



## Oral and maxillofacial metastasis of male breast cancer: Report of a rare case and literature review

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Oral and maxillofacial metastatic tumors are uncommon, with the breast, prostate, lung, and kidney representing the most common primary sites. Less than 1% of all breast cancers occur in male patients, and to date, only 8 cases of metastatic breast adenocarcinoma to the oral and maxillofacial region in a male patient have been reported in the literature. An 88-year-old male with previous history of a successfully treated primary breast adenocarcinoma 12 years earlier was referred for evaluation of an oral swelling lasting 6 months. Intraoral examination revealed a 2-cm reddish, pedunculated nodule with a smooth surface located in the left retromolar region. Imaging revealed maxillary sinus involvement. The patient underwent incisional biopsy, and microscopic evaluation revealed invasive tumor islands compounded by malignant epithelial cells, sometimes exhibiting ductal arrangement, which were positive for the estrogen receptor and gross cystic disease fluid protein 15. The final diagnosis was metastatic breast adenocarcinoma. Breast metastases are exceedingly rare in the oral and maxillofacial region of male patients; however, clinicians should consider breast metastasis when evaluating reddish oral nodules in older patients, including men, especially those with a history of malignancy. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;127:e18–e22)

Metastatic tumors in the oral and maxillofacial (OMF) region are uncommon. These represent approximately 1% of all oral tumors, with the jaws, particularly the mandible, being more frequently affected compared with soft tissues.<sup>1,2</sup> The clinical differential diagnoses include common inflammatory and reactive lesions, and microscopic analysis is usually required for diagnosis. This may be challenging, especially in patients with an unknown cancer history.<sup>1,2</sup> Patients with OMF metastases are usually treated with surgical resection, which is sometimes combined with radiation therapy and/or chemotherapy. This cancer has a poor prognosis, with an average survival period of 7 months.<sup>1–3</sup> Malignant tumors from almost any site can metastasize to the OMF region, the most common of which originate from the breast, genital organs, kidney, and colorectum in women and from the lung, kidney, liver, and prostate in men.<sup>3–13</sup>

Male breast cancer (MBC) is a rare disease accounting for less than 1% of all mammary malignancies.<sup>3</sup> Our understanding of the epidemiology, treatment, and prognosis of MBC is still limited, with distant metastases usually observed in bone and the lungs.<sup>4</sup> Breast metastasis to the OMF region in a male is an even rarer event, and to the best of our knowledge, only 8 cases

have been reported in the English language literature to date (Table I).<sup>4–11</sup> Here, we describe an additional case of metastatic MBC to the OMF region.

### CASE REPORT

An 88-year-old male, originally from the Republic of Cabo Verde, presented with a painless swelling of 6 months' duration in the left retromolar region. His past medical history included primary breast adenocarcinoma in the left breast 12 years earlier; the tumor had been successfully treated with surgery and axillary lymph node dissection. In addition, the patient had prostate carcinoma that had been surgically treated 6 years earlier. The patient reported hypertension and no history of tobacco or alcohol use, and his familial history was deemed noncontributory. Extraoral examination showed slight asymmetry of the left midface, with elevation of the nose wing. Intraorally, there was a well-circumscribed, pedunculated, reddish nodule measuring 2 × 1 cm, located between the left buccal mucosa and retromolar region and covered by smooth mucosa (Figure 1). The lesion was asymptomatic and fibroelastic in consistency, and there was no hardening of surrounding tissues. Imaging revealed a hypodense expansile lesion in the left maxillary sinus region, with cortical expansion of the orbital floor and destruction of the nasal fossa and maxillary sinus cortices (Figure 2). Scintigraphy also revealed an area of enhanced captation in the left maxillary sinus. Because of clinical suspicion of either sinonasal or oral squamous cell carcinoma or metastasis, an incisional biopsy under local anesthesia was performed. We observed well-defined fibrous tissue that exhibited an irregular cut surface with a whitish to brownish color (Figure 3). Microscopic examination revealed proliferation of

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Received for publication Apr 3, 2018; returned for revision May 4, 2018; accepted for publication May 21, 2018.

