Case Report

Maxillary Ameloblastoma with Lung Metastasis: Case Report of a Rare Tumor

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Abstract

Ameloblastomas are low-grade neoplasms of odontogenic epithelium that account for about 1% of all oral tumors and about 10% of odontogenic tumors. Rarely, these tumors have a potential of distance metastasis, and once they do metastasize, they are termed as *metastatic ameloblastoma.* This article aims at describing a case of a rare form of maxillary ameloblastoma that metastasized to the lung and challenges in its management in settings with limited resources. A 24-year-old African male presented with a massive swelling on the right side of the face for 2 years in 2018. He was previously operated on for a swelling on the right side of the maxilla in 2012, which was histologically diagnosed as ameloblastoma. Clinical and radiological evaluation revealed a massive maxillary tumor that had a local extension to the brain. X-ray and computed tomography (CT) scan of chest pointed out to metastatic mass in the lungs. Histology of the recurrent tumor mass revealed it to be follicular ameloblastoma, and CT-guided fine-needle aspiration cytology of the lung mass showed microscopic features of ameloblastoma similar to the primary jaw tumor.

Keywords: *Lungs, maxilla, metastatic ameloblastoma*

Introduction

Ameloblastomas are low-grade neoplasms of odontogenic epithelium that account for about 1% of all oral tumors and about 10% of odontogenic tumors.[1] They commonly occur in the mandible and involvement of the maxilla is about 20%.[2,3] Although they are considered to be benign tumors with a slow growth rate, they are locally aggressive with a high tendency for local recurrence if not removed completely.[1,4] Rarely, these tumors have the potential of distance metastasis,[3] whereby this phenomenon is associated with a prolonged tumor duration and multiple recurrences following surgical interventions.[2] When histologically benign-appearing ameloblastoma does metastasize, it is referred to as *metastatic ameloblastoma.*[5] According to the 2005 World Health Organization (WHO) classification, metastatic ameloblastoma was classified as a malignant odontogenic tumor, however, in the 2017 WHO classification, it was moved to benign ameloblastoma subtypes.[6]

The management of metastatic ameloblastoma is challenging partially due to its rarity.[7] The treatment options include close observation, surgical resection, and chemotherapy/radiotherapy.[8] Generally, if the metastatic lesions are resectable, then surgery is the treatment of choice, but for inoperable cases, radiotherapy and/or chemotherapy may be used despite unpredictable and poor results.[7,9,10]

Herein, we describe a very rare case of maxillary ameloblastoma that had metastasized to the lungs. We describe the challenges in the diagnosis and management of such cases in a developing country setting.

Case Report

A 24-year-old African male presented to our institute in December 2018 with a complaint of a swelling on the right side of the face for about 2 years. The patient reported that the swelling had started spontaneously as a painless nodule around the region of right cheek in 2016, and it gradually but consistently increased in size, resulting in obvious facial deformity. In about a year, the swelling was involving the entire right side of the face and started to become painful. The pain was localized and dull in nature. By mid-2018, the swelling extended to involve the right eye causing

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it to be pushed up and outward, but there was no loss of vision. This was followed by an outward extension of the swelling around the region of the right cheek, which later ulcerated and started to bleed. The patient also reported that, in 2012, he was admitted to our hospital due to a swelling in the right side of the upper jaw which was surgically treated.

Clinical examination of the patient revealed a young man, who was sick looking, slightly wasted, and pale. He was well oriented to his surroundings. On local examination, the patient presented with facial asymmetry due to a massive irregular exophytic mass on the right side of the face that measured approximately 23 by 14 cm. The overlying skin was hyperemic and shiny, with an area of ulceration. There were visible surgical marks of previous surgery as well. The right eye was displaced superiorly and outward; however, the vision was not lost. The nose was displaced toward the left side, with occlusion of the right nostril. The overstretched overlying skin had a normal temperature and could not be folded. The swelling was mildly tender, firm and fixed to the underlying structures. There was an ovalish outgrowth/extension of the swelling at its lower border, which was ulcerated and was profusely bleeding [Figure 1a and b].

Intraorally, the lesion was occupying the entire right side of the upper jaw extending just a few millimeters beyond the midline to the left side of the palate. The lesion was oval in shape, with an otherwise hyperemic overlying mucosa. Based on these clinical findings, a provisional diagnosis of ameloblastic fibrosarcoma was made.

