Case Report

A Rare Case: Isolated Metastasis of Laryngeal Cancer to the Breast in a Male Patient

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Abstract

Laryngeal cancer is one of the common cancer types, and distant organ metastasis is extremely rare. We present a 65-year-old male patient who received five cycles of cisplatin and radiotherapy after surgery for laryngeal cancer. In the positron emission tomography-computed tomography examination performed during the follow-up, we observed a newly developed mass with increased fluoro-D-glucose uptake in the right breast. A hypoechoic lesion with irregular borders of approximately 17 mm × 11 mm × 17 mm was observed in the retroareolar region of the right breast in ultrasound. Calcification was not observed in mammography. In the pathological evaluation after biopsy, it was seen that the neuroendocrine type of laryngeal cancer was compatible with breast metastasis. Although rare, metastases to the breast should be kept in mind in cases with a primary tumor.

Keywords: Breast metastasis, laryngeal cancer, magnetic resonance imaging, male breast metastasis, positron emission tomography-computed tomography

Introduction

Nowadays, larynx cancer is one of the common cancer types and can be a source of morbidity and mortality.[1] In the last three decades, according to a study, the incidence and prevalence of the disease have increased from 12% to 24%.[1] According to the American Cancer Society, approximately 12,380 new laryngeal cancer cases were detected in the United States in 2023 (9900 in men and 2480 in women). Laryngeal cancer is more common in males than females.[1,2] Most patients diagnosed with laryngeal cancer are 55 years or older, with an overall average age of 66.[1,2] The etiology of laryngeal cancer involves many factors, including smoking and alcohol consumption as the leading causes, along with anatomical malformations, gastroesophageal reflux, exposure to hot substances, certain viral infections, chemicals, and ionizing radiation.[1,2]

The main symptom of laryngeal cancer is hoarseness. The most common type of laryngeal cancer is squamous cell carcinoma.[3] However, there may be other rare forms of laryngeal cancer, such as adenocarcinomas, sarcomas, lymphoma, and neuroendocrine tumors.[3] Neuroendocrine tumors of the larynx are quite rare, comprising approximately 1% of all types of laryngeal tumors.[4]

While distant organ metastasis of laryngeal cancer is not very common, according to the conducted study, distant organ metastasis was observed in approximately 19% of all cases.[5] The lung is the organ where laryngeal cancer most frequently metastasizes.[5]

Metastasis of laryngeal cancer in the breast is extremely rare. In fact, this case report represents the first case in English literature to our knowledge. In this case report, we present the case of a male patient with a neuroendocrine type of laryngeal cancer who developed isolated breast metastasis.

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Case Report

A 65-year-old male patient has a history of smoking 100 packs/year but does not consume alcohol. There is no known history of cancer in his family. He visited the doctor in July 2022 with complaints of hoarseness. Apart from hoarseness, no pathological physical examination features were identified. After the physical examination performed by the otolaryngologist (ear, nose, and throat) doctor, asymmetric pathological thickening in the glottic region was observed with rigid laryngoscopy, and a biopsy was taken from here. The biopsy result showed compatibility with the large cell subtype of the neuroendocrine type of laryngeal cancer.

A positron emission tomography-computed tomography (PET-CT) examination performed in July 2022 showed a 19 mm × 17 mm mass with increased fluoro-D-glucose (FDG) uptake at the laryngeal glottic level (standardized uptake value [SUV]$_{max}$: 14.1) [Figure 1]. In addition, multiple pathological lymph nodes with increased FDG uptake were observed on the left side of the neck, the larger one measuring approximately 16 mm × 13 mm at cervical level 2–3 (SUV$_{max}$: 8.4).

He underwent left hemilaryngectomy – Neck lateral dissection and received five courses of cisplatin and radiotherapy treatment. During the patient's follow-up, the first postoperative PET was taken in September 2022 [Figure 2a]. There was no finding suggestive of metastasis. In February 2023, a repeat PET-CT scan (Siemens, Horizon MCT PET-CT, Germany) was conducted to evaluate the treatment response. This PET-CT examination revealed a new hypermetabolic nodular breast lesion of approximately 6 mm in size adjacent to the right nipple (SUV$_{max}$: 4.3) [Figure 2b]. Furthermore, in this PET-CT examination, millimetric nodules have been observed in both lungs that do not exhibit significant FDG uptake. In addition, increased FDG uptake with indistinctly defined boundaries has been observed at the posterior level of the left vocal cord in the larynx, at the posterior wall of the hyoid bone-vocal cord level, and in both lateral sections. These findings are considered suspicious for recurrence or residue. In the contrast-enhanced neck magnetic resonance imaging performed on March 23, 2023, the areas mentioned in the PET-CT examination have also been evaluated as suspicious for recurrence or residue in terms of PET-CT findings. The patient was referred to the breast radiology clinic due to the mentioned FDG uptake in the right breast in the PET-CT examination, and a palpable mass in the right breast was noticed.