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2212-4403/\$-see front matter

<http://doi.org/10.1016/j.oooo.2018.05.006>

**Table I.** Clinical features of 8 cases of oral and maxillofacial metastatic breast adenocarcinoma in male patients reported in the English language literature and the present case

<i>N</i>	<i>Author (year)</i>	<i>Age</i>	<i>Site</i>	<i>Clinical features</i>	<i>Breast cancer history; immunomarkers</i>
1	Franklin & Kunkler (1992) <sup>4</sup>	52	Posterior mandible	Severe pain, Third molar was loose	Yes; absent
2	Choukas et al. (1993) <sup>5</sup>	43	Posterior mandibular	Ulcerated swelling	Yes; absent
3	Morris et al. (2001) <sup>6</sup>	61	Anterior submental triangle	Soft tissue mass and hyperesthesia	Yes; absent
4	Kesting et al. (2006) <sup>7</sup>	86	Submandibular region	Painless mass	Yes; negative: ER, PR, HER-2. Positive: mammoglobin, E-caderin
5	Fontana et al. (2007) <sup>8</sup>	69	Mandible	Multiple oral fistulae Osteolytic lesions	Yes; absent
6	Gonzalez-Perez et al. (2012) <sup>9</sup>	73	Posterior mandible	Painful swelling	No; absent
7	Sahoo et al. (2012) <sup>10</sup>	60	Masticator space	Pain and limitation of mouth opening	Yes; absent
8	Lee et al. (2014) <sup>11</sup>	85	Left buccal mucosa and cheek	Hard fixed mass	Yes; negative: ER,PR,CK20; positive: CK7, HER-2
9	Present case (2018)	88	Left maxillary sinus and retromolar region	Asymptomatic reddish nodule. Destructive sinonasal lesion	Yes; negative: CK7, CK20, PSA; positive: ER, GCDFP15

CK, cytokeratin; ER, estrogen receptor; GCDFP15, gross cystic disease fluid protein 15; HER-2, herceptin receptor-2; PR, progesterone receptor; PSA, prostate specific antigen.

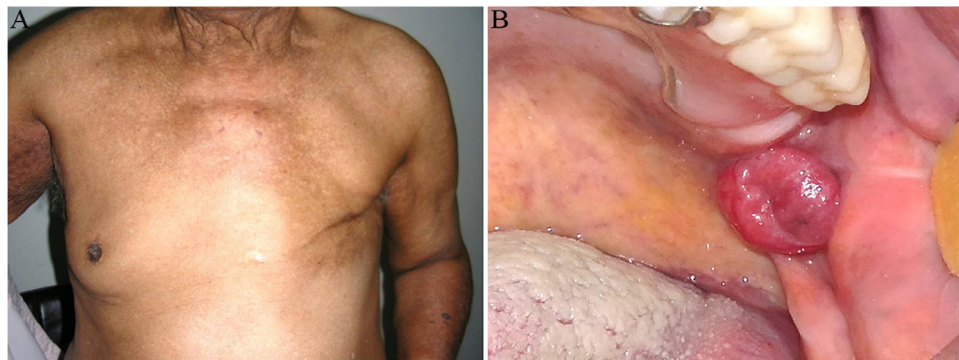


Fig. 1. Clinical features of oral and maxillofacial metastatic breast adenocarcinoma in a male patient. **A**, Scar from the mastectomy and axillary lymph node dissection associated with primary breast carcinoma treatment. **B**, Intraoral examination revealed a well-circumscribed, pedunculated, reddish nodule measuring 2 × 1 cm, located at the transition between the left buccal mucosa and retromolar region and covered by intact smooth mucosa.

infiltrative tumor cells characterized by an eosinophilic cytoplasm and hyperchromatic nucleus containing conspicuous nucleoli that were organized in islands and nests, sometimes exhibiting ductal arrangement and areas of comedonecrosis. Immunohistochemical staining revealed that tumor cells were positive for the estrogen receptor in a nuclear pattern and gross cystic disease fluid protein 15 (GCDFP-15) in the cytoplasmic granules but were negative for cytokeratin 7 (CK7), CK20, and prostate-specific antigen (PSA). The Ki-67 labeling index was 30% (Figure 4). The final diagnosis was metastasis of male breast adenocarcinoma to the OMF region. The patient was referred to the Oncology service, where he had previously been treated for the primary breast cancer. Treatment with hormone therapy, including Zoladex every 3 months and tamoxifen (20 mg/day), was started. At 2 years'

follow-up, the lesion had slightly decreased in size. The patient is clinically healthy, with no pain or any signs of fever, fatigue, weight loss, or prostration.

