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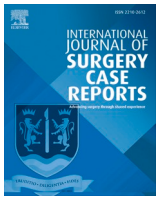

Case report

Metastasizing ameloblastoma of the breast: A case report

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ABSTRACT

Introduction: Ameloblastomas are slow growing and locally aggressive odontogenic tumors with a high propensity for recurrence. It frequently arises in the mandible and has been reported to metastasize commonly in the lungs. An updated World Health Organization classification re-categorized metastasizing ameloblastomas under benign tumors. Other rare metastatic sites include the skull, maxilla, kidney, and liver.

Case presentation: We present a 53-year-old female with a gradually enlarging right breast mass for 2 years. She previously underwent right hemimandibulectomy with clavicular bone grafting 15 years ago for a primary ameloblastoma. Preoperative imaging showed a resectable, heterogenous right breast mass with a biopsy revealing spindle cell neoplasm. She subsequently underwent radical mastectomy with a latissimus dorsi myocutaneous flap as a reconstructive procedure. Histopathologic findings were consistent with a metastasizing ameloblastoma. The patient remains disease-free as of most recent follow-up.

Discussion: There are several proposed mechanisms for metastasizing ameloblastomas. Based on the history and location of the tumor, we surmised that tumor seeding from the first surgery done 15 years ago may explain this rare occurrence. Preoperative imaging and biopsy determine resectability and surgical approach. Radical surgery is frequently performed which largely depends on the site of the tumor. Complete primary resection with adequate margins remains to be the treatment of choice to prevent recurrence or metastasis. The role of adjuvant radiotherapy or chemotherapy are still to be established.

Conclusion: This case highlights the value of history-taking and having a high-index of suspicion for metastasis several years after primary resection of ameloblastomas.

1. Introduction

Ameloblastomas are infrequent, painless, and insidious odontogenic tumors that are commonly located in the jaw or maxilla. They arise in the dental lamina and present as large, bulky, often disfiguring tumors with a high propensity for local recurrence if not removed completely. In 2017, the World Health Organization (WHO) updated its classification into four subtypes: conventional ameloblastoma, unicystic ameloblastoma, peripheral or extraosseous ameloblastoma, and metastasizing ameloblastoma [1]. Although benign, they often cause functional impairment and cosmetic issues. Metastasizing ameloblastoma is a variant of benign ameloblastomas with similar histologic characteristics and can present decades later in life. It is extremely rare and current experience is only limited to case reports with variable treatment options and outcomes. Majority (80 %) of reported metastasis involve the lungs followed by the cervical lymph nodes (15–20 %) [2]. Other sites, however less common, are skull, maxilla, heart, vertebrae, kidney, and liver. Herein we describe the first reported case of a metastasizing ameloblastoma of the breast presenting 15 years after primary resection. This case presents an opportunity to emphasize the diagnostic dilemma, importance of history-taking and discuss the approach and options in management of such a rare case. This report has been written in line with the recent SCARE criteria for case reports [3].

2. Case

A 53-year-old female (G5P4) presented with a two-year history of gradually enlarging right breast mass. She has no known comorbidities

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as well as familial cancer however, she previously underwent right hemimandibulectomy with bone grafting for ameloblastoma in 2004. Physical examination showed a 16 × 13 cm breast mass extending to the upper chest wall and right neck with no palpable lymphadenopathy (Fig. 1). Computed tomography (CT) scan revealed a heterogenous solid and cystic mass arising from the superior region of the right breast measuring 15 × 15 × 10 cm with involvement of the pectoralis major muscle. There were no other lesions nor lymphadenopathy noted (Fig. 2). A punch biopsy was done which yielded spindle cell neoplasm for which an en bloc radical mastectomy was performed (Fig. 3). Intraoperatively, the mass was adherent to the sternocleidomastoid muscle, innominate and jugular veins with note of axillary lymphadenopathies (Levels I–III). A latissimus dorsi myocutaneous flap was then performed to cover the resulting anterior chest wall defect (Fig. 4). Postoperatively, the patient developed surgical site infection and partial flap necrosis for which debridement and daily wound care were performed together with culture-guided intravenous antibiotics. She was eventually discharged after 2 weeks and presently with no recurrence at 2 years of follow-up. Final histopathology was consistent with ameloblastoma (Fig. 5).