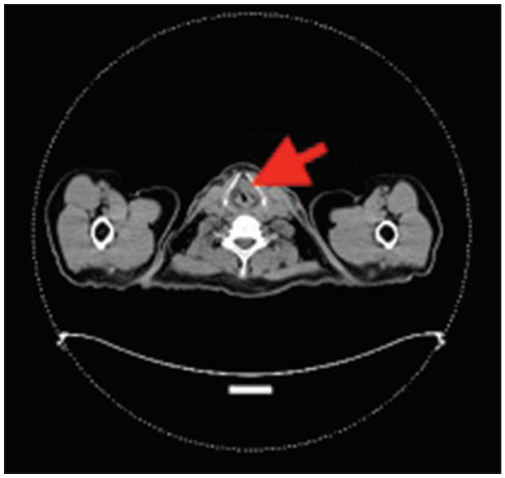

Figure 1: In the positron emission tomography-computed tomography examination, a lesion with dimensions of 19 mm × 17 mm was observed in the larynx at the glottic level, extending from the anterior commissure to the left vocal cord, with indistinct borders (red arrow)

On June 02, 2023, mammography (Siemens, Mammomat inspiration, Germany) was taken for the patient; however, due to the patient's lack of cooperation and pain, only the cranio-caudal (CC) image could be obtained. In the CC image, a lobulated contoured nodular opacity located near the nipple in the retroareolar area of the right breast is observed [Figure 3].

In the mammography, the skin thickness was normal, and no pathological microcalcifications were observed.

When an ultrasound (US) (Toshiba Aplio 500, USA) was performed, a hypoechoic lesion with irregular borders of approximately 17 mm × 11 mm × 17 mm was observed in the retroareolar region of the right breast [Figure 4]. The skin and subcutaneous tissue appeared normal, and no microcalcifications were observed. No focal lesion was detected in the left breast. There were no pathological lymph nodes identified bilaterally in the axilla. When comparing the dimensions of this lesion between the US examination conducted in June and the PET scan evaluated in February, it is observed that the size of the lesion has increased by more than twice in a very short period, and therefore, it is considered an aggressive tumor.

After a tru-cut biopsy was performed on this lesion visible in the US, the biopsy result is compatible with isolated metastasis of neuroendocrine larynx cancer to the breast [Figure 5].

After confirming the biopsy result compatible with breast metastasis, chemotherapy was initiated with carboplatin and etoposide. The patient continues to follow-up at the Medical Oncology Clinic.

Discussion

Breast metastases from extramammary primary tumors are rare and constitute 0.5%–2.0% of all breast malignancies.[6] The most common source of a metastatic breast lesion is contralateral breast cancer. The most common extramammary cancers that metastasize to the breast are lymphoma/leukemia, melanoma, sarcomas, prostate cancer, lung cancer, gastric cancer, ovarian cancer, renal cell cancer, malignant mesothelioma, carcinoid tumor, carcinoma of the cervix, rectal cancer, and papillary thyroid cancer.[7] Among the sources, lymphomas/leukemias and melanomas are the most common.

