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Case Report

Metastasis to an odontogenic cyst: case report and review of literature

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ABSTRACT

Metastatic disease to the jawbone is relatively uncommon. However, its occurrence within a pre-existing odontogenic cyst or tumor is extremely rare. We present a case of a 61-year-old woman experiencing fatigue and nocturnal diaphoresis with an otherwise asymptomatic radiolucent lesion of the mandible. Radiographic features were suggestive of a benign odontogenic cyst. A biopsy revealed a metastatic nidus within the wall of a benign odontogenic cyst. Further investigations confirmed the presence of a primary pulmonary adenocarcinoma. Diagnosis of metastases to the orofacial region may be challenging because of their various clinical and radiographic features. Thorough histopathological analysis of any routine cystic tissue from the maxillofacial structures, even seemingly benign, is necessary to rule out more aggressive disease.

Keywords: Dentigerous cyst, Metastasis, Adenocarcinoma, Odontogenic cyst, Mandible

INTRODUCTION

Metastatic disease to the maxillofacial region is rare and represents almost 1% of all oral malignancies.[1,2] The prevalence is increased among individuals between the fourth and sixth decades. Among women, the most common primary sources for metastatic disease are the breast, reproductive organs, kidney and colon while among men, the most common primary sites are the lung, kidney, liver and prostate.[3]

The most commonly affected site of metastasis to the jawbones is the mandibular molar area. The most common reported symptoms are pain, swelling, paresthesia, spontaneous bleeding and teeth mobility; however, metastasis to the jaws can also be asymptomatic. Radiographic features are varied; nonetheless, ill-defined osteolytic lesions are the most common radiographic finding.[3-6]

Odontogenic cysts include a range of osteolytic lesions of the jawbones that can be classified as either developmental, inflammatory or even neoplastic. Most developmental cysts are thought to be derived from remnants of odontogenic epithelium. For example, dentigerous cysts are generally classified as developmental cysts and are thought to arise from the epithelial lining of the follicle of an unerupted tooth and are more common in the pediatric population. In contrast, inflammatory cysts are more common in adults and usually have an infectious origin. In these instances, a chronic endodontic or periodontal infection initiates an inflammatory response leading to the formation of a benign cyst. A residual cyst is a subtype of inflammatory odontogenic cyst that persists after removal of the causative tooth.[7-10]

Some benign odontogenic cysts, such as odontogenic keratocysts, display biological and clinical features more akin to neoplasia. Several investigators regard odontogenic keratocysts as cystic neoplasms rather that cysts, although this opinion is still actively debated to this day.[10-13]

Metastases and odontogenic cysts may occur simultaneously in the same patient. However, the

occurrence of a metastatic nidus within a benign odontogenic cyst is exceedingly rare.[14-16]

CASE REPORT

A 61-year-old Caucasian woman was referred to an oral and maxillofacial surgeon for the evaluation of an asymptomatic radiolucent lesion in the left mandible. The patient reported fatigue and nocturnal diaphoresis but did not have any weight loss. The patient denied having any orofacial pain or paresthesia.

Her medical history was otherwise non-contributive. She had stopped smoking 3 years prior to the consultation and had an average alcohol intake of 3 drinks per day.

Physical examination was unremarkable. Cranial nerve and intraoral examinations were within normal limits.

A panoramic radiograph (Figure 1) revealed a large, well-defined and corticated unilocular radiolucency in the left premolar mandibular region. The epicenter of this radiolucency was likely associated with a missing second premolar. The lesion extended anteriorly and crossed the midline.

Figure 1: Panoramic radiograph showing an extensive radiolucent lesion in the left and anterior mandible involving dental roots and reaching the mandibular inferior cortex.

A cone-beam computed tomography (CBCT) scan of the mandible (Figure 2) showed expansion and thinning of the cortical bone surrounding the lesion. There was no perforation of the cortical plates, nor any dental resorption. Based on these findings, a preliminary diagnosis of benign odontogenic cyst was favored, such as a residual cyst or an odontogenic keratocyst. However, because of systemic symptoms, malignancy could not be entirely ruled out.

An incisional biopsy was performed. Histological examination revealed fragments of a fibrocollagenous capsule lined by non-keratinizing stratified squamous epithelium (Figure 3 A), consistent with a benign odontogenic cyst.