3. Discussion

Ameloblastomas are locally aggressive tumors of odontogenic origin and frequently recurs in 50–70 % of cases. Regional and distant metastasis are rare however, occurring in about 2 % of reported cases [4]. The recent WHO update re-classified metastasizing ameloblastomas as a benign epithelial head and neck tumor as they always show benign histological features even at the site of metastasis, in contradistinction to ameloblastic carcinoma which manifests malignant features such as pleomorphism, nuclear hyperchromatism, increased mitotic activity and perineural or vascular invasion. There are no specific histologic features which differentiate a metastasizing ameloblastoma from a benign ameloblastoma, and that the paucity of malignant cytologic transformation of this tumor explains its indolent metastatic site growth [5]. There is a slight predilection for males and in the Asian or African population. In a recent review by Zambrano, in the last decade there were only 18 reported cases of metastasizing ameloblastomas worldwide which were primarily mandibular tumors [6]. To our knowledge, this is the first reported case of a metastasizing ameloblastoma to the breast.

Proposed mechanisms by which ameloblastomas metastasize are the following: (1) implantation of tumor cells (tumor seeding) during surgery, (2) heterotropy, in which ectopic odontogenic epithelial cells would undergo benign neoplastic transformation, (3) lymphatic spread, (4) hematogenous and (5) theory of lung aspiration, wherein tumor cells are aspirated during surgery [7]. Based on the patient's history and location of the metastatic tumor, we assumed that this may be due to tumor seeding from the primary surgery done 15 years ago. The initial operation performed was a mandibulectomy with reconstruction using a clavicular bone graft. Clinically, the metastatic tumor was located superior to the right breast, which corresponds to the location of the donor site.

The diagnosis in this case requires a biopsy as well as a CT scan to assess for surgical resectability. Imaging revealed a heterogenous mass that had clear planes of dissection allowing us to proceed with the resection and planned reconstruction. With the initial biopsy result of a spindle cell tumor, our differential diagnosis included phyllodes tumor or breast sarcoma. Molecular markers and gene mutations are also currently being studied to aid in establishing the diagnosis of ameloblastomas as well as understand its pathophysiology. Increased Ki-67 staining and CD10 reactivity have been reported to be associated with recurrence while mutations within the mitogen-activated kinase protein kinase (MAPK) pathway, particularly the BRAF V600E mutation are found in as high as 96 % mandibular ameloblastomas [8,9]. Consequently, these advances have allowed molecular targeted therapies to be introduced such as vemurafenib and dabrafenib with recent reports of benefit for multiple recurrent ameloblastomas [10].

Surgery for primary ameloblastomas usually involves wide resection with a 1 to 1.5 cm margin followed by an immediate or delayed bone reconstruction. Meticulous tissue handling is paramount to prevent tumor seeding and possible metastasis. In a retrospective study by Bi et al., risk factors identified that were associated with recurrence were primary treatment modality performed (e.g., radical resection, enucleation), presence of impacted tooth and presence of root resorption [11]. Further studies are still needed though as they had limited study population. Extent of initial disease, multiple surgeries and history of radiation therapy have also been associated with the tendency to develop metastases [12]. Currently, complete resection with adequate margins remains to be the primary method of reducing recurrence.

