesion of size 4x3cm^2

Department of Oral Pathology and Microbiology, Government Dental College, Kottayam, Kerala, India.

Corresponding Author: Bhagya J, Department of Oral Pathology and microbiology, Government Dental College Kottayam, Kerala, India. E-mail: bhagya.bj333@gmail.com

How to cite the article: Cherian LM, Bhagya J, Indu M, Sudharani, Rasla PC, Krishnapriya S.An Intraosseous Neoplasm Masquerading as a Cyst: A Rare Presentation of Adenoid Cystic Carcinoma of the Jaws.Oral MaxillofacPathol J 2024; 15(2);266-269.

Source of Support: Nil

Conflict of Interest: None

extending from the distal aspect of partially impacted 38 to the ramus. The lesion was confined within the mandibular bone with intact cortical plates. (Figure 2)

On extra oral examination, left submandibular lymph nodes were firm and tender. Extraoral salivary glands appeared normal. His past medical history, personal history, and family history were non-contributory. On correlating the history and clinical findings, a provisional diagnosis of an odontogenic cyst or an osteolytic lesion was considered. The lesion was excised and sent for histopathological examination. (Figure 3)

The hematoxylin and eosin-stained sections revealed the connective tissue stroma infiltrated with tumor cells arranged predominantly in a cribriform pattern separated by hyaline stroma. Tumor cells were basaloid with small, uniform, hyperchromatic nuclei, and eosinophilic cytoplasm. Cyst-like spaces filled with eosinophilic mucin-like material were also noted. (Figure 4,5A) Aggregates of tumor cells were seen around the blood vessels and nerve bundles suggesting angioinvasion and PNI respectively. (Figure 5B)

Microscopy of the decalcified section shows necrotic bony trabeculae infiltrated with basaloid tumor cells at areas. (Figure 5C) The histologic features were consistent with a cribriform variant of ACC.

Subsequent examination, including MRI and CT scan of the salivary glands, did not disclose additional neoplastic deposits in the head and neck; and the major or minor salivary glands appeared normal; following which a final diagnosis of primary intraosseous adenoid cystic carcinoma was made.

The patient was referred to the Department of Oral and Maxillofacial Surgery for further management. However, they refused to undergo surgery in our institution and maintained no contact. Hence, the case couldn't be followed up postoperatively, and distant metastasis could not be ruled out.

Discussion

Theodor Bilroth in 1856 was the first to describe the long amorphous compartments of ACC as cylinders and coined the term cylindroma.[6] The term adenoid cystic carcinoma was first used by Spies in 1930.[7] Despite ACC of the head and neck region being a common malignant salivary gland tumor, PIACC arising from the jawbones with no major or minor salivary gland involvement is rare. They occur in a wide age range from 24 to 82 years and have equal sex distribution. The clinicopathologic and radiographic findings of PIACC are comparable to other malignant or borderline-malignant mandibular tumors, hence thorough histopathologic examination is mandatory to arrive at a definitive diagnosis.[5]

The gnathic origin of salivary gland tumors remains controversial, and the popular theories are i) neoplastic

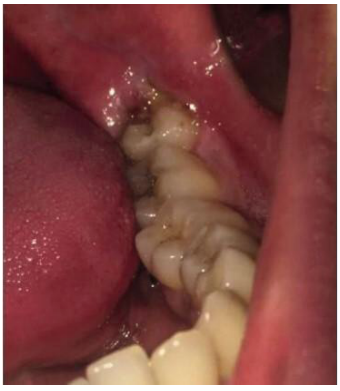

Fig. 1: Clinical examination showing pericoronitis in relation to 38 no apparent swelling.

