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Malignant Ameloblastoma with Hepatic Metastasis in a 38-Year-Old Haitian Woman

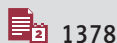
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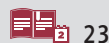
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Corresponding Author: Andrew P. Collins, e-mail: Andrewcollins@knights.ucf.edu**Conflict of interest:** None declared**Patient:** Female, 38-year-old
Final Diagnosis: Hepatic metastasis • malignant ameloblastoma
Symptoms: Abdominal pain • ascites • hepatic cyst
Medication: —
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology • Pathology**Objective:** Rare disease**Background:** Primary malignant ameloblastoma is a very rare tumor of the dental lamina epithelium. Similar to the benign ameloblastoma, the mass is without significant histological atypia, but the malignant type may present with metastases, most commonly to the lungs. The average age of diagnosis is 34 years, and the malignancy affects men and women equally. The tumors often present with an insidious growth and have a median survival from time of diagnosis of 17.6 years. Due to the rarity of this lesion, a standard of care has not yet been established.
Case Report: A 38-year-old Haitian woman, who initially presented with a large primary malignant ameloblastoma of the angle of the mandible, experienced a recurrence in the floor of the mouth 30 months after surgical resection. In 2018, 2 years after the removal of the recurrent tumor, the patient presented with ascites, right-sided abdominal pain, weight loss, and a palpable liver mass. Laparoscopic exploration demonstrated a complex lateral right liver lobe cyst, suspicious for parasitic infection. Cytological analysis showed positive staining for cytokeratin 5/6, P63, and CD56, indicative of metastatic ameloblastoma of the liver. Consistent cell morphology from the primary tumor and liver cyst was also noted. Following drainage of the cyst, the patient returned to Haiti, where she died in 2020. In Haiti, she lacked appropriate local medical care, leading to the severe progression of her initial primary ameloblastoma and disease recurrence.**Conclusions:** Malignant ameloblastoma accounts for less than 2% of all odontogenic tumors, as the benign variant is much more common. Distant metastases of these lesions are rare; to date, few cases have presented with hepatic metastases.**Keywords:** Ameloblastoma • Neoplasm Metastasis • Rare DiseasesFull-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/929422>

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Background

Ameloblastomas arise from the dental lamina epithelium and most frequently occur as either a benign or malignant ameloblastoma. Malignant lesions lack significant histological atypia, like the benign type, but they may metastasize and can present as locally aggressive tumors with a high recurrence rate [1-3]. Malignant ameloblastomas commonly metastasize through a hematogenous route to the lungs [4] and are very rare, constituting less than 2% of all odontogenic tumors and roughly 4% of ameloblastoma [5,6]. In 2005, the World Health Organization (WHO) further classified malignant ameloblastoma into 2 categories: ameloblastic carcinoma and malignant ameloblastoma [3]. Unlike malignant ameloblastoma, ameloblastic carcinoma presents with significant cytological atypia, increased mitoses with atypical forms, and a high N: C ratio [7].

Localized ameloblastoma is treated with surgical resection, while metastatic disease is commonly treated with radiation therapy and chemotherapeutic agents. Due to the few cases of malignancy, defined treatment protocols have been difficult to develop, and results have been unpredictable.

In this report, we present a rare case of extremely aggressive recurrent malignant ameloblastoma of the mandible and floor of the mouth in a 38-year-old woman, with cytology confirming metastasis to the right lobe of the liver.

Case Report

In April 2018, a 38-year-old woman presented to the Halifax Health Emergency Department in Daytona Beach, Florida, with constant right-sided abdominal pain (6/10), significant ascites, weight loss, and a palpable mass. A large complex cyst measuring 21.9×14.4×17.3 cm in the lateral right lobe of the liver was identified with CT (**Figure 1**). Laparoscopic drainage of the cyst removed 2000 cc of brown-red fluid (**Figure 2**). Initial differential diagnoses included bacterial or parasitic infection; however, the biopsy had negative serology (echinococcus and entamoeba IgG) and cultures.

