

# Breast Carcinoma Metastasis to the Submandibular Glands in a Male Patient: A Case Report and a Literature Review

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## Abstract

Female breast cancer is the most frequently diagnosed tumor while in the male population breast cancers are uncommon, as men account for less than 1% of all breast carcinomas. The leading predisposing factors for the development of breast cancer in men are: (1) chest radiation exposure, (2) estrogen use, diseases associated with hyperestrogenism, such as cirrhosis or Klinefelter syndrome, and (3) family health history. Male breast cancer (MBC) is more prevalent in elderly men. It occurs most often in the elderly population and resembles postmenopausal breast cancer in women based on its behavior. A higher incidence of breast cancer was recorded in men who have a larger number of relatives with BRCA mutations in the family, although the risk appears to be greater with inherited BRCA-2 mutations than inherited BRCA-1 mutations. Breast cancer rarely metastasizes to the oral region. If metastases occur in the oral region, they are localized in the maxillary and mandibular bones, less often in soft tissues. Male breast cancer is almost always positive for hormone receptors. A worse prognosis is associated with a more advanced stage at diagnosis for men with breast cancer. We describe a case of breast cancer metastasis to the submandibular glands. Examination of both masses of a 75-year-old Serbian male patient in both of the submandibular glands was suggestive of breast cancer metastasis, and a breast tumor mass was detected. We decided on operative treatment and successfully removed the tumor masses.

**Keywords:** Breastcancer; Malebreastcancer; Metastasis; Submandibular glands; Maxillofacial surgery

## Introduction

Male breast cancer is rare and not so frequent in comparison with the female breast cancer. People often assume that men don't get breast cancer. Men and women both have breasts that are made up of fatty tissue, fibrous tissue called stroma, nipples, ducts, and lobules, hence men do have a small amount of breast tissue and can develop breast cancer as well. From a biological point of view, hormones in girls enable the growth of breasts during puberty, while in boys they prevent them, so their breast tissue stays smaller. According to the CDC about 1 out of every 100 breast cancers diagnosed in the USA is found in a man. The most common kinds of breast cancer in men are the same kinds in women: invasive ductal carcinoma, invasive lobular carcinoma, ductal carcinoma *in situ* (DCIS). Most breast cancers in men are ductal carcinomas, which begin in the milk ducts[1- 2].

Breast cancer is one of the most frequent malignant tumors in women, and it has been reported to metastasize to bone. It's reported that 3.6% of all breast cancers develop bone metastasis [3].

While breast cancer as primary tumor is the most common source of metastasis to the oral cavity in women, metastasis to the head and neck area of the male population is uncommon. [4].

It's rarity occasionally makes it's diagnosis difficult for both clinicians and pathologist. Herein, we report a case in which breast cancer metastasis to the right and left submandibular gland was diagnosed and identified postoperatively.

## Materials and Methods

In order to present the clinical case as efficiently as possible, we conducted a search of the official literature available to us on the subject

of breast cancer in men in English, as well as reference databases. The last literature search was conducted on October 23, 2022. A scientific article of importance as a starting point of the search was "An Update on the General Features of Breast Cancer in Male Patients—A Literature Review" (published: 26 June 2022.) written by Sinziana Ionescu, Alin Codrut Nicolescu, Marian Marincas, Octavia-Luciana Madge, and Laurentiu Simion [5].

As the aforementioned authors of the scientific article, we conducted an identical data search and did not encounter any significant statistical deviations, and we hereby thank the authors of the scientific article who conducted the research.

The databases we searched are: (1) On [www.sciencedirect.com](http://www.sciencedirect.com), the search terms were: "breast cancer in male systematic review" between 2000. and 2022. and also "male breast cancer", with the mention that "review" as type of article between 2018. And 2022. and having "medicine and dentistry" as a domain. Furthermore, another association of terms that was searched for was "breast cancer in men systematic review". (2) On [www.pubmed.gov](http://www.pubmed.gov), the terms "male AND breast AND cancer" and also "breast cancer in men" were looked up

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with the settings: systematic reviews from the year 2000., in humans, articles in English. (3). Other quests on: [www.pubmed.ncbi.nlm.nih.gov](http://www.pubmed.ncbi.nlm.nih.gov), [www.oxfordjournals.org](http://www.oxfordjournals.org), and [www.sciencedirect.com](http://www.sciencedirect.com), and having as settings: reviews, in humans, article in English, domain medicine and dentistry, looked also for meta-analysis and randomized control trials, using the terms: "male AND breast AND cancer" and "male breast cancer surgery", and "male breast cancer (treatment) (systematic) review study".

Tumor masses from the patient biopsy were pathohistologically analyzed and a diagnosis was made.