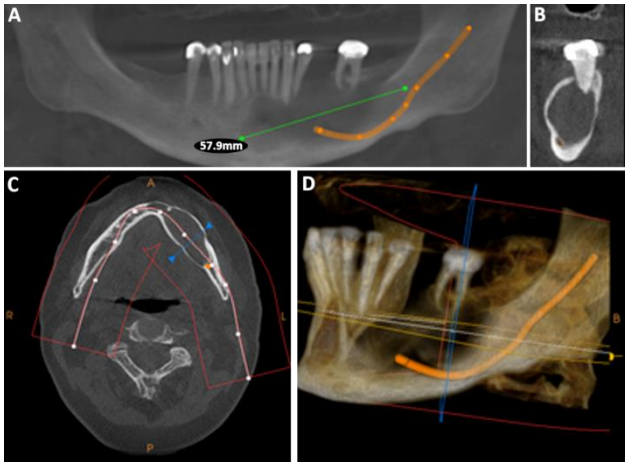

Figure 2: Cone-beam computed tomography of the lesion and its relation with the inferior dental nerve, colored in orange. (A) Reconstructed panoramic view exhibiting the lesion in its greatest dimension. (B) Cross-sectional view of inferior left molar region and (C) axial section showing cortical expansion. (D) The mandibular canal in periphery of the lesion shown in a 3-dimensional reconstruction.

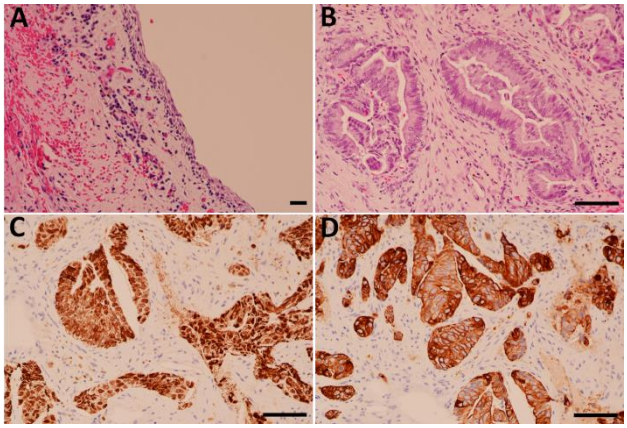

Figure 3: Histopathological analysis after incisional biopsy. (A) Hematoxylin-eosin-stained sections reveal a benign cyst lining of stratified squamous epithelium and (B) malignant ductal structures within the cyst wall. (C) Immunohistochemistry shows positive staining of tumoral clusters with anti-thyroid transcription factor 1 and (D) anti-cytokeratin 7.
Scale bar=20 µm.

However, in one area of the capsule, a cluster of atypical ductal structures was noted, consistent with metastatic adenocarcinoma (Figure 3 B). These structures stained positively for thyroid transcription factor-1 (TTF-1) and cytokeratin 7 (CK7), suggesting either a thyroidal or pulmonary origin (Figure 3 C-D).

Subsequent advanced imagery and lung biopsy revealed a primary pulmonary adenocarcinoma in the pulmonary lingula (Figure 4). Alas, the patient died 12 months after the initial diagnosis.

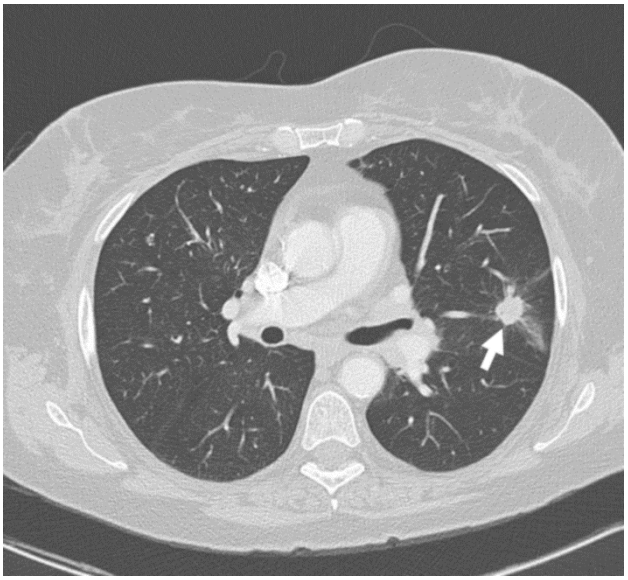

Figure 4: Thoracic computed tomography with contrast showing a nodular radiopacity (arrow) representing the primary malignancy in the lingula region.