In 2014, the patient had presented to the same medical facility with a large ameloblastoma of the mandible that spread locally to involve the jaw, neck, and floor of her mouth. This original mass measured over 30 cm AP×30 cm laterally and weighed over 1 kg (**Figure 3**). It contained both soft tissue and numerous ossifications. The local invasion also involved her mandibular molars and premolars, and protruded anteriorly from her mouth with floating teeth, impacting speech and eating. Maxillary teeth and tongue muscles were not invaded by the tumor; however, the mass effect prevented full range of motion of the lingual muscles. The tumor encompassed

the entire mandible from angle to angle, down to the lower tracheal region, with the lower lip displaced inferiorly to her chest (**Figure 3**). This mass was surgically removed in 2014. Cytological markers of the mass displayed a lack of significant atypia and stained positive for CK 5/6 and P63 (**Figure 4**). Morphological analysis demonstrated odontogenic epithelial islands without dentin or enamel, consistent with malignant ameloblastoma. Postoperatively, the patient developed a left-sided deep vein thrombosis and pulmonary embolism. An IVC filter was placed, but the patient returned to Haiti without appropriate anti-coagulation therapy.

Two years later, in 2016, she presented to the same medical center and another mass was surgically excised. The patient experienced a recurrence of the malignancy in the floor of her mouth, deep strap muscles of her neck, and minor salivary glands, but showed no mandibular infiltration. The mass was highly vascular and demonstrated extremely rapid growth. The recurrent tumor involved only soft tissues and appeared roughly one-third of the size of the original mass. She has no history of smoking or drinking, no allergies, and no family history of any malignancies.

At the current presentation, cytology of the liver cyst fluid demonstrated positive staining for CK 5/6, P63, and CD56, indicating metastasis of malignant ameloblastoma (**Figure 4**). The cystic cells displayed odontogenic epithelial islands and lacked dentin or enamel formation, similar to cytology seen in the patient's previous masses. Following drainage, the patient's corrected serum calcium was severely elevated (13.3) and she was started on calcitonin. Three days postoperatively, she experienced shortness of breath and a CT pulmonary angiogram was negative for pulmonary embolism; however, there was re-accumulation of intrahepatic fluid within the right lobe, and right hemidiaphragm elevation with submaximal inspiration. The patient returned to Haiti prior to full resolution of respiratory symptoms and she did not return for post-operative care or chemotherapy. She died in 2020, potentially due to complications of the metastatic ameloblastoma; however, there was no post-mortem autopsy.

Discussion

Odontogenic neoplasms are uncommon tumors affecting the oral cavity. While the odontoma is the most common odontogenic neoplasm, the ameloblastoma falls a close second in incidence [2]. The first case of malignant ameloblastoma was described in 1923, and approximately only 100 cases have been described since [8]. On average, patients with ameloblastoma are diagnosed at 34 years of age, with a range from 5 to 74 years [9,10]. Both men and women have been shown to be equally affected. The most common site of primary



Figure 1. Computed tomography scan of hepatic cyst.

ameloblastoma is the angle of the mandible, while the maxilla is less frequently involved [11]. Approximately 75-88% of metastatic sites include the lungs, often following multiple local recurrences [12]. Clinically, this lung involvement may present with cough, dyspnea, hemoptysis, and rarely paraneoplastic syndrome. These lung metastases often show indolent clinical behavior and long median survival times [7]. Cervical lymph nodes are the second most common site of metastasis, while other rare sites include vertebrae, pleura, the skull, parotid glands, diaphragm, and liver [13].

Although our patient presented with an extremely aggressive and rapidly-growing recurrent ameloblastoma 2 years after initial resection, ameloblastoma are often described as slow-growing with a high likelihood for local recurrence. Following initial therapy, 50% to 72% of patients experienced local recurrence of the ameloblastoma [3]. Due to these high recurrence rates, post-operative follow-up is mandatory for managing ameloblastoma. Although the recommended therapy for localized cases is surgical resection, the anatomical complexity of the mandibular region often causes difficulty for attaining recommended surgical excision margins. In the case of incomplete resection, adjuvant radiotherapy can be considered [14].

However, treatment regimens for metastatic ameloblastoma have not been well established. While removable metastases should be surgically resected with wide margins, as attempted in our case, radiotherapy and chemotherapy results have been unpredictable. Some therapies that have shown activity include cisplatin combination with cyclophosphamide, vinblastine, bleomycin, paclitaxel, and carboplatin [15-20]. There are far too few cases of metastatic ameloblastoma to consider randomized trials analyzing treatment methodology. Despite this, the median survival from the time of diagnosis is 17.6 years, and increased age at diagnosis is associated with poor survival [21]. Our patient returned to Haiti following each surgical resection and after the liver cyst drainage, so, unfortunately, adjuvant therapy was not utilized. Additionally, in Haiti, she lacked appropriate local medical care. Thus, routine follow-up