## Case Representation

Here we report a case of male breast cancer metastasis in a 75-year-old patient. The patient was admitted to the Department of Neurotraumatology of the Emergency Center of the University Clinical Center of Serbia. The first symptoms that the patient noticed began in May 2022 in the form of difficulty swallowing, dry mouth, and poor appetite.

In the initial stages, the tumor mass was sensitive to palpation and slightly noticeable visually. In the meantime, the patient contracted COVID-19. During the illness, he noticed an expansive growth of the tumor mass in the submandibular glands .

During hospitalization, the patient underwent detailed diagnostic procedures. The anamnestic data we received from the patient is that the patient was aware of a tumor mass in the left breast. He knew about the tumor mass on the breast for the last 10 years .

Due to the tumor masses in the submandibular region, the doctors declared that it was inoperable and recommended radiotherapy. As the patient turned to us for help, we decided on operative treatment. The patient was operated on on September 23, 2022. We removed the tumor mass in its entirety and sent it for histopathological analysis, as well as the perimandibular tissue . During the intervention, 750ml of fluid was collected (blood, hydrogen and physiological solution calculated together. The operation lasted 7 hours.

The histopathological findings of the right submandibular region showed infiltration of the soft tissues of the neck and submandibular gland by tumor tissue, which morphologically and immunohistochemically corresponds to HPV negative squamous cell carcinoma. Also the histopathological findings of the perimandibular tissue on the right side showed the infiltration of necrotic tumor tissue of HPV negative squamous cell carcinoma.

The histopathological findings of the left submandibular region also showed the presence of HPV negative squamous cell carcinoma. Then the histopathological findings of the perimandibular tissue of the left side showed the infiltration of necrotic tumor tissue of HPV negative squamous cell carcinoma.

Postoperative CT examination of the neck, chest, abdomen, and pelvis, performed before and after the application of intravenous contrast in the arterial phase, showed a necrotically altered lymph node on the left side of the neck with a diameter of 12mm x 10mm in group IV-B. CT signs of reactive lymphadenopathy in the form of individual lymph nodes with a diameter of up to 13mm x 7mm can be seen in other regions of the neck. In the lower lobe of the right lung, a solid nodule with a diameter of 8 mm is visible, which is suspicious for a secondary deposit. Scarring changes with calcifications can be seen in the tips of both lung wings as a sequel of the old tubercular process. In the upper inner quadrant of the left breast, a relatively clear

limited tumor change with a diameter of 48mm x 36mm can be seen without signs of infiltration of the pectoral muscle, but with a close relationship with the artery which is a side branch of the contralateral right mammary artery.

The patient was referred for further treatment at the Institute for Oncology and Radiology of the Republic of Serbia.

## Etiology of Breast Cancer

When it comes to the etiology of breast cancer, predisposition factors play a key role, as well as environmental factors. It is also important to be mindful that the majority of males diagnosed with male breast cancer (MBC) have no identifiable risk other than increasing age (average age of diagnosis of 71 years) [6].

Males have also a higher risk like women, of getting breast cancer if they have a first- or second-degree relative with breast cancer. Bevier et al. (2012.) noted in their study that the relative risk (RR) of breast cancer was similar in either offspring when the father or mother was affected (RR = 1.73 and 1.74, respectively), but the risk was slightly higher in the females when the brother is affected as opposed to when the sister is affected (RR=2.48 and 1.39, respectively) [7].

In addition to a positive family history of breast cancer, males with a BRCA mutation appear to have increased risk for breast cancer as well. Those with BRCA-2 carrier mutation have a 6% increased risk, and BRCA-1 with a 4% risk of developing the disease [8].

Other genetic disorders have been implicated in increasing the risk of MBC, including Klinefelter sy. (47, XXY), Cowden syndrome (PTEN tumor suppressor gene), Li-Fraumeni sy. (TP53), Lynch sy. (PALB2 and mismatch repair genes) [6, 8].

The alterations in estrogen to androgen ratios are important to note when discussing the etiology of male breast cancer. Estrogen, which stimulates ductal development in breasts, has also been implicated as a potential risk factor for MBC similarly to women. Klinefelter syndrome, as previously mentioned, may increase the risk of MBC through excess estrogen stimulation. Other potential triggers have also been identified and include obesity, marijuana use, hepatic dysfunction, thyroid disease, and estrogen-containing medications.

Likewise, a decrease in circulating androgens would result in elevations of the estrogen ratios, and this may occur from conditions such as cryptorchidism, orchitis, and orchiectomy [9].

Environmental factors have also been implicated in the possibility of increasing the risk of male breast cancer. Previous radiation therapy has been noted as a potential risk factor. Radiotherapy has been used to treat gynecomastia, but these patients have been found to have a 7-fold increase in the risk of MBC [10].