Due to the rarity of such cases, treatment is highly dependent on the site of metastasis and would frequently entail an en bloc resection if deemed resectable. Collaboration with other specialties (e.g., plastic surgery, vascular surgery) is often warranted. Radical surgery often leads to functional impairment, aesthetic deformities, or even psychological stress. These were clearly an issue for the patient as she had a prolonged postoperative course because of a surgical complication. The role and benefit of chemotherapy and/or radiotherapy as adjuvant treatment are still limited and not clearly defined as results have been varied. Suffice is to say that the best method to treat a metastasizing

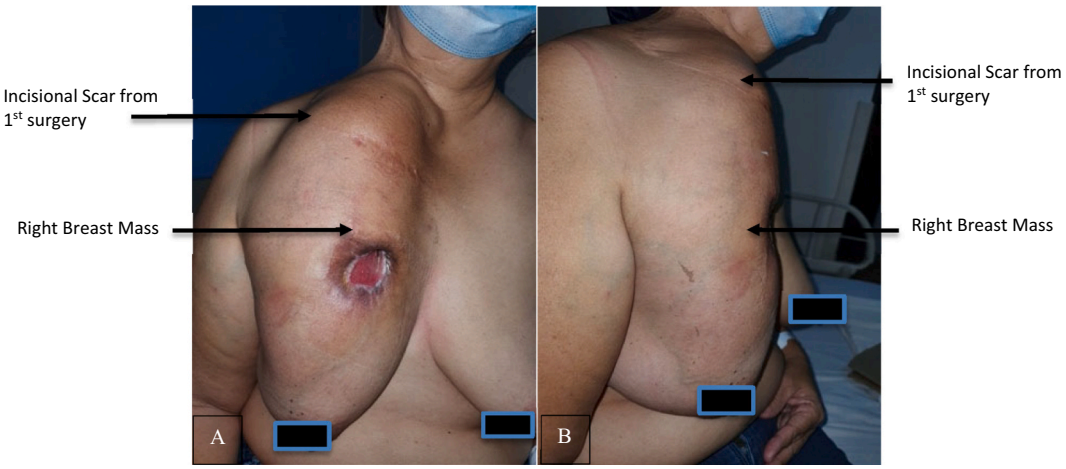

Fig. 1. Preoperative photograph showing the right breast mass extending to the anterior chest wall with an ulcerated area which was the site of the previous punch biopsy. Anterior view (A). Lateral view (B).

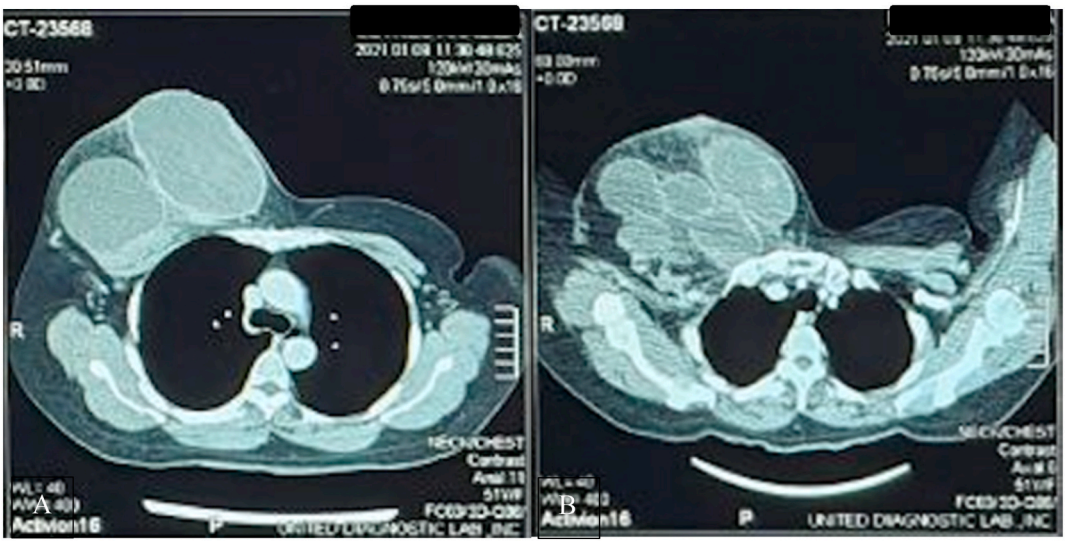

Fig. 2. CT scan showing multi-cystic mass arising from the superior region of the right breast involving the adjacent cutaneous region (A) and pectoralis muscles with no evidence of lymphadenopathy (B).