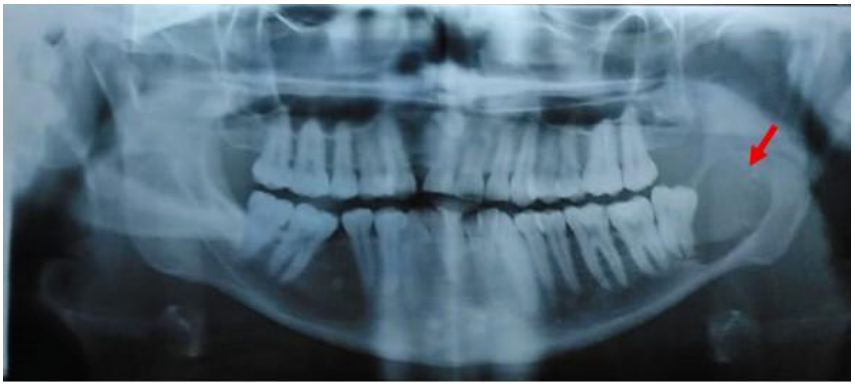

Fig. 2: OPG shows a radiopaque-radiolucent lesion of size 4x3 cm2extending from distal aspect of partially impacted 38 to ramus.

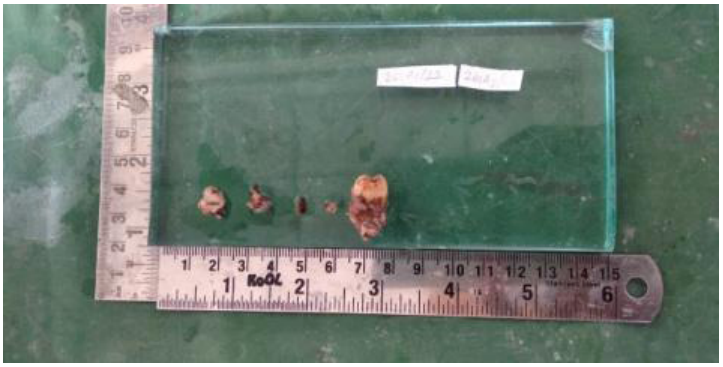

Fig. 3: Gross examination showing three firmbrownish soft tissue bits, one hard tissue bitand the associated tooth (38).

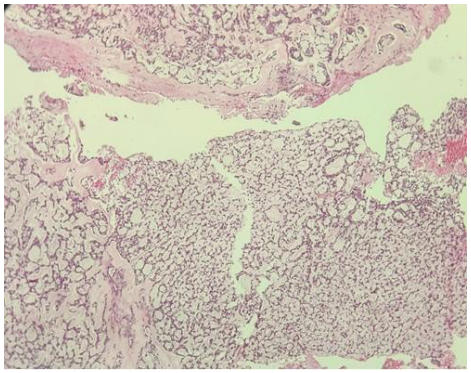

Fig. 4: Connective tissue stroma infiltrated with tumor cells in a sheet-like pattern with numerouscyst-like spaces (Hematoxylin and eosin stain, magnification x10).

transformation of mucous cells of dentigerous cyst lining, ii) ectopic entrapment of retromolar salivary glands or developmentally included embryonic remnants of submandibular salivary gland, and iii) metaplasia and malignant transformation of epithelial cells in the mandible, like the cell rests of Malassez and reduced enamel epithelium. Although different scholars support different theories, strong evidence to support none of these is available.[8,9]

Regardless of the controversial origin, strict diagnostic criteria by Batsakis et al. in 1979 for central salivary gland neoplasm have been established namely: a) radiographic evidence of bone destruction; b) the presence of intact cortical plates; c) absence of any primary lesion within the major or minor salivary glands; and d) histologic confirmation of the typical architecture and morphological features of a salivary gland tumor.[10] All the criteria of Batsakis et al. were satisfied in this case.

Brookstone and Huvos recommended a staging system for the central salivary gland neoplasm where stage I: lesions located within the undisturbed, intact cortical bone and overlying periosteum without any sign of cortical expansion, II: lesions with some degrees of expansion but intact cortical bone, and stage III: lesion characterized by cortical perforation, breakdown of overlying periosteum, or nodal metastatic spread.[11] In regard to this, the current case was diagnosed as a stage II lesion.