DISCUSSION

Odontogenic cysts are benign lesions that may, on rare instances, undergo malignant transformation. There have been numerous reports of primary squamous cell carcinoma arising from a benign odontogenic cyst.[17,18] By contrast, metastatic disease within a pre-existing benign odontogenic cyst is exceedingly rare.[14-16]

Lung cancer is the most prevalent malignancy among men and the third most common among women worldwide, after breast and colorectal cancer. It is also the main cause of death from cancer among men and the second among women. Men experience nearly a two-fold increase in both incidence and mortality rate compared to women.[19,20] For lung metastases to the jaws, Gultekin et al.[21] reported a men to women ratio of (3.9:1) in a review of the literature.

Adenocarcinoma is the most common subtype of lung cancer, representing more than 40% of all pulmonary malignancies.[22-24] This tumor typically stains positively with pancytokeratin AE1/AE3, CK7, TTF-1 and Napsin A while it is typically negative for cytokeratin 20 (CK20) and paired box 8 (PAX8).[25-27]

In the present case, the mandibular nidus was the first evidence of pulmonary adenocarcinoma. Hirshberg et al[3], in their analysis of 673 cases of metastases to the oral cavity, found that in approximately 23% of cases, oral metastases were the first sign of disease. Metastases to the jaws display a wide range of clinical and radiographic features and may mimic benign lesions and odontogenic infections.[25]

To our knowledge, the present case is the fourth report of metastatic disease arising within a benign odontogenic cyst in the English literature, and the first case of pulmonary metastasis within a pre-existing odontogenic cyst. [14-16] Clinical features of previously reported cases of metastasis within odontogenic cysts are detailed in Table 1. In two of these cases, paresthesia was reported, while the third was associated with pain. Benign odontogenic cysts are seldom associated with systemic signs or symptoms, unless secondarily infected.[28] Therefore, in presence of benign radiographic features accompanied with paresthesia or systemic symptoms, the possibility of a superimposed malignancy must be considered.

Dahl and Terakado et al also reported cases of metastases to the jaws presenting as periapical radiolucencies.[29,30] However, histologic evidence of pre-existing odontogenic lesions is lacking; it is impossible to state whether the radiolucencies were purely metastatic or if they arose within odontogenic lesions. Incidentally, cases of metastatic disease presenting as periapical lesions have been widely reported.[31-33]

In our case, aside from the wall of the residual cyst, there was no other detectable metastatic implant in the jawbones. Even though this may be a simple coincidence, there might be some underlying mechanism for this occurrence. In the context of inflammatory odontogenic cysts, it is possible that a cascade of pro-inflammatory cytokines and byproducts of osteolysis at the periphery of the lesion may facilitate chemotaxis and proliferation of metastatic cells in the previously diseased bone. Chemoattracting factors produced during natural bone turnover may recruit circulating cancer cells. Examples of these chemoattractants are C-X-C Motif Chemokine ligand 12 (CXCL12), Osteopontin (OPN), receptor activator of nuclear factor κ-B Ligand (RANKL) and bone morphogenic proteins (BMPs) secreted by osteoblasts.[34, 35] Once the metastatic cells acquire adaptive traits to grow in their new microenvironment, a vicious cycle of paracrine and autocrine signaling is established among cancer cells, osteoblasts and osteoclasts, thereby maintaining the metastatic colonization in bone tissue.[36,37] Growth factors such as transforming growth factor beta (TGF-β) and insulin-like growth factors (IGF) may play a key role in the survival of cancer cells in these conditions.[38] In addition, the reactive formation of leaky neocapillaries associated with inflammatory lesions, often present around inflamed odontogenic cysts, may further increase the likelihood of a metastatic implant via hematogenous routes.[16,39,40]

Table 1: Characteristics of metastasis cases arising within a benign odontogenic cyst.