The workup done on the patient included hematological investigations, radiological investigations, and histopathological analysis of the tissue. The complete blood count result was normal, except that he had low levels of hemoglobin (7.1 g/dl). The liver function test and renal function tests were within normal ranges. Initial radiological investigations included a computed tomography scan (CT scan) of the head-and-neck region and chest X-ray. The CT scan images revealed a massive heterogeneous lesion that eroded the cortical plate with an extension to the anterior cranial fossa [Figure 2a and b]. The chest X-ray showed features of lung metastasis [Figure 3a]. A wedge biopsy from the lesion revealed it to be follicular ameloblastoma [Figure 4a and b]. The biopsy results of the previously operated lesion were traced, and they were also indicative of follicular ameloblastoma. Due to its clinical aggressive nature, a panel of oral and maxillofacial surgeons requested another tissue biopsy to be taken which and was reviewed by a panel of different pathologists and similar results were obtained. Immunohistochemistry for Ki67 revealed an aggressive tumor with 60%–80% reactivity in neoplastic cells [Figure 5]. A chest CT scan [Figure 3b] was taken, and a CT-guided fine-needle

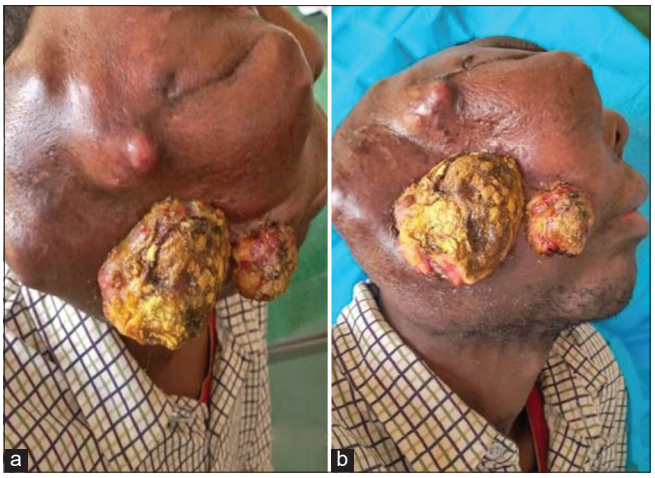

Figure 1: (a and b) Clinical presentation of the patient showing a massive irregular exophytic mass on the right side of the face. There is an ulcerated ovalish outgrowth/extension of the swelling at its lower border and the right eye is displaced superiorly and outwards

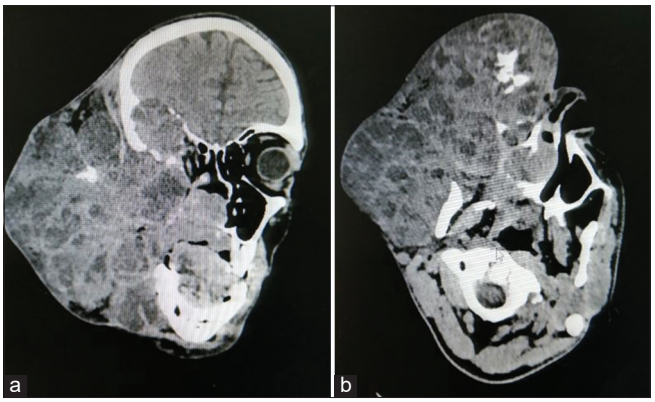

Figure 2: Computed tomography scan appearance of the maxillary lesion. (a) A coronal computed tomography scan demonstrates a heterogeneous soft-tissue mass, originating from the maxilla, involving the right maxillary sinus and the orbital roof, and extending into the cranial fossa. (b) Axial computed tomography scan showing a huge heterogeneous soft-tissue mass eroding the walls of the maxillary sinus and displacing the nasal septum to the left

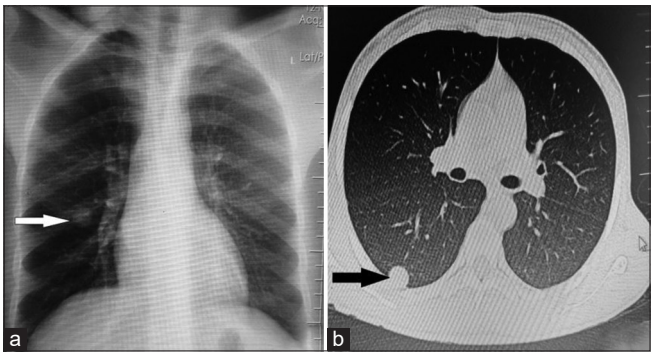

Figure 3: Chest X-ray and computed tomography scan of the metastatic lesions. (a) X-ray showing a solitary nodular opacity in the middle zone of the right lung (white arrow). (b) Computed tomography showing soft-tissue mass in the posterior aspect of the right lung presenting as a nodule (black arrow)

aspiration cytology of the lung mass was performed. The results of the aspirates were indicative of ameloblastoma as well [Figure 6]. The final diagnosis was thus metastatic ameloblastoma.