Histologically, ACC is identified as a tumor with biphasic differentiation of epithelial and myoepithelial cells in cribriform, tubular, and solid patterns. The cribriform or tubular growth patterns are known to have a healthier prognosis, but the solid variant (>30-50% areas) indicates an aggressive clinical course.[12-14] The presence of a solid pattern regardless of its quantity is proposed to be a poor prognosticator by Van Weert et al.[15] The predominant cribriform pattern in the present case favors a fair prognosis. Ki-67, PCNA, AgNOR associated proteins can also act as independent prognostic markers.[16]

However, ACC needs to be differentiated from its analogous histopathological entities such as polymorphous adenocarcinoma (PAC), basal cell adenocarcinoma, basaloid squamous cell carcinoma (BSCC), and metastatic lesions from other organs.[17,18] PAC is an accountable differential diagnosis of ACC given that PAC shows similar histological patterns, growth patterns, and perineural spread.[17] However, the characteristic polymorphous architecture, single-file/single-cell infiltration, and whirling "targetoid pattern" of a single cord of cells were absent in the present case, ruling out the possible histopathological diagnosis of PAC.

The solid variant of ACC is more likely to be confused with basal cell adenocarcinoma. Additionally, tubular and cribriform variants of basal cell adenocarcinomas have also been described. The differentiation between the two may best be accomplished using cytomorphologic criteria. Basal adenocarcinoma has a nested arrangement with smaller and darker cells at the periphery exhibiting palisading and cells with paler cytoplasm in the center. The nuclei of ACC are angular rather than rounded and the cell arrangements are not palisaded.[18]

Basaloid squamous carcinoma and ACC may mimic each other since each of these may exhibit a dominant adenoid pattern which may be selectively represented in small biopsies. However, the presence of peripheral palisading and foci of squamous metaplasia with a striking absence of ductal and myoepithelial components suggests the diagnosis of BSCC.[19]

Abnormalities in the MYB gene were recently reported as a unique feature of ACC. The study by Han et al. investigated the histopathology and molecular features of 4 cases of PIACC using IHC and FISH. They observed a high MYB protein expression few translocations and deletions in the MYB gene locus in PIACC. These were identical to the abnormalities observed in the ACC derived from the salivary glands, suggesting a similar origin of both lesions.[20]

ACC displays a good 5-year survival rate, despite poor clinical outcome after prolonged observation (10 to 20 years). Neural invasion can be seen even in early-stage tumors and has been regarded as an unfavorable prognostic factor, associated with distant metastasis and adverse outcome. Teymoortash et al. reviewed 22 cases of ACC with documented PNI and proposed a new classification scheme for ACCs. They classified tumors as p1 when a true perineural or endoneurial invasion was observed and p2 when the tumor was adjacent to nerves without invading them where p1 tumors had a higher recurrence rate in comparison with p2 tumors.[21] The present case displayed p2 PNI.