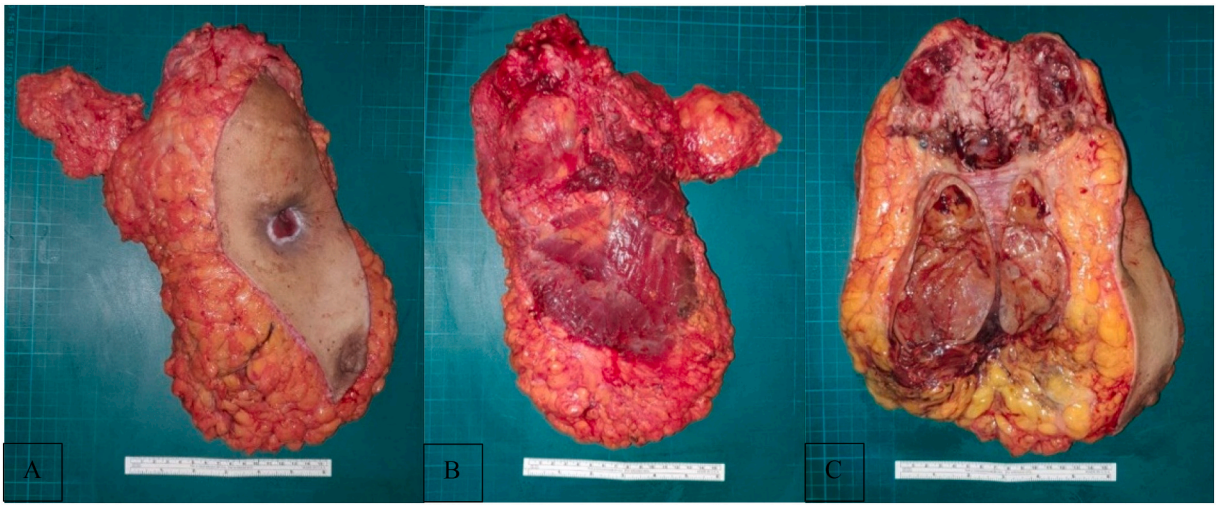

Fig. 3. En bloc radical mastectomy specimen. Anterior (A). Posterior (B). Cut section (C).

ameloblastoma, is to prevent its occurrence. Continued follow-up and surveillance are essential to detect further recurrences for these slow-growing and indolent tumors.

4. Conclusion

In conclusion, our case describes a patient who underwent radical surgery for a metastasizing ameloblastoma to the breast occurring several years after the initial surgery for primary ameloblastoma. A multidisciplinary approach for such cases is often employed to optimize patient outcomes. This case further highlights the significance and importance of careful history taking in every patient encounter.

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CRediT authorship contribution statement

Emmanuel T. Limpin, MD. MD: writing of paper, draft preparation.
Edna L. Lasap-Go, MD MD: data collection, draft preparation.
Ferri P. David-Paloyo, MD: draft preparation, supervision.
Eduardo C. Ayuste, Jr. MD: study concept, writing of paper.
Orlino C. Bisquera, Jr., MD: draft preparation, data collection.
Siegfredo Paloyo, MD, MPH: final editing, supervision, reviewing.
Research registration: N/A.