It was also noticed that certain professions have been found to increase the risk of MBC, including steel and rolling mills, as well as occupations involved with organic solvents such as trichloroethylene [11].

## Epidemiology

Male breast cancer is a relatively rare malignancy compared to breast cancer in women with a known ratio of 1 male case to 100 in females and occurs in about 1% of all breast cancers. Regarding male cancers in general, it accounts for 0.5% of all cancer diagnosis in men, however, recently there has been some concern about an increase in incidence in the past few decades [12].

Studies have hypothesized that in addition to obesity and alcohol, dietary factors may be exacerbating the incidence of male breast cancer, but concrete research and evidence regarding specific dietary patterns have yet to be established [13].

Despite the aforementioned risk factors and potential cause-and-effect correlations, many individuals who are diagnosed with male breast cancer have no identifiable risk factors [12].

## Histopathology

The most common type of breast cancer diagnosed in men is invasive ductal carcinoma, which constitutes approximately 90% of all male breast cancer. In regards to hormone expression in male breast cancer, approximately 90% express the estrogen receptor, and 81% express the progesterone receptor [14].

Studies have also found that the expression of these hormone receptors is more prevalent than female breast cancer [15].

In a literature review by Sinziana Ionescu et al., general information on the common types found and an exhaustive list of uncommon types versus their prognosis and clinical significance were presented [5].

Shaaban AM finds that the most prevalent histology is grade 2 ductal carcinoma with no special subtype. Male breast cancer is frequently of the luminal A phenotype comparable to postmenopausal breast cancer in women [5, 16].

A study by Fentiman showed that using hierarchical clustering, estrogen receptor was clustered with progesterone receptor in female breast cancer, but with estrogen receptor and androgen receptor in male breast cancer [5, 17].

Oncotype DX appears to be effective in determining recurrence risk in selected male breast cancer based on limited data. A study by Cho looked at the use of HE images, a deep-learning algorithm that may be able to predict the efficacy of adjuvant chemotherapy in cancer patients. The Lunit SCOPE algorithm was developed using HE slides from 1343 breast cancer patients. Lunit SCOPE was trained using the 21-gene assay (Oncotype DX) and histological parameters to predict recurrence. The risk prediction model accurately predicted the Oncotype DX score >25 and the recurrence survival of the validation cohort and TCGA cohorts. The predicted risk was positively associated with proliferation-associated Oncotype DX genes and negatively correlated with estrogen-related prognostic genes. The risk of cancer recurrence and the early-stage hormone receptor-positive breast cancer patients who would benefit from adjuvant chemotherapy were predicted by an integrative analysis utilizing Lunit SCOPE [5, 18].

Papillary in situ and invasive carcinomas are not uncommon in the male breast, unlike the female breast. Zhong finds in a review that papillary lesions of the male breast papillary carcinomas span a wide clinic-pathological spectrum, and both invasive and noninvasive papillary carcinomas have a favorable prognosis, as it is also reported by Avau [5, 19, 20].

Other types of tumors are medullary, papilloma, and lobular. Ductal carcinoma in situ is not so commonly found due to a lack of awareness and stigmas related to male breast cancer, hence we have delayed diagnosis and poorer outcomes of the patients.

## Patient History and Physical Examination

Men usually go to the doctor for a check-up with the complaint of a painful lump in the breast unilaterally. Other accompanying symptoms

that may occur are: include nipple retraction, nipple discharge, ulceration, and pain [6].

Tumor masses in men are easier to diagnose precisely because of the smaller size of the breasts compared to women, although gynecomastia may mask the condition. It's also vital to discuss the potential family history of breast cancer, the patient's past medical history, profession, and whether there has been previous estrogen or radiation exposure.

## Evaluation

The diagnosis of male breast cancer is made by a triple assessment, which includes clinical assessment, mammography, or ultrasonography, and core biopsy. Mammography is an effective diagnostic method with a sensitivity of 92% and a specificity of 90%; due to size and volume differences in male breasts, and as well as for the promotion of breast screening among women, this modality may be limited at times. Given this, ultrasound-guided core biopsy gives the most definitive diagnosis of male breast cancer and is preferred over fine-needle aspiration. Most male breast cancers are hormone receptor-positive [14].

## Discussion

Most malignant tumors that occur in the oral cavity are salivary gland tumors, such as adenoid cystic carcinoma, acinic cell carcinoma, and mucoepidermoid carcinoma [21].

Therefore, metastasis of a tumor to the head and neck region is uncommon, and challenging for maxillofacial surgeons, oral surgeons, otorhinolaryngology surgeons, and pathologists. Metastatic tumors differ by gender. The most common primary sites in women are the breasts, genitourinary or gynecologic sites, kidneys, and colorectum; in males, the lung, kidneys, liver, and prostate are predominant [22-23].