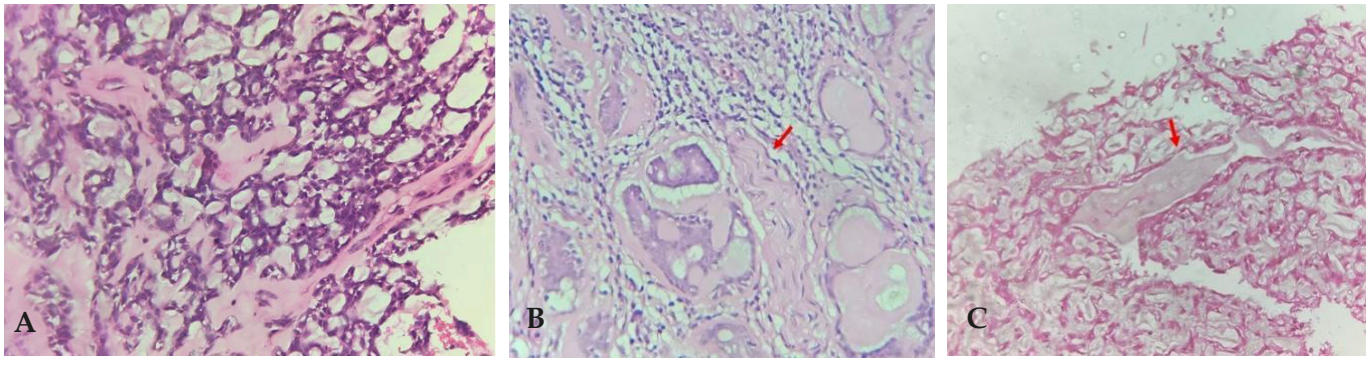

Fig. 5 : A - Basaloid cells with hyperchromatic nuclei and eosinophilic cytoplasmarranged in cribriform patterns. Numerous cystic spaces are seen filled with eosinophilic mucin-like material. **B** - Perineural invasion. **C** - Tumor cells invading the necrotic bony trabeculae in the decalcified sections. (Hematoxylin and eosin stain, magnification x40).

The pathogenesis of PNI is based on two theories, "the path of low resistance" and "reciprocal signaling interactions". The anatomical proximity between the salivary glands and cranial nerves alongside certain factor-based interactions between tumor cells and nerves provides a microenvironment suitable for PNI. Recently, studies have indicated that the tight junction in the perineurium may also act as a barrier against cancer invasion, and dismantling the tight junctions can facilitate PNI.[22]

In contrast to this, a survey by Mark Zupancic stated that age, gender, smoking, PNI, and radical surgery are not prognostic factors for disease-free survival and overall survival of ACC. Instead, patients of early clinical stages (stage I and II), patients of major salivary gland subsites, and patients who have taken multimodal treatment (surgery and post-operative radiotherapy) have the best prognosis.[23]

PIACC is primarily treated with surgery, which can be supplemented with radiotherapy, although a few cases can be treated with chemotherapy or radiotherapy alone. ACC is radiosensitive but not radio-curable and attention is needed to obtain clear margins around regional nerves. Due to the historically low incidence of occult nodal metastasis, neck dissection should only be performed in patients with clinical or radiologic evidence of cervical lymphatic metastasis. Prophylactic neck dissection is generally not recommended. Radical surgery followed by postoperative radiation therapy results in 5- and 10-year survival rates of 77% and 57%, respectively.[3,4]

Despite combined treatment with surgery and radiotherapy, local recurrences occur and are uniformly linked to the failure to control distant disease. The reported rates of distant metastasis (lung, bone, and soft tissues) vary from 20% to 55%; with lung metastasis being most common varying from 67.0% to 92.9%. The risk of lung metastasis increases when PNI is present, tumor size is greater than 2.5 cm, and locally recurs. Bone metastases usually correspond to an aggressive clinical course with rapid tumor dissemination and death of the patient.[24] Owing to the small size and innocuous histopathology, a fair prognosis is expected in this case.

Conclusion

The present case calls attention to the possible occurrence of malignant salivary gland neoplasms like ACC at intraosseous sites and to its intriguing clinical-radiological presentation which may lead to late diagnosis. This stresses the importance of systematic histopathological examination and complete clinical-radiological workup of apparently benign lesions.