The clinically observed rate of breast metastases from nonmammary malignancies is rare because it occurs in the late

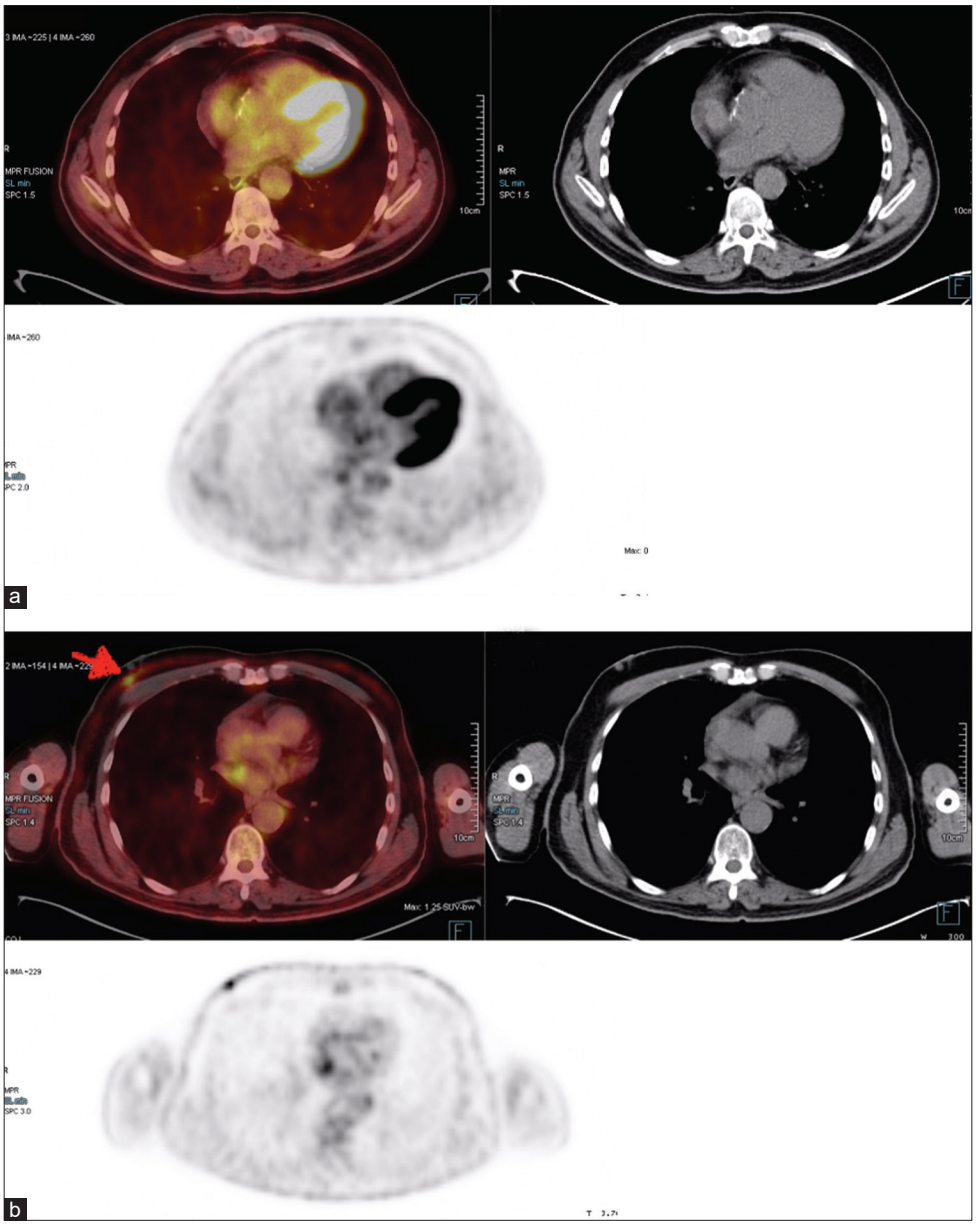

Figure 2: (a and b) In the February 2023, positron emission tomography (PET), PET-computed tomography (CT) examination (b), increased fluoro-D-glucose uptake was observed in the right breast retroareolar region (standardized uptake value max: 4.3) (red arrow). This finding was considered a new finding compared to the September 2022 PET-CT examination (a)

stage of nonmammary malignancies.[7] This rare occurrence of metastases to the breast is suggested to be due to the presence of large areas of fibrous tissue with a relatively poor blood supply. Estrogen is able to increase the vascularity and stroma of the breast due to this situation predisposing factor in the development of metastasis. As a result of this hypothesis, most cases occur in young women. Some rare cases of the development of breast metastases have been reported in male patients with prostate carcinoma who received estrogen therapy.[8] Metastatic breast masses arising from nonmammary malignancies can spread through both hematogenous and lymphatic pathways.[8]