Due to unresectability of the primary lesion, the patient was presented in the tumor board and planned for palliative chemoradiotherapy in February 2019. The patient was referred to us in April 2019, following episodes of profuse bleeding per oral cavity after receiving three cycles of chemotherapy and radiotherapy. Hematological investigation revealed pancytopenia. He received 4 units of whole blood and was returned to the cancer institute for further management. The patient was seen again in early 2020, and the ovalish outgrowth/extension of the swelling at its lower border had significantly regressed.

Discussion

Metastatic ameloblastoma refers to a lesion that metastasizes to a distant organ, but the histology of both primary and metastatic tissues is benign.[11] It is an infrequent entity, accounting for approximately 2% of ameloblastoma cases.[12] The commonly reported site for metastasis includes the lungs, cervical lymph nodes, diaphragm, liver, brain, and bone.[5] The lung is the most common site for metastasis, and in approximately 80% of the cases, the primary site is the mandible.[4] The case which has been presented here is considered rare not only because of being metastatic ameloblastoma but also because the maxilla was the primary site.

The mechanism by which a histologically benign-looking lesion spreads to a distant organ is unclear.[13] Proposed mechanisms of metastatic spread include hematogenous and lymphatic routes and aspiration of tumor cells from the primary oral lesion.[4,13,14] Another possible mode of metastasis is tumor implantation during surgical procedures.[8] In the current case reported, direct implantation of tumor cells in the lung and aspiration from the endotracheal tube during previous surgery (hemimaxillectomy) cannot be ruled out.

Metastatic ameloblastoma may occur at any age, ranging between 5 and 94 years.[13,15] However, the third decade of life seems to be the most affected age group.[8,10,12,16,17] The number of years between the diagnosis of the primary tumor and metastases varies between 0 and 15 years.[15] In the case presented here, the patient presented with a primary tumor at the age of 17 years, and at the age of 24 years, he developed metastasis. This falls within the same range of time, as documented in the literature.

Unlike in the case reported by Rabo *et al*.,[8] where the patient had intermittent, nonradiating, sharp, and piercing upper back pains, our patient did not have any signs or symptoms that could raise suspicious of lung metastasis. This coupled with the clinical-radiological behavior of the tumor led us to an initial working diagnosis was ameloblastic fibrosarcoma. Ameloblastic fibrosarcoma commonly presents with facial swelling, which is often accompanied by pain, paresthesia, dysesthesia, and ulcer.[18,19] Radiologically, it appears as a uni- or multilocular radiolucent mass with an ill-defined border. It tends to

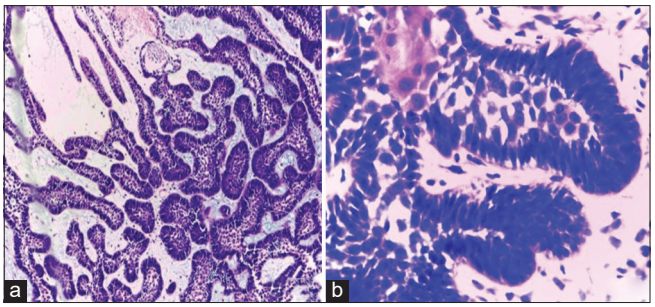

Figure 4: Histopathological images (H and E) of the maxillary lesion: (a) Islands of odontogenic epithelium with peripheral palisading and stellate reticulum at the center (×10). (b) Foci of abnormal mitoses in both the peripheral palisading cells and the central stellate reticulum (×40)

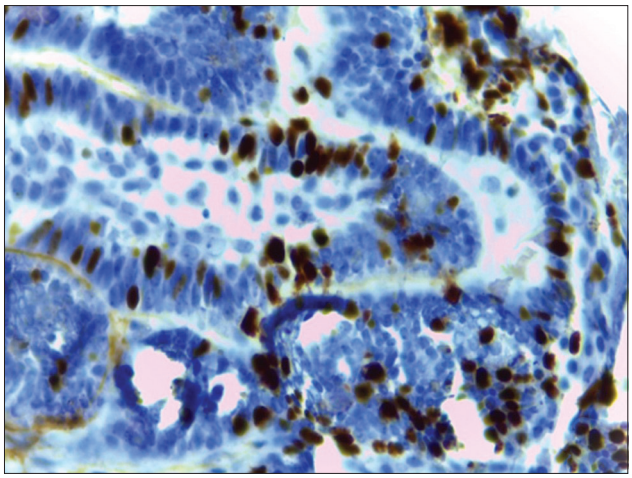

Figure 5: Immunohistochemistry staining of the maxillary lesion: Ki67-positive staining with the labeling index reaching 60%–80% reactivity in neoplastic cells