Study	Sex	Age (in years)	Site of primary disease	Cancer type	Type of odontogenic cyst	Site	Orofacial symptoms
Welch et al, 1985[14]	Male	23	Skin	Melanoma	Periapical cyst	Maxilla-anterior	Pain
Chatterjee et al, 2006[15]	Female	44	Breast	Adenocarcinoma	Dentigerous cyst	Mandible-posterior	Paresthesia
Eichhorn et al, 2009[16]	Female	67	Breast	Ductal carcinoma	Periapical cyst	Mandible-posterior	Paresthesia
Current case	Female	61	Lung	Adenocarcinoma	Residual cyst	Mandible-posterior	None

CONCLUSION

Metastatic disease to the jaws may present with a wide variety of clinical and radiographic features. On rare instances, it may be masked by a superimposed benign condition, thereby posing a diagnostic challenge to the clinician. This case illustrates the necessity for thorough examination of any tissue submitted during routine jaw surgery, even in presence of asymptomatic and seemingly benign odontogenic cysts.

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REFERENCES

1. Meyer I, Shklar G. Malignant Tumors Metastatic to Mouth and Jaws. Oral Surg Oral Med Oral Pathol. 1965;20:350-62.
2. Servato JP, de Paulo LF, de Faria PR, Cardoso SV, Loyola AM. Metastatic tumours to the head and neck: retrospective analysis from a Brazilian tertiary referral centre. Int J Oral Maxillofac Surg. 2013;42(11):1391-6.
3. Hirshberg A, Shnaiderman-Shapiro A, Kaplan I, Berger R. Metastatic tumours to the oral cavity-pathogenesis and analysis of 673 cases. Oral Oncol. 2008;44(8):743-52.
4. Hirshberg A, Berger R, Allon I, Kaplan I. Metastatic tumors to the jaws and mouth. Head Neck Pathol. 2014;8(4):463-74.
5. Irani S. Metastasis to the Jawbones: A review of 453 cases. J Int Soc Prev Community Dent. 2017;7(2):71-81.
6. Andabak Rogulj A, Tomasovic Loncaric C, Muller D, Blivajs I, Andabak M, Vucicevic Boras V, et al. Solid malignant metastases in the jaw bones. Br J Oral Maxillofac Surg. 2018;56(8):705-8.
7. Johnson NR, Gannon OM, Savage NW, Batstone MD. Frequency of odontogenic cysts and tumors: a systematic review. J Investig Clin Dent. 2014;5(1):9-14.
8. Jones AV, Craig GT, Franklin CD. Range and demographics of odontogenic cysts diagnosed in a UK population over a 30-year period. J Oral Pathol Med. 2006;35(8):500-7.
9. Li N, Gao X, Xu Z, Chen Z, Zhu L, Wang J, et al. Prevalence of developmental odontogenic cysts in children and adolescents with emphasis on dentigerous cyst and odontogenic keratocyst (keratocystic odontogenic tumor). Acta Odontol Scand. 2014;72(8):795-800.
10. Bilodeau EA, Collins BM. Odontogenic Cysts and Neoplasms. Surg Pathol Clin. 2017;10:177-222.
11. Stoelinga PJW. The odontogenic keratocyst revisited. Int J Oral Maxillofac Surg. 2022;51(11):1420-3.
12. Polak K, Jedrusik-Pawlowska M, Drozdzowska B, Morawiec T. Odontogenic keratocyst of the mandible: A case report and literature review. Dent Med Probl. 2019;56(4):433-6.
13. Pogrel MA. The keratocystic odontogenic tumor. Oral Maxillofac Surg Clin North Am. 2013;25(1):21-30.
14. Welch RD, Hirsch SA, Davis RG. Melanoma with metastasis to an apical periodontal cyst. Oral Surg Oral Med Oral Pathol. 1985;59(2):189-93.
15. Chatterjee M, Balaraman K, McDermott P. Metastatic breast carcinoma discovered in a dentigerous cyst - a case report. Br Dent J. 2006;201(6):349-50.
16. Eichhorn W, Wehrmann M, Blessmann M, Pohlenz P, Blake F, Schmelzle R, et al. Metastases in odontogenic cysts: literature review and case presentation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;109(4):582-6.
17. Bodner L, Manor E, Shear M, van der Waal I. Primary intraosseous squamous cell carcinoma arising in an odontogenic cyst: a clinicopathologic analysis of 116 reported cases. J Oral Pathol Med. 2011;40(10):733-8.
18. Zapala-Pospiech A, Wyszynska-Pawelec G, Adamek D, Tomaszewska R, Zaleska M, Zapala J. Malignant transformation in the course of a dentigerous cyst: a problem for a clinician and a pathologist. Considerations based on a case report. Pol J Pathol. 2013;64(1):64-8.
19. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer

Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71:209-49.
20. Nasim F, Sabath BF, Eapen GA. Lung Cancer. Med Clin North Am. 2019;103:463-73.
21. Gultekin SE, Senguven B, Isik Gonul I, Okur B, Buettner R. Unusual Presentation of an Adenocarcinoma of the Lung Metastasizing to the Mandible, Including Molecular Analysis and a Review of the Literature. J Oral Maxillofac Surg. 2016;74:2007-e1-8.
22. Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger KR, Yatabe Y, et al. International association for the study of lung cancer/american thoracic society/european respiratory society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol. 2011;6:244-85.
23. Hutchinson BD, Shroff GS, Truong MT, Ko JP. Spectrum of Lung Adenocarcinoma. Semin Ultrasound CT MR. 2019;40:255-64.
24. Meza R, Meernik C, Jeon J, Cote ML. Lung cancer incidence trends by gender, race and histology in the United States, 1973-2010. PLoS One. 2015;10:e0121323.
25. Kaplan I, Raiser V, Shuster A, Shlomi B, Rosenfeld E, Greenberg A, et al. Metastatic tumors in oral mucosa and jawbones: Unusual primary origins and unusual oral locations. Acta Histochem. 2019;121(8):151448.
26. Kandukuri SR, Lin F, Gui L, Gong Y, Fan F, Chen L, et al. Application of Immunohistochemistry in Undifferentiated Neoplasms: A Practical Approach. Arch Pathol Lab Med. 2017;141(8):1014-32.
27. Inamura K. Update on Immunohistochemistry for the Diagnosis of Lung Cancer. Cancers (Basel). 2018;10(3):72.
28. Rajendra Santosh AB. Odontogenic Cysts. Dent Clin North Am. 2020;64(1):105-19.
29. Dahl EC. Diagnosing inflammatory and non-inflammatory periapical disease. J Indiana Dent Assoc. 1991;70(6):22-6.
30. Terakado N, Shintani S, Nakashiro K, Hamakawa H. Malignant pleural mesothelioma metastasis to the mandible. Int J Oral Maxillofac Surg. 2004;33(8):798-800.
31. Thompson IO, Phillips VM, Kalan M. Metastatic squamous carcinoma manifesting as a periapical lesion. J Dent Assoc S Afr. 1992;47(11):481-3.
32. Poulias E, Melakopoulos I, Tosios K. Metastatic breast carcinoma in the mandible presenting as a periodontal abscess: a case report. J Med Case Rep. 2011;5:265.
33. Khalili M, Mahboobi N, Shams J. Metastatic breast carcinoma initially diagnosed as pulpal/periapical disease: a case report. J Endod. 2010;36(5):922-5.
34. Obenauf AC, Massague J. Surviving at a Distance: Organ-Specific Metastasis. Trends Cancer. 2015;1:76-91.
35. Joyce JA, Pollard JW. Microenvironmental regulation of metastasis. Nat Rev Cancer. 2009;9(4):239-52.
36. Nicolson GL. Cancer progression and growth: relationship of paracrine and autocrine growth mechanisms to organ preference of metastasis. Exp Cell Res. 1993;204(2):171-80.
37. Patel LR, Camacho DF, Shiozawa Y, Pienta KJ, Taichman RS. Mechanisms of cancer cell metastasis to the bone: a multistep process. Future Oncol. 2011;7(11):1285-97.
38. Yoneda T. Cellular and molecular basis of preferential metastasis of breast cancer to bone. J Orthop Sci. 2000;5(1):75-81.
39. Johnson RC, Augustin-Voss HG, Zhu DZ, Pauli BU. Endothelial cell membrane vesicles in the study of organ preference of metastasis. Cancer Res. 1991;51(1):394-9.
40. Nagy JA, Brown LF, Senger DR, Lanir N, Van de Water L, Dvorak AM, et al. Pathogenesis of tumor stroma generation: a critical role for leaky blood vessels and fibrin deposition. Biochim Biophys Acta. 1989;948(3):305-26.

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