It is difficult to distinguish the second primary tumor from breast metastasis radiologically. In our case, the histological subtype of laryngeal cancer and breast lesion was neuroendocrine, suggesting metastasis in the foreground. While systemic treatment is considered primarily in metastasis, surgical treatment is considered primarily in second primary breast cancer according to the cancer stage. Histological examination has an important role in distinguishing between second primary breast cancer and extramammary metastasis. It is important to be able to recognize the signs of metastatic lesions to avoid unnecessary surgery.[7]

Hematogenous breast metastases arising from nonmammary malignancies are usually located in the upper outer quadrant and are superficially found in the subcutaneous tissue or just adjacent to the breast parenchyma, which is relatively rich

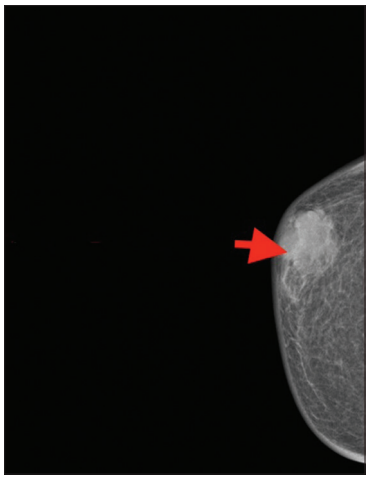

Figure 3: Craniocaudal mammography revealed a lobulated contoured nodular opacity near the nipple in the retroareolar region of the right breast (red arrow)

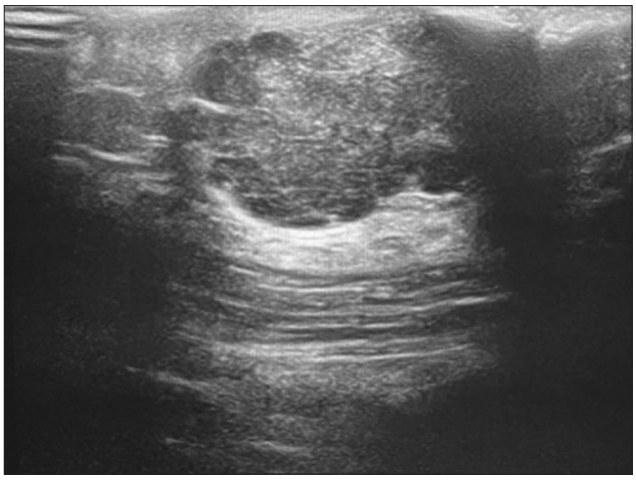

Figure 4: According to the ultrasound, a hypoechoic lesion with irregular borders, measuring approximately 17 mm × 11 mm × 17 mm, was observed in the retroareolar region of the right breast

in blood supply.[8] Metastatic breast masses tend to enlarge rapidly.

Axillary lymph node involvement is less common in metastases than in primary breast cancers.[9] The appearance of lymphatic metastasis makes it different from nonmammary malignancies. It includes a thick trabecular pattern with diffusely and heterogeneously increased density of subcutaneous fat and glandular tissue, and secondary skin thickening, lymphedema, and lymph node enlargement indistinguishable from inflammatory breast cancer.[8-10] Malignant-type microcalcifications are not common, as is often reported in primary inflammatory breast cancer.

Typical US features include single or multiple, round-to-oval-shaped, well-circumscribed, occasionally micro-lobulated hypoechoic masses without spiculations, calcifications, architectural distortion, retrotumoral acoustic shadowing, or secondary skin or nipple changes.[11] Unlike primary breast tumors, desmoplastic reactions and spiculation on mammography are not seen in metastases.[8] Rare tumoral calcifications found in metastases may help distinguish metastases from primary breast cancers, except for rare examples of metastases from ovarian, thyroid, or mucin-producing gastrointestinal tract carcinomas that may contain intratumoral calcifications.[8,12,13]

On mammography, metastatic lesions may appear as single or multiple masses or as diffuse skin thickening. Metastases usually present as round masses with well or ill-defined borders. Microcalcifications may rarely occur in some primary types.[14]

Larynx cancer is the most common type of cancer in the respiratory tract.[1] Distant metastases are seen in up to 19% of all cases. The most common site of metastases from laryngeal cancer is the lung. Distant metastasis to skeletal muscle is extremely rare.[4] We thought that the cause of this rare breast metastasis was due to the neuroendocrine subtype of laryngeal cancer. In the literature, we have seen that neuroendocrine laryngeal cancer tends to be locally aggressive and distant metastases.[4]