References

1. Vinuth D, Agarwal P, Dhirawani RB, Dube G. Atypical case of primary intraosseous adenoid cystic carcinoma of mandible. J Oral MaxillofacPathol2013;17:436-9.
2. Indu S, Roy ID. Intraosseous adenoid cystic carcinoma of the mandible: A rare presentation. J Oral MaxillofacPathol 2020;24:S37-41.
3. Favia G, Maiorano E, Orsini G, Piattelli A. Central (intraosseous) adenoid cystic carcinoma of the mandible: report of a case with periapical involvement. Journal of endodontics. 2000 Dec 1;26(12):760-3.
4. Al-Sukhun J, Lindqvist C, Hietanen J, Leivo I, Penttilä H. Central adenoid cystic carcinoma of the mandible: case report and literature review of 16 cases. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2006 Mar 1;101(3):304-8.
5. Li Y, Li LJ, Huang J, Han B, Pan J. Central malignant salivary gland tumors of the jaw: Retrospective clinical analysis of 22 cases. J OralMaxillofac Surg 2008;66:2247-53.
6. Bumstead WD. Cylindroma of the mandible. Oral Surg1955;8:546.
7. Clark JM, Triana RJ, Meredith SD. Uncontrolled central adenoid cystic carcinoma: case report. Ear Nose Throat J 2000;79:784.
8. Jafek BW, Strife JL. Accessory lobe of the submandibular gland. DiagnRadiol 1973;75-7.
9. Cohen JI: Submandibular accessory salivary gland causing Warthin's duct obstruction. Head Neck 2000;717-21.
10. Hu HY, Liu YY, Wang H, Jiang M. Primary intraosseous adenoid cystic carcinoma of the mandible: a comprehensive review with analysis of 2 additional cases. Journal of Oral and Maxillofacial Surgery. 2017 Aug 1;75(8):1685-701.
11. Brookstone MS, Huvos AG, Spiro RH. Central adenoid cystic carcinoma of the mandible. J Oral Maxillofac Surg 1990;48:1329–33.
12. Langdon JD, Henk. JM. Malignant tumours of the mouth, jaws and salivary glands. London: Edward Arnold; 1995.
13. Szanto PA, Luna MA, Tortoledo ME, White RA. Histologic grading of adenoid cystic carcinoma of the salivary glands Cancer 1984;54:1062-9.
14. Spiro RH, Huvos AG, Strong EW. Adenoid cystic carcinoma of salivary origin: a clinicopathologic study of 242 cases. The American Journal of Surgery. 1974 Oct 1;128(4):512-20.
15. van Weert S, Bloemena E, van der Waal I, de Bree R, Rietveld DH, Kuik JD, Leemans CR. Adenoid cystic carcinoma of the head and neck: a single-center analysis of 105 consecutive cases over a 30-year period. Oral oncology. 2013 Aug 1;49(8):824-9.
16. Coca-Pelaz A, Rodrigo JP, Bradley PJ, Vander Poorten V, Triantafyllou A, Hunt JL, Strojan P, Rinaldo A, Haigentz Jr M, Takes RP, Mondin V. Adenoid cystic carcinoma of the head and neck–An update. Oral oncology. 2015 Jul 1;51(7):652-61.
17. Tasoulas J, Tsourouflis G, Klijanienko J, Theocharis S. Polymorphous adenocarcinoma of the salivary glands: an overview of immunohistochemical features and insights on molecular pathology.
18. Wilson TC, Robinson RA. Basal cell adenocarcinoma and Basal cell adenoma of the salivary glands: a clinicopathological review of seventy tumors with comparison of morphologic features and growthcontrol indices. Head and neck pathology. 2015 Jun;9:205-13.
19. Madur BP, Jambhekar NA. Basaloid squamous carcinoma simulating adenoid cystic carcinoma: diagnostic dilemma. Oral Oncology Extra. 2006 Jul 1;42(6):227-30.
20. Han J, Gu T, Yang X, Hu L, Xia R, Tian Z, Li J, Zhu L, Xu L, Zhang C. Primary intraosseous adenoid cystic carcinoma of the mandible: a comprehensive review and analysis of four new cases with emphasis on morphologic, immunophenotypic, and molecular characteristics. Oral surgery, oral medicine, oral pathology and oral radiology. 2017 Mar 1;123(3):365-73.
21. Teymoortash A, Zieger L, Hoch S, Pagenstecher A, Hofer MJ. Distinct microscopic features of perineural invasion in adenoid cystic carcinoma of the head and neck. Histopathology 2014;64:1037–9.
22. Liu X, Yang X, Zhan C, Zhang Y, Hou J, Yin X. Perineural invasion in adenoid cystic carcinoma of the salivary glands: where we are and where we need to go. Frontiers in Oncology. 2020 Aug 18;10:1493.
23. Zupancic M, Näsman A, Berglund A, Dalianis T, Friesland S. Adenoid cystic carcinoma (AdCC): a clinical survey of a large patient cohort. Cancers. 2023 Feb 27;15(5):1499.
24. Seok J, Lee DY, Kim WS, Jeong WJ, Chung EJ, Jung YH, Kwon SK, Kwon TK, Sung MW, Ahn SH. Lung metastasis in adenoid cystic carcinoma of the head and neck. Head & Neck. 2019 Nov;41(11):3976-83.