Oral cavity metastasis is mostly to the jaw, mandible, or maxilla, and far more cases of metastatic lesions in the jawbone rather than soft tissue have been reported, despite jawbone metastases being more difficult to detect because of their relative invisibility. In oral soft tissues, the most frequent site is the gingiva, and it has been speculated that inflammation such as periodontitis may contribute to the attraction of metastatic cells [23].

A literature review done by de Almeida Freire has put the attention towards metastatic sites. For example, in the oral and maxillofacial region of male patients, breast metastases are exceedingly rare; however, clinicians must consider breast metastasis when evaluating oral nodules in older patients, including men, especially those with a history of malignancy. From the point of view of clinical approach to have in mind, even if some metastatic sites are very rare, they can be the first clinical manifestation of an occult male breast cancer. This previous aspect was underlined by Kesting and Gonzalez-Perez [24-26].

Metastases to the parotid gland, for example, are extremely rare. According to Hyun Kyung Jung et al., 24 cases of breast cancer metastasis to the parotid gland have been reported from 1982. to 2018 [27-28].

Malignant salivary tumors account for 0.5–1% of all cancers, and less than 10% of them are metastatic [27, 29].

Metastatic disease of the parotid gland accounts for 9-14% of all parotid tumors [27, 30].

The most common malignancies metastasizing to the parotid gland are tumors arising from the head and neck, such as squamous cell carcinoma and malignant melanoma, and rare malignancies that

metastasize to the parotid includes tumors arising from the breast, kidney, gastrointestinal tract, and prostate [27, 31, 32].

After a thorough data search, we found that there are only 15 recorded cases of metastases to the submandibular gland whose origin is from breast carcinoma, and all of them were women. Our presentation of the clinical case is the 16<sup>th</sup> recorded case of metastases in the submandibular glands and the first ever recorded in a male, and it was bilateral, unlike the previous.

As mentioned before, metastatic tumors to the major salivary glands are very rare. Conley and Arena reviewed 81 cases of parotid metastases in 1963. In most cases the primary tumors were malignant melanomas of the skin of the temple, ear or scalp (45.7%), or squamous cell carcinomas from the oral cavity, accessory nasal sinuses, ear or pharynx (37%). The remaining primary tumors arose in other head and neck structures [33, 34].

Until the year of 1987., 9 cases were well-reported in the literature of submaxillary metastases from a distant tumor [33- 42].

A case report from March 1985, “*Metastases to the Submaxillary Gland from Breast Cancer: Case Report*” written by Giovanni Rosti et al., documented a 68-year-old female patient who was admitted to the Department of Medical Oncology at the Ravenna Hospital because of a mass in the left submandibular region. She had undergone left radical mastectomy for a stage II ductal breast cancer 4 years before she noticed the mass in the submandibular gland. There was no pain, slurred speech or difficulty moving the tongue. There was a mild peripheral paresis of the facial nerve. At 26 months follow-up (May 1987) there was a clinical complete remission of the mass, with no evidence of disease elsewhere [33].

In 1995 a case report “*Submandibular gland metastasis of breast carcinoma: a case report and review of the literature*” was published by G. Vessecchio et al. They’ve reported a 49-year-old female patient who developed a solitary metastasis in the submandibular salivary gland 2 years after primary surgery for a grade II T1 NO M0 breast cancer. Vessecchio et al. conducted a literature search and found that there were approximately 100 cases of metastases in the submandibular glands, of which 14 (including their clinical case report) were metastases as a result of breast cancer. All 14 cases were women. The metastases were unilateral [43].

Including the previously mentioned case report from 1995, the total number of patients with metastases in the submandibular gland, with primary breast cancer in question, was 14.

In 2011, another clinical case of breast cancer metastasis to the submandibular gland was recorded, and making it 15th overall. The case report “*Breast cancer metastatic to the submandibular gland. Case report.*” was presented by Erra, S, and D Costamagna [44].

Erra, S, and D Costamagna reported a case of breast cancer metastasis to the right submandibular gland in a 50-year-old woman with a past history of ductal G3 T1c N0 ipsilateral breast carcinoma. In 1999 she underwent right mastectomy and axillary lymphadenectomy. She was well and free of disease for nine years [44].

Our clinical case report of a 75-year-old male patient represents the first male case of breast cancer metastases in both submandibular glands and as such the 16th case overall.

## Conclusion

Breast cancer metastases, although rare, in the orofacial region are

possible and should not be excluded even in the male population. Oral surgeons, and otorhinolaryngology surgeons should be aware of this possibility even in the male population.

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