

Breast Cancer Recurrence Presenting as Solitary Intraparotid Nodal Metastasis Detected by 18F-Fluorodeoxyglucose Positron Emission Tomography: A Very Unusual Occurrence

Abstract

Primary malignancies of the salivary gland itself are uncommon, while secondary metastatic deposits are further very rare with description of only few case reports in the literature. The most common site of metastatic deposit to parotid gland is from squamous cell malignancies of head and neck, while secondary deposits from primary in infraclavicular location are very rarely described. We herein describe the case of an elderly lady who while on adjuvant endocrine therapy developed metastatic disease with right intraparotid node as the sole site of metastasis detected on FDG PET scan. This type of presentation of recurrence is very uncommon, especially in hormonal receptor-positive cases, with <30 cases described in the literature to the best of our knowledge. This patient underwent metastasectomy followed by palliative the second-line hormonal therapy and achieved long-term survival more than usually seen with other metastatic breast cancers highlighting the importance of metastasectomy in metastatic breast cancer patients on hormonal therapy who develop metachronous oligometastatic disease.

Keywords: Intraparotid node, metastasectomy, oligometastatic, parotidectomy

Introduction

Malignancies of the salivary gland are very uncommon and constitute only 3%–6% of all head-and-neck malignancies.^[1] Most of them are primary salivary gland tumors and metastatic involvement of the salivary glands is very uncommon. Among them, most commonly involved is parotid gland followed in decreasing frequency by submandibular and sublingual glands. Metastatic tumors to parotid gland have already been described in the literature from hepatocellular carcinoma, breast cancer, renal cell carcinoma, bronchogenic carcinoma, and cutaneous malignancies; however, these are rare and seen only in cases of diffusely metastatic diseases.^[2]

We herein report a 60-year-old female patient, who was on adjuvant hormonal therapy after treatment of an early right breast cancer developed metastatic disease solely at the right parotid gland with right intraparotid gland and no evidence of disease elsewhere in the body on positron-emission tomography (PET) imaging. She was managed with

surgical excision of solitary metastasis (superficial right parotidectomy with Level II and Level III neck node dissection) followed by palliative the second-line hormonal therapy achieving long-term recurrence-free survival. Such a pattern of recurrence is very uncommon and described in the literature only in few case reports. Long-term survival after parotidectomy potentially highlights this as valuable therapeutic option which needs further validation through large series.

Case Report

A 60-year-old multiparous postmenopausal female patient, with no prior known medical or surgical comorbidities or any drug allergy, presented with a history of lump in the right breast of 4 weeks' duration which is gradually increasing in size. The lump was not associated with any pain, deformity, or bloody nipple discharge. There was no history of any axillary swelling, trauma, surgery, or systemic symptoms such as fever or weight loss. Family history was insignificant. On examination, there was 4 cm × 3 cm lump in the lower quadrant

**Chaturbhuj
Ramanand Agrawal,
Kumardeep Dutta,
Dinesh Chandra
Doval,
Sunil Pasricha¹,
Manoj Gupta²**

*Departments of Medical
Oncology, ¹Pathology and
²Nuclear Medicine,
Rajiv Gandhi Cancer Institute
and Research Centre,
New Delhi, India*

Address for correspondence:
Dr. Chaturbhuj Ramanand
Agrawal,
Department of Medical
Oncology, Rajiv Gandhi
Cancer Institute and Research
Centre, Sector 5, Rohini,
New Delhi - 110 085, India.
E-mail: chaturbhujagrwal06@
rediffmail.com

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of the breast, not fixed to underlying structures or skin. The fine-needle aspiration cytology (FNAC) of lump was suspicious of malignancy, while biopsy revealed invasive ductal carcinoma Grade III, which demonstrated estrogen and progesterone receptor positive and HER2/Neu receptor negative. She underwent right breast conservation surgery with oncoplastic reconstruction. Final histopathology report revealed an invasive ductal carcinoma Grade III, with tumor size of 2.3 cm × 3.0 cm and node negative status, that is, Stage IIA (T₂N₀M₀) breast cancer. She received six cycles of adjuvant chemotherapy with five fluorouracil, epirubicin, and cyclophosphamide followed by adjuvant radiation therapy and then started on adjuvant hormonal therapy with tablet anastrozole 1 mg OD.