**DISCUSSION**

The incidence of MBC has increased significantly over the past 2 decades. Although the etiology remains unknown, the risk factors that may predispose an individual to breast cancer have been suggested to include diseases that alter the estrogen-to-testosterone ratio in males. Men with Klinefelter syndrome have 50-times higher risk and account for 3% of all patients with MBC.<sup>9,14</sup> Similarly, cirrhosis and exogenous administration of estrogen (either in transgender individuals or as therapy for prostate cancer) have been implicated as causative factors for MBC.<sup>3</sup> Other risk factors include mutations in the BRCA2 gene, exposure to radiation,

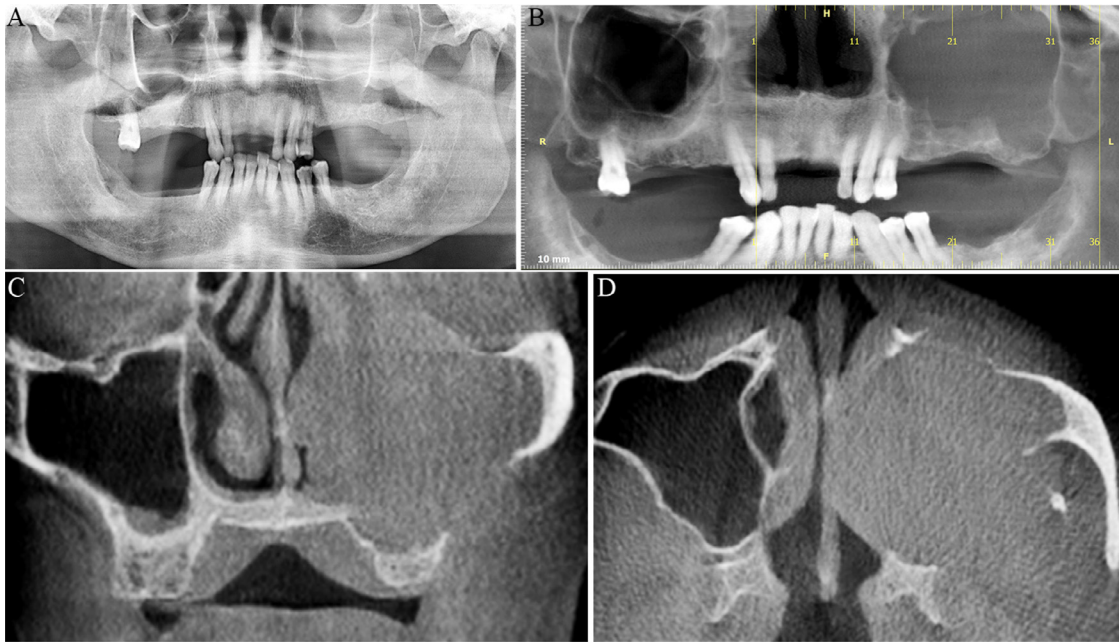


Fig. 2. Radiographic features of oral and maxillofacial metastatic breast adenocarcinoma in a male patient. **A,B**, Panoramic radiograph showing destruction of the left nasal maxillary sinus cortices. **C**, Cone beam computed tomography in the coronal plane revealed a hypodense lesion in the left maxillary sinus with medial–lateral and inferior–superior bone expansion, cortical expansion of the orbital floor and cortical destruction of the nasal fossa and of the lateral cortex of the maxillary sinus. **D**, Cone beam computed tomography in the axial plane showed extension of the lesion to the posterior region of the tuberosity.

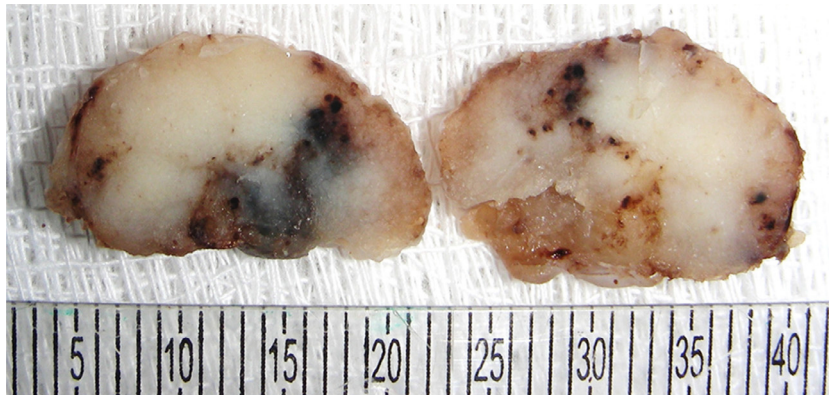


Fig. 3. Gross appearance of oral and maxillofacial metastatic breast adenocarcinoma in a male patient, which appeared as a 2 × 1 cm well-circumscribed nodule, fibrous in consistency, exhibiting irregular cut surface with a whitish to brownish color.