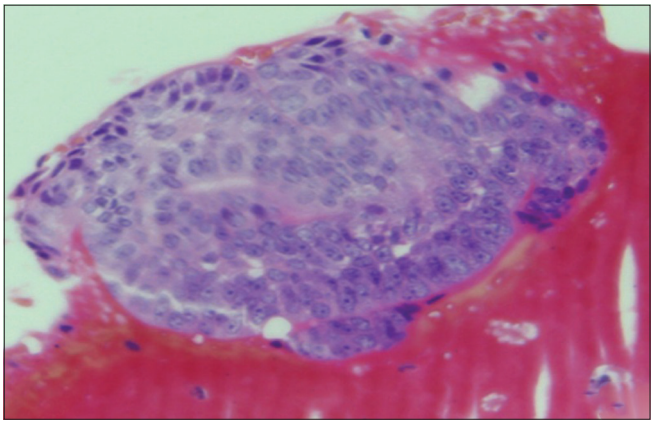

Figure 6: Histocytological images (H and E) of the lung mass showing cellular smear with clusters of odontogenic epithelium characterized by peripheral palisading and loose pale nuclei at the center

cause gross expansion and/or erosion of the cortical bone with a tendency to invade adjacent soft tissues, the base of the cranium and intracranial and orbital tissues.[18,19]

Based on the clinical-radiological behavior of the tumor that did not match with the histological diagnosis of ameloblastoma, further workup including a chest X-ray and CT scan were carried out. These investigations led to the identification of a lesion on the chest raising suspicion of metastasis that was later confirmed by cytology. The diagnosis of metastatic ameloblastoma is almost always made retrospectively after metastasis has occurred and not otherwise.[14] It is difficult to predict which cases would metastasize and which would not, and this is among the challenges in managing these lesions.

Histopathologically, it is difficult to differentiate between metastatic ameloblastoma and nonmetastatic ameloblastoma; however, there are specific markers that show strong positivity in metastatic ameloblastoma.[4,20,21] Immunohistochemical markers that are strongly positive in ameloblastoma but not in metastatic ameloblastoma include extracellular signal-regulated kinase 5 and KRSA, whereas N-terminus-truncated p73 isoform (Δ*Np73*) was reported to be found in 100% of metastatic ameloblastomas.[21] In the current reported cases, however, these investigations could not be carried out due to reasons such as the unavailability of reagents for carrying such investigations and the cost of acquiring these reagents. Immunohistochemistry for Ki67 was done; however, it does not specifically point out to metastatic ameloblastoma but rather indicates local invasiveness and recurrences of ameloblastoma, thereby its prognosis.[22,23]

There is no therapeutic gold standard for treating metastasizing ameloblastoma due to the small number of cases reported.[20] Radical surgery remains the mainstay of therapy, while the role of chemo- and radiotherapy still is yet to be defined.[10,20] In some cases, surgery has been successfully combined with additive and adjuvant radiotherapy.[10] Radiotherapy has been recommended for inoperable metastatic deposits, but because the response is unpredictable, it is used only for palliative care.[8] In the case reported herein, surgery could not be done as the tumor had already extended to the cranium, thus palliative chemoradiotherapy was chosen, which showed some significant benefit, as the size of the tumor did decrease. Since surgery was not done, the prognosis was expected to be poor, as it has been reported that with adequate resection and radiotherapy, the median survival is 6 years compared to 2 years when resection is not done.[17]

There may be a role for routine annual chest X-rays when assessing patients with ameloblastomas;[24] however, in our case, this could not be done as the patient did not turn up for follow-up clinics after the first surgery, and only came back with a huge tumor 6 years later. Delay in seeking health care and failure to attend the follow-up clinics is attributed mainly to financial difficulties that most of the patients in developing countries face.[25]

Conclusion

This case reports a rare case of maxillary ameloblastoma that metastasized to the lungs. Metastatic ameloblastoma is a rare tumor characterized by an indolent clinical course. It is difficult to predict metastasis, even with adequate surgery of the primary lesion. Close and long-term follow-up is mandatory in patients diagnosed with ameloblastoma even years after primary resection since there is no clear protocol to prevent or detect metastatic ameloblastoma.

Consent

Informed consent was obtained from the patient for the publication of the case report and accompanying images.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. The patient understands that name and initials will not be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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