Within 9 months of adjuvant endocrine therapy, she presented with swelling over right preauricular region which she noticed incidentally. There was no history of any associated pain, trauma, sialorrhea, or difficulty in chewing food. PET scan revealed a focus of increased avidity in the right parotid gland without any metastatic focus elsewhere in the body [Figure 1] while contrast-enhanced computed tomography (CT) fused 18F-fluorodeoxyglucose (¹⁸F-FDG) PET/CT axial and coronal sections showed a well-defined nodular lesion measuring 1.8 cm × 1.7 cm × 1.6 cm in the right parotid gland with good postcontrast enhancement and mild FDG avidity [Figure 2]. She underwent right superficial parotidectomy with Level II and Level III neck node dissection which revealed metastatic infiltrating ductal carcinoma involving the right parotid gland with intraparotid node [Panel A, Figure 3]. On immunohistochemistry, cells were positive for CK 7 and GATTA 3, while negative for CK 20, PAX 8, and TTF1 suggesting metastasis from breast primary [Panel B, Figure 3]. In view of limited parotid metastasis and no other evidence of any visceral crisis, she was started on second-line hormonal therapy with tablet exemestane 25 mg OD and tablet everolimus 5 mg OD. At present, she is on regular follow-up on same

second-line hormonal therapy and disease free for the last 16-month postsurgery.

Discussion

The most common tumors arising in parotid gland are benign neoplasms, most common being pleomorphic adenoma.^[3] Although metastatic tumors of salivary glands are very rare, among them, the mandibular gland is a common source of distant metastatic site while the majority of reports of parotid gland metastasis are from squamous cell carcinoma of head-and-neck region. The possible explanations for this difference in the pattern of metastases are the differences in the anatomic relationships, number of the lymph nodes, and their drainage between the parotid gland and submandibular gland.^[4] Parotid gland has abundant lymphatic supply with rich lymphatic network around the gland. Embryological development of lymph nodes precedes the parotid development and the average number of parotid lymph nodes is around 20–30 in a healthy individual which is further divided into paraglandular and intraglandular nodal subgroups.^[5] These nodes drain from the lateral and frontal aspects of the scalp, lateral aspects of the lids, lacrimal gland, conjunctiva, external auditory canal, parotid gland, and paraglandular nodes. This forms the logical explanation of the most common primary site for parotid secondaries being squamous cell carcinoma of head and neck. On the other hand, the most common nodes involved in breast cancer are axillary nodes, while the most common sites of metastasis in decreasing order of occurrence are bones, lung, liver, and brain. In view of



Figure 1: Coronal 18F-fluorodeoxyglucose positron emission tomography image shows a focus of increased fluorodeoxyglucose avidity in the right parotid gland with no fluorodeoxyglucose avid focus elsewhere in the body

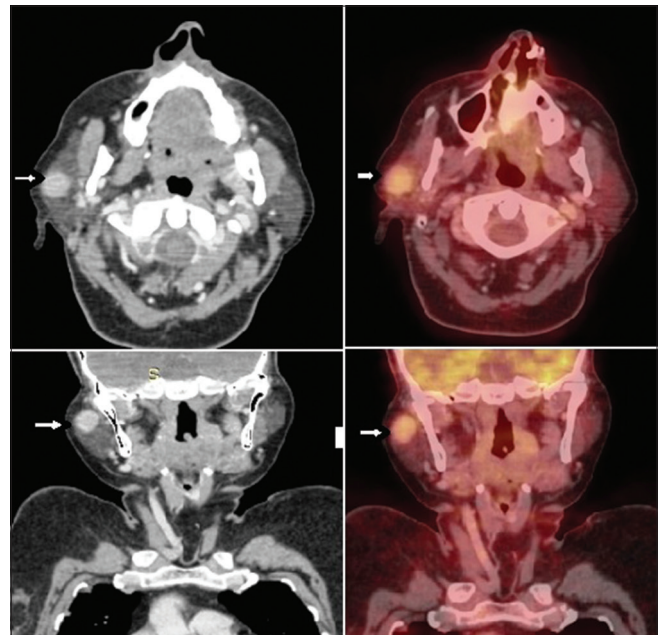


Figure 2: Contrast-enhanced computed tomography and fused 18F-fluorodeoxyglucose positron emission tomography/computed tomography axial and coronal sections show a well-defined nodular lesion measuring 1.8 cm × 1.7 cm × 1.6 cm in the right parotid gland showing good postcontrast enhancement and mild fluorodeoxyglucose avidity