and a family history of the disease.<sup>9,15</sup> Interestingly, MBC accounts for up to 14% of all breast cancers in sub-Saharan Africa, with the highest incidence observed in African American men in the United States. However, the specific factors responsible for the increased incidence in Africans and African Americans are not well understood.<sup>3</sup> The present patient was originally from the Republic of Cabo Verde and had a past history of breast and prostate cancers.<sup>3</sup>

Oral metastases are uncommon, generally affecting both men and women with an overall median age of

60 years.<sup>13,16-19</sup> Clinical signs and symptoms include asymptomatic ulcerated swellings in the gingiva or tongue for soft tissue metastases, and ill-defined radiolucent lesions in the posterior mandible for intraosseous metastases, which cause pain, paresthesia, and numbness, as well as misleading presentations, such as toothache, dentoalveolar swelling, and loose teeth.<sup>1,13</sup> In men, oral soft tissue and jaw metastases usually originate from the lung, prostate, kidney, and liver and in women from the breast, kidney, adrenal, genital organs (uterus, cervix, ovaries), and colorectum.<sup>19</sup>



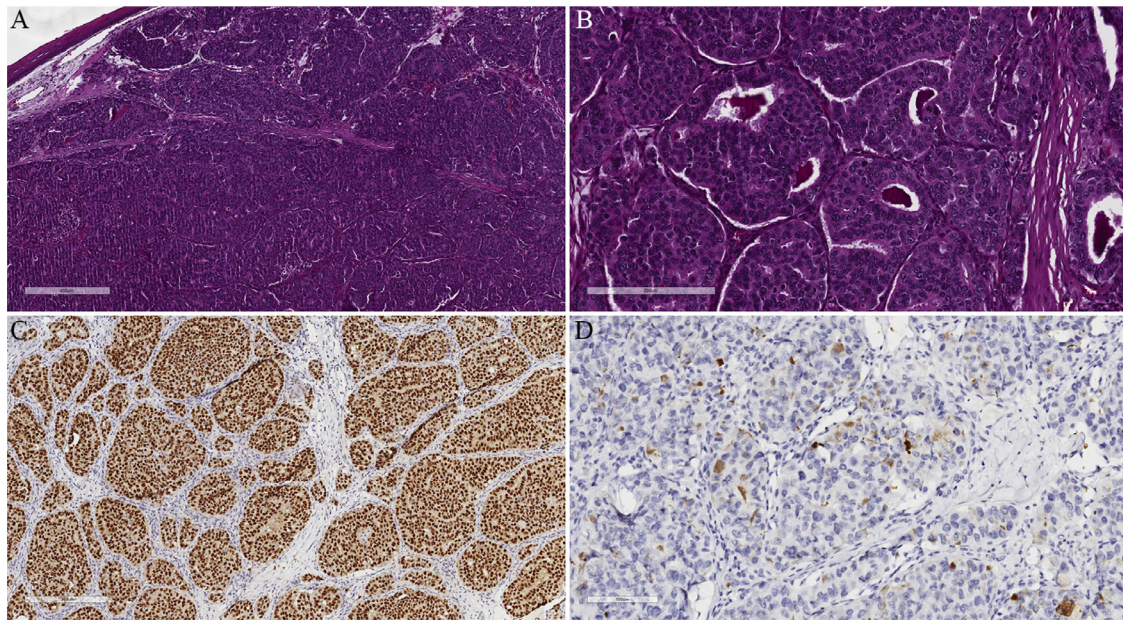


Fig. 4. Histopathologic and immunohistochemical aspects of oral and maxillofacial metastatic breast adenocarcinoma in a male patient. **A**, Oral mucosa fragment covered by parakeratinized, stratified squamous epithelium, with proliferation and infiltration of tumor cells organized in islands and nests in the lamina propria (hematoxylin and eosin [H&E], original magnification  $\times 100$ ). **B**, Tumor cells with hyperchromatic nuclei, evident nucleoli and eosinophilic cytoplasm exhibiting a ductal arrangement (hematoxylin and eosin [H&E], original magnification  $\times 200$ ). A high-resolution version of these slides for use with the Virtual Microscope is available as eSlide: [VM04957](#). **C**, Tumor cells were positive for estrogen receptor (immunoperoxidase, original magnification  $\times 100$ ). A high-resolution version of these slides for use with the Virtual Microscope is available as eSlide: [VM04959](#). **D**, Tumor cells were positive for GCDFP-15 (immunoperoxidase, original magnification  $\times 200$ ). A high-resolution version of these slides for use with the Virtual Microscope is available as eSlide: [VM04962](#).