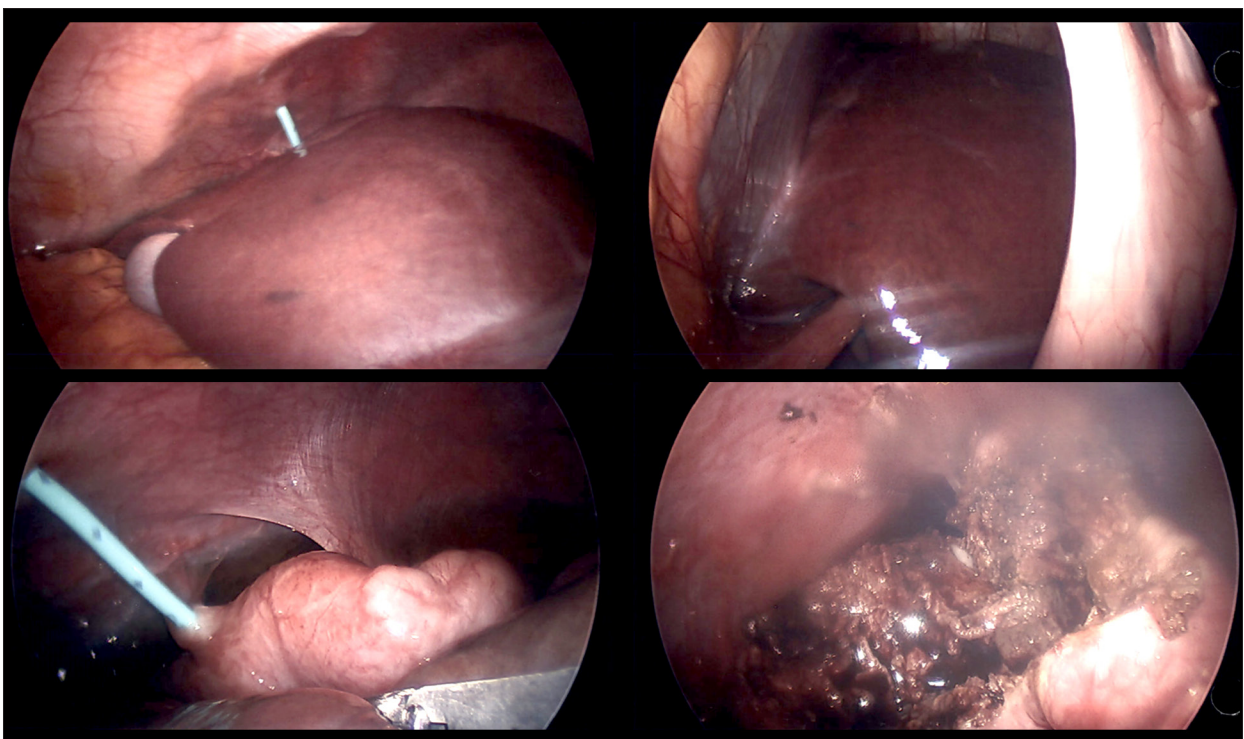


Figure 2. Intra-abdominal laparoscopic view of lateral right lobe of liver metastatic ameloblastoma and cystic drainage.