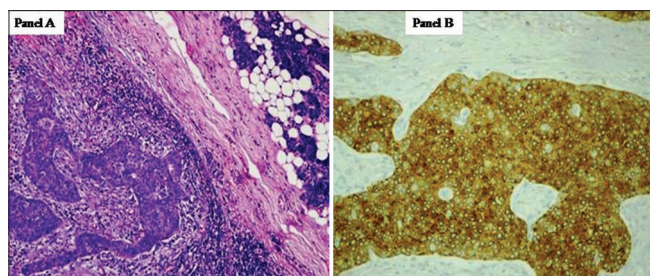


Figure 3: Panel A: Intraparotid lymph node with metastatic infiltrating ductal carcinoma (H and E, ×40) Panel B: Immunohistochemistry for GATTA-3 shows positive staining of tumor cells (×40)

these complex anatomical landscapes, metastatic cancer to parotid from breast primary is very rare and hematogeneous route appears to be the predominant mode of spread in view of noninvolvement of axillary nodes in the majority of the previous series.

An extensive search of the literature revealed <30 similar cases reported so far with most of the data from case reports only. Considering parotid masses, the largest series has been studied by Seifert *et al.* who examined 108 cases of metastatic parotid and submandibular tumors and reported metastatic disease limited to glandular parenchyma in 47% cases; while in remaining 53% cases, there was involvement of intraglandular lymph nodes also. In this large series, the majority of tumors had primary in head-and-neck region followed by skin, while only six cases were found to have mammary gland as the primary site of origin.^[6] Bergersen *et al.* have reported that up to 80% metastatic disease in parotid results from cutaneous lesions evenly distributed between squamous cell carcinoma and melanoma.^[7] Nuyens *et al.* reported 34 metastatic cases out of 520 parotid masses examined and found 23 cases having primary from squamous cell carcinoma of the skin, 7 from metastatic melanoma while only 2 from ductal carcinoma of breast.^[8] These two patients in their series had dismal outcome despite being treated optimally with parotidectomy with neck node dissection followed by postoperative radiation. Most of the cases are missed as benign causes which mimics similar presentation are far more common than malignant causes which includes inflammatory conditions such as acute or chronic sialadenitis, sialolithiasis, benign neoplasms such as pleomorphic adenoma, Warthin's tumor, hemangiomas, and hemangioendotheliomas. However, the presence of metastatic-appearing lymph nodes accompanying a tumor in the salivary gland strongly suggests a malignancy.^[9]

FNAC can adequately distinguish between benign and malignant parotid masses and is very useful in therapeutic decision-making, but it requires expertise.^[10] On histopathology, although primary parotid tumors resemble immunohistochemical features of intraductal breast carcinoma (including Her2/Neu overexpression), diffuse and strong GATTA 3 positivity is seen only in salivary duct carcinoma and mammary analog secretory carcinoma^[11]

which were excluded on the basis of histomorphological features favoring metastasis from breast primary.

The role of metastasectomy in metastatic breast cancer is not so clear like in renal cell carcinoma or soft tissue and bony sarcomas where it has definite therapeutic benefit in oligometastatic disease. However, metastasectomy has been successfully performed for oligometastatic disease limited to the lung, bone, or brain.^[12] In case of unusual metastatic sites such as parotid, well-defined guidelines are lacking due to rarity of the situation, but the previous case-based management reports have clearly shown the role of parotidectomy followed by palliative therapy.^[13] In our case, in view of favorable molecular subtype (hormone-receptor positive and Her2/Neu negative status) with parotid as sole recurrent site and the previous literature search (which is although from case reports and small series), we went ahead with parotidectomy followed by change of hormonal therapy to the second-line agents on which patient achieved long-term recurrence-free survival.

Conclusion

Diagnosis of solitary parotid metastasis requires high index of suspicion, in the view that benign causes mimicking malignancy are far more common and leads to false diagnosis unless investigated properly. This holds more clinical relevance, especially with tumors, with favorable disease biology such as hormone positive status with Her2/Neu negativity. Metastasectomy followed by palliative therapy forms the backbone of treatment as far as existing literature is concerned although this treatment approach requires validation through large studies.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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