We present the case of a 66-year-old male patient with neuroendocrine histological subtype laryngeal cancer that has isolated and metastasized to the breast, which has no previous report in the literature to our knowledge. Williams *et al*. show that the mean age of metastatic breast malignancy patients was 51 (range 13–85) and 91% of them were female.[15] In our case, contrary to the literature, the metastatic mass was in the retroareolar area of the right breast.[8] On mammography, approximately 30 mm × 25 mm lobulated contoured nodular opacity located close to the nipple in the right breast retroareolar region is observed. In our case, microcalcification was not found on mammography, like secondary breast cancers in the literature.[8]

Lee *et al*. describe 18 metastatic tumors in the breast ultrasonographically. Poorly defined (8 cases, 53.3%), irregularly shaped (8 cases, 53.3%), hypoechoic (14 cases, 93.3%), and heterogeneous (8 cases, 53.3%) lesions were predominantly distributed superficially. In our case, the lesion is hypoechoic, poorly defined, irregularly shaped, and superficially located, which is compatible with literature.[8]

The use of radiolabeled 2-deoxy-2-[18F] FDG for imaging in oncological patients constitutes the majority of all PET-CT imaging procedures for many cancers, as increased FDG accumulation relative to normal tissue is a useful marker. SUV is often used as a measure to indicate FDG accumulation.[16,17] SUV_{max} value is associated with certain pathological features such as the largest diameter of the mass, histology, and number of mitosis.[18] In our case, the lesion in the right breast had increased SUV_{max} values (SUV_{max} 4.3) in favor of malignancy, consistent with the literature.[19]

Conclusion

Secondary breast cancer is much rarer than primary breast cancer. Many cancers can distant metastasize to the breast. We presented laryngeal cancer with neuroendocrine histological subtype with isolated breast metastasis, which is the first case in the English literature to our knowledge.

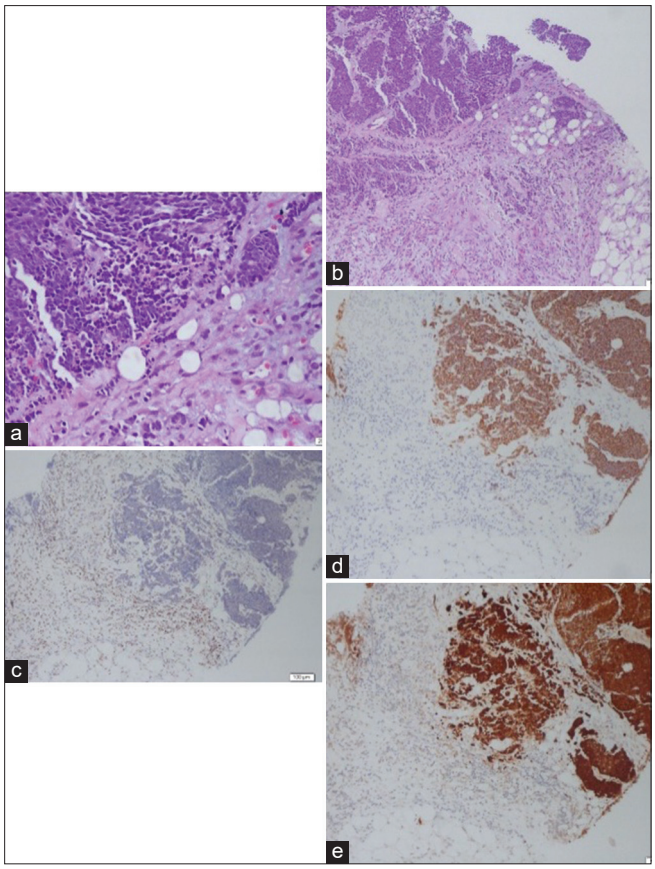

Figure 5: In H and E preparations, invasion of tumor cells into breast stroma (a) and thin chromatin structure (b) is seen. Immunohistochemical study shows loss of GATA3, (c) unlike breast tumors. There is an immunoreaction with P16 (d) and synaptophysin (e) consistent with the original tumor

Ethics statement

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its amendments. The authors certify that they have obtained all appropriate patient consent form. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his 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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