Metastases to the nasal cavity and paranasal sinuses are rare and may represent the first manifestation of an otherwise clinically occult carcinoma, mainly occurring in males (mean age 57 years).<sup>19</sup> The main clinical features include nasal obstruction, headache, painful facial swelling, visual disturbances, exophthalmos, cranial nerve deficits, and epistaxis.<sup>13</sup> The most common primary sites of tumors that disseminate to this region are the kidney, lung, breast, thyroid, and prostate. In the OMF region, the maxillary sinus is most frequently involved, followed by the sphenoid, ethmoid, and frontal sinuses.<sup>19</sup> The present case involved metastatic MBC, with an epicenter in the left maxillary sinus causing disruption to the lateral and inferior bone cortices, contiguous extension into the oral cavity, and presentation as a reddish, polypoid swelling in the retromolar region.

To the best of our knowledge, only 8 cases of metastatic MBC to the OMF region have been reported in the English language literature (see [Table I](#)).<sup>4-11</sup> The most common clinical feature reported in 5 cases was painful swelling that affected the mandible, followed by involvement of the submandibular region, buccal mucosa, and masticator space, all reported in older men (median age 66 years; range 43-85 years).<sup>4-11</sup> In 7 cases,

the primary tumor in the breast was already known before metastatic spread, and immunohistochemical studies had been performed in only 2 cases.<sup>4-11</sup> The present case is the first description of metastatic MBC to the maxillary sinus with oral involvement.

Ductal carcinoma, as observed in the present case, is the most prevalent histopathologic subtype, making up greater than 90% of all cases of MBC, followed by the mucinous, papillary, and lobular subtypes.<sup>7,9</sup> In addition to review of the clinical history of the patient and histologic evaluation of hematoxylin and eosin-stained sections, immunohistochemical studies employing sensitive and specific antibodies may aid in identifying the primary site in a high percentage of cases of metastases.<sup>17</sup> Breast carcinomas usually stain positive for CK7 and the estrogen receptor and are negative for CK20. Interestingly, the present case was positive for the estrogen receptor but negative for CK7, a finding previously reported in MBC.<sup>7</sup> Positive staining for GCDFP-15 and negative staining for PSA confirmed the breast as the origin in the present case.<sup>16-18</sup>

An interesting finding in the present case was the long interval of 12 years between the primary diagnosis of MBC and its OMF metastasis. Similarly, Gondim et al.<sup>16</sup> also observed that in 16 women with head and

neck breast metastases, 9 cases were detected at a mean interval of 10.9 years after their primary breast cancer diagnosis. Therefore, the long interval for metastasis of breast cancer to bone and other organs, such as the lung and the brain, as noted in women, is similar to MBC metastasis to the OMF region, as in the present case.<sup>16</sup>

MBC is thought to have a less favorable outcome compared with breast cancer in women because it is usually more advanced at the time of diagnosis and has a higher incidence of lymph node metastasis.<sup>3</sup> Although the outcome is usually poor, prognosis is dependent, in part, on whether the oral or sinonasal metastasis is localized or is part of widespread disseminated disease. If the sinonasal metastasis is localized and treated aggressively, average survival may be extended. The present patient underwent a clinical checkup and positron emission tomography—computed tomography, which confirmed that the OMF metastasis was localized to the maxillary sinus. Considering the advanced age of the patient, hormone therapy with zoladex and tamoxifen was a conservative choice in line with the wishes of the patient's family. The patient remains alive after 2 years of follow-up.

## CONCLUSIONS

In summary, we have presented here an exceedingly rare case of OMF metastasis of MBC, the first case reported in Brazil. Clinicians and pathologists should be aware of the increasing incidence of MBC and its potential for late metastasis, particularly to the OMF region. Careful correlation of clinical, microscopic, and immunohistochemical features are required for proper diagnosis of oral and sinonasal metastases.

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