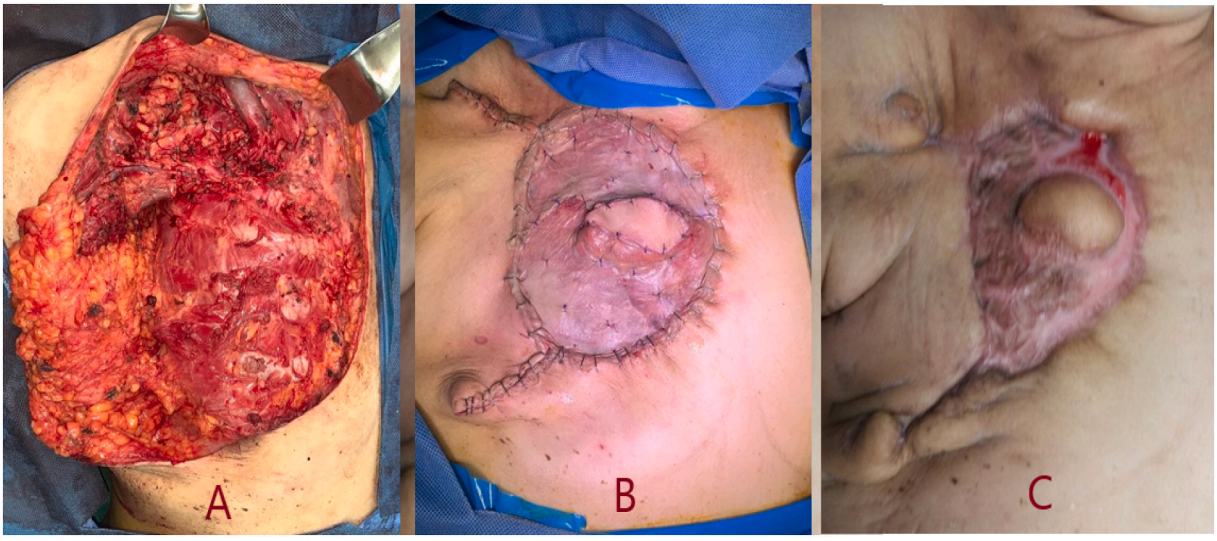

Fig. 4. Wound defect with exposed chest wall, subclavian and internal jugular veins (A). Closure using latissimus dorsi myocutaneous flap (B). Wound contracture 6 weeks after surgery (C).

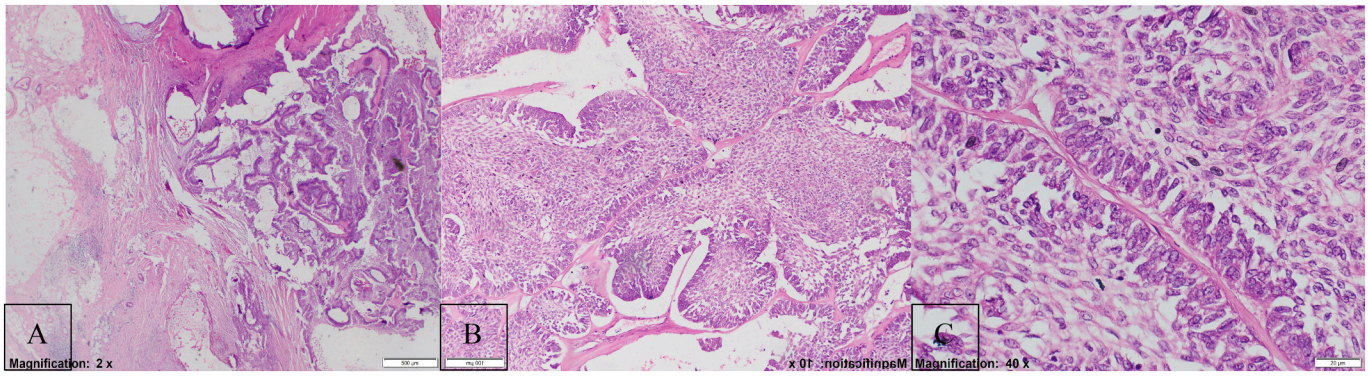

Fig. 5. Hematoxylin and Eosin (H & E) stain. Scanning view, the tumor is infiltrating the breast parenchyma (A). H & E stain, original magnification ×20 – Low-power microscopic view showing tumor is solid with papillary configuration. Stellate reticulum is prominent (B). H & E stain, original magnification ×200 – High-power microscopic view demonstrating columnar cells with hyperchromatic nuclei at basal layer, exhibiting peripheral palisading and reverse polarization characteristic of ameloblastoma (C).

Declaration of competing interest

None.

Acknowledgments

None.

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