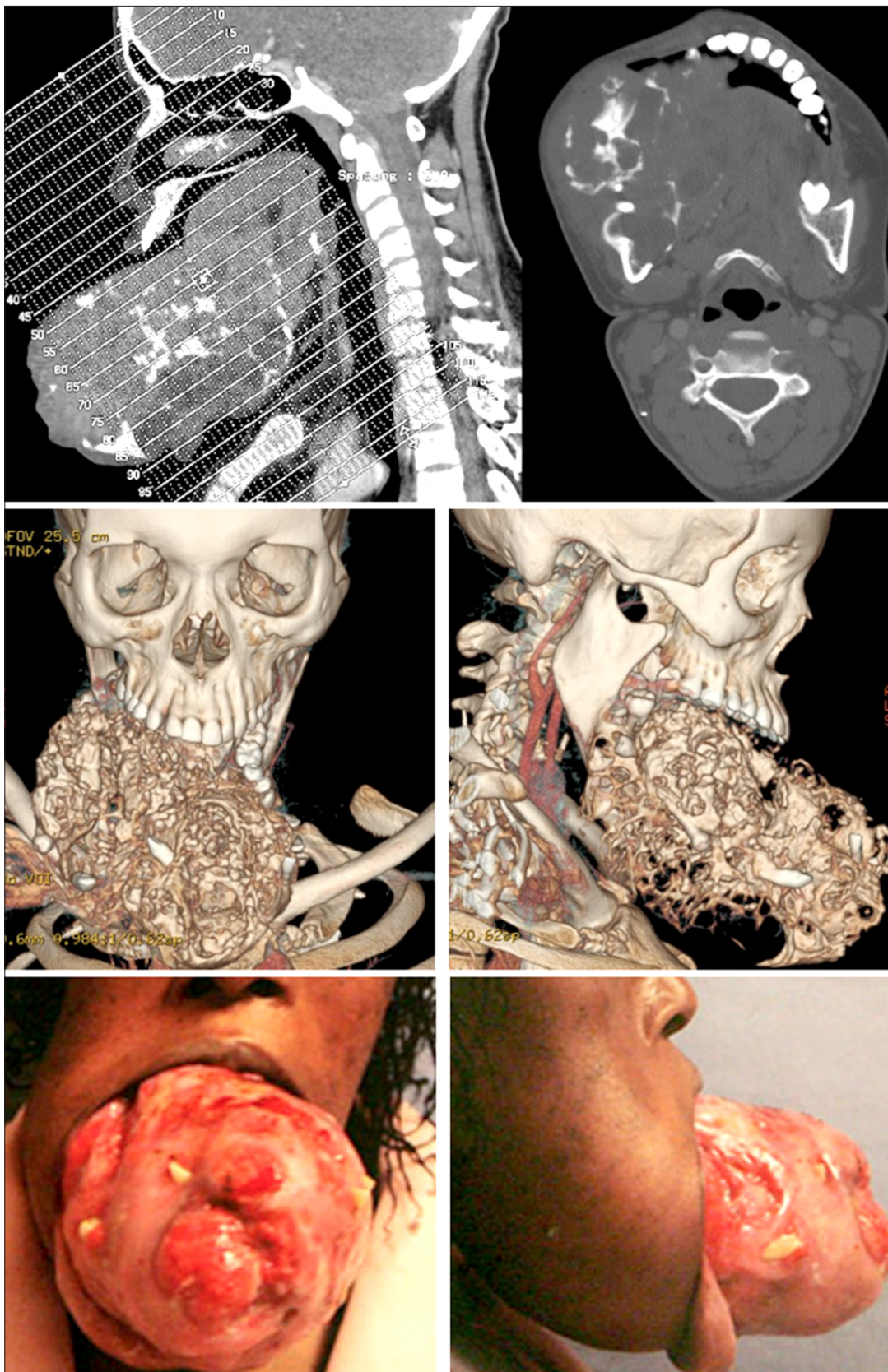


Figure 3. Computed tomography imaging of primary ameloblastoma with measurement and 3-dimensional reconstruction.

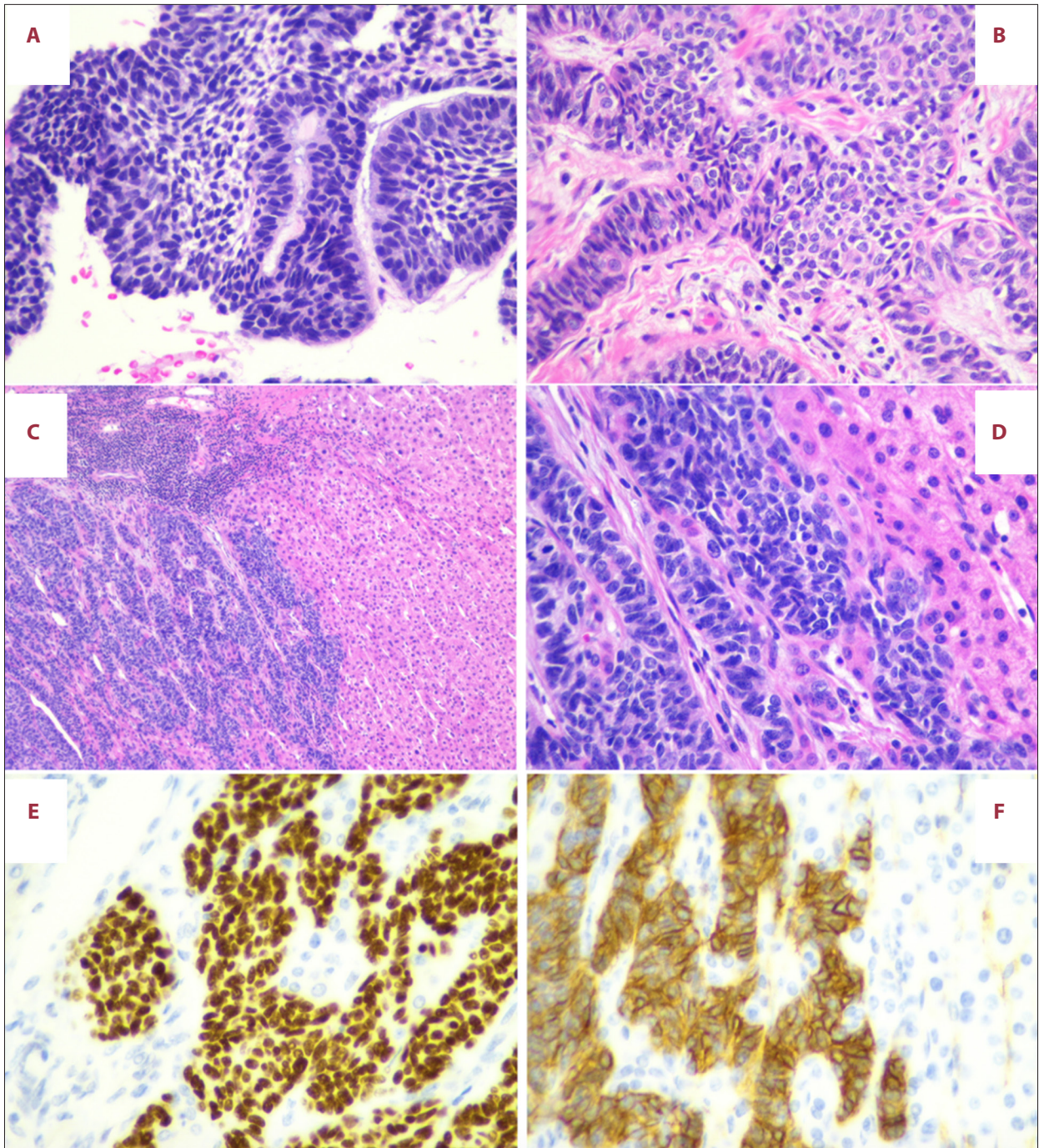


Figure 4. Histology images of ameloblastoma. (A) Floor of mouth mass (400×). (B) Mandible mass (400×). (C) Hepatic ameloblastoma metastasis (100×). (D) Hepatic ameloblastoma metastasis (400×). (E) Hepatic mass positive CK 5/6 staining (400×). (F) Hepatic mass positive P63 staining (400×).

was difficult, leading to the severe progression of the initial primary ameloblastoma and recurrence.

Our case followed an atypical malignant ameloblastoma pattern; the initial primary mandibular carcinoma was radically removed, but a highly vascular, extremely aggressive, and

rapidly-growing lesion recurred in the floor of her mouth within 2 years. The ameloblastoma cytology demonstrating positive staining for CK 5/6, P63, and CD56 was consistent with typical ameloblastoma features [22,23], confirming the diagnosis of hepatic metastatic malignant ameloblastoma.

Conclusions

This report describes a rare example of hepatic metastasis of malignant ameloblastoma 4 years after primary mass in the mandible, and 2 years following a recurrent mass in the floor of the mouth. Histopathological and cytologic features of this case were similar to previously reported features, showing odontogenic epithelial islands lacking major histological atypia. The patient underwent 2 radical surgical resections for the mandibular and mouth ameloblastomas, and a laparoscopic liver drainage of the complex malignant ameloblastoma cyst. While very rare diseases may not be included in our original differential diagnoses, this case demonstrates the importance of obtaining a detailed medical history to determine the etiology. Once treated, establishing frequent follow-up to manage

disease progression can limit the extreme development seen with this patient. Unfortunately, due to the patient residing in Haiti, follow-up care was difficult, and she died within 2 years after discovery of her hepatic metastasis.

The authors report no sources of external funding and have no conflicts of interest to disclose. We declare that written informed consent was obtained and the patient permitted us to publish the case details and any related images, the safety of our procedure, and the probable complications.

Conflicts of Interest

None.

References:

1. Gardner DG, Pecak AM. The treatment of ameloblastoma based on pathologic and anatomic principles. *Cancer*. 1980;46:2514-19
2. Jordan RCK, Speight PM. Current concepts of odontogenic tumours. *Diagn Histopathol*. 2009;15(6):303-10
3. Effiom OA, Ogundana OM, Akinshipo AO, Akintoye SO. Ameloblastoma: Current etiopathological concepts and management. *Oral Dis*. 2018;24(3):307-16
4. Henderson JM, Sonnet JR, Schlesinger C, Ord RA: Pulmonary metastasis of ameloblastoma: Case report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999;88(2):170-76
5. Jing W, Xuan M, Lin Y, et al. Odontogenic tumours: A retrospective study of 1642 cases in a Chinese population. *Int J Oral Maxillofac Surg*. 2007;36:20-25
6. Mosqueda A, Meneses A, Ruiz LM, et al. Malignant odontogenic tumors. A retrospective and collaborative study of seven cases. *Med Oral*. 2003;8:110-21
7. Magliocca K, Martinez A. Metastasizing ameloblastoma. PathologyOutlines.com website. <https://www.pathologyoutlines.com/topic/mandiblemaxilla-malignantameloblastoma.html> [Accessed February 13th, 2021]
8. Laughlin EH. Metastasizing ameloblastoma. *Cancer*. 1989;64:776-80
9. Van Dam SD, Unni KK, Keller EE. Metastasizing (malignant) ameloblastoma: Review of a unique histopathologic entity and report of Mayo Clinic experience. *J Oral Maxillofac Surg*. 2010;68:2962-74
10. Gilijamse M, Leemans CR, Winters HA, et al. Metastasizing ameloblastoma. *Int J Oral Maxillofac Surg*. 2007;36(5):462-64
11. Hall JM, Weathers DR, Unni KK. Ameloblastic carcinoma; An analysis of 14 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103:799-807
12. Ricard AS, Majoufre-Lefebvre C, Siberchicot F, Laurentjoye M. A multirecurrent ameloblastoma metastatic to the lung. *Rev Stomatol Chir Maxillofac*. 2010;111:98-100
13. Zhang G, Zhao L, Wang X, et al. Pulmonary resection for multiple lung metastasis from ameloblastoma: A rare case report and literature review. *Postgrad Med*. 2021;133(1):117-22
14. Amzerin M, Fadoukhair Z, Belbaraka R, et al. Metastatic ameloblastoma responding to combination chemotherapy: Case report and review of the literature. *J Med Case Rep*. 2011;4:491
15. Grünwald V, Le Blanc S, Karstens JH, et al: Metastatic malignant ameloblastoma responding to chemotherapy with paclitaxel and carboplatin. *Ann Oncol*. 2001;12(10):1489-91
16. Houston G, Davenport W, Keaton W, Harris S. Malignant ameloblastoma: Report of a case. *J Oral Maxillofac Surg*. 1993;51:1152-55, discussion 1156-57
17. Gall JA, Sartiano GP, Shreiner DP. Ameloblastoma of the mandible with pulmonary metastasis. *Oncology*. 1975;32(3-4):118-26
18. Ramadas K, Jose CC, Subhashini J, et al. Pulmonary metastases from ameloblastoma of the mandible treated with cisplatin, adriamycin and cyclophosphamid. *Cancer*. 1989;66:1475-79
19. Eliasson AH, Moser RJ, Tenholder MF. Diagnosis and treatment of metastatic ameloblastoma. *South Med J*. 1989;82(9):1165-68
20. Hendra FN, Natsir Kalla DS, Van Cann EM, et al. Radical vs conservative treatment of intraosseous ameloblastoma: Systematic review and meta-analysis. *Oral Dis*. 2019;25(7):1683-96
21. Rizzitelli, A. Incidence and overall survival of malignant ameloblastoma. *PLoS One*. 2015;10(2):e0117789
22. Hunter KD, Speight PM. The diagnostic usefulness of immunohistochemistry for odontogenic lesions. *Head Neck Pathol*. 2014;8(4):392-99
23. Martínez-Martínez M, Mosqueda-Taylor A, Carlos-Bregni R, et al. Comparative histological and immunohistochemical study of ameloblastomas and ameloblastic carcinomas. *Med Oral Patol Oral Cir Bucal*. 2017;22(3):e324-32