



Invasive Lobular Carcinoma of Male Breast Presenting with Cerebellar Metastasis

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Abstract

Breast cancer is very rare in males and constitutes only 1% of the diagnosed cancer. Of these, only 0.8% have a pathologic diagnosis of invasive lobular carcinoma (ILC). We present a case of ILC that presented with necrotizing cervical lymphadenopathy and brain metastases.

Background

Breast cancer is very rare in males and constitutes only 1% of the diagnosed cancers. Out of every 100,000 males in the United States, 1 dies of breast cancer. 90 to 93% of breast cancers in men are of invasive ductal carcinoma (IDC) subtypes, 2% are papillary and the rest are ductal carcinoma in situ (DCIS) [1,2]. Only 0.8% of the breast cancers in male are invasive lobular type (ILC) [2]. The most common presentation is a painless subareolar mass. There has been increasing incidence of male breast cancer [3]. This may be due to advancement in diagnostic modalities and higher suspicion for breast cancer in males than in the past. The median age of breast cancer diagnosis in male is 10 years later than in females (67-71) [4]. There are only 20 cases of invasive lobular carcinoma reported in the English literature with each one having a different presentation. The first official case report was published in 1989 [5]. This is the first known invasive lobular breast cancer in male patient presenting with cervical lymphadenopathy and having brain metastases at diagnosis.

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Case Presentation

A 63 year old male without significant past medical history presented to our for evaluation of a left neck mass which appeared 2 months earlier. He had the mass evaluated at another hospital and had a biopsy showing malignant cells of unknown origin. Initial evaluation was at the Ear, Nose, and Throat (ENT) clinic. Since the ENT doctor did not have access to outside medical records, the patient was discharged with orders for neck and chest CT with contrast, as well as image-guided biopsy for further evaluation. The patient came to the emergency room 2 months later presenting with enlargement of the neck mass, now extending from his left lateral neck to his anterior left neck. He reported development of erythema over the same area, for which he had been started on amoxicillin-clavulanate (Augmentin) days earlier. Computed tomography (CT) scan of the neck showed extensive left neck inflammation and necrotic lymphadenitis with phlegm on development in the lateral mid neck soft tissue. Patient was subsequently admitted and started on antibiotics. The next day the patient complained of dysphagia to solids and inability to breathe. Repeated neck CT showed interval development of a retropharyngeal fluid collection/abscess with possible involvement of the prevertebral space at the C4-C5 level, and new severe effacement of the airway at the level of C2-C3. In addition, the CT showed a likely neoplastic process involving lymph nodes in the left masticator space, parotid space (superficially and deep), and post styloidparapharyngeal space, as well the deep cervical musculature (left longuscolli), left lateral paraspinous musculature, and left prevertebral musculature, which appeared to enhance more avidly than on prior exam. ENT was consulted and the patient was noted to have edematous airway with retropharyngeal fullness. The patient was admitted to the ICU and started on dexamethasone for swelling as well as broad-spectrum antibiotics. However given absence of fever and other systemic symptoms per consulting ENT physician, suspicion for infection was low and proximity of the tumor to the retropharyngeal

edema may have explained presence of fluid. It was also suggested that incision and drainage of the fluid collection would carry a higher risk than benefit ratio. If the tumor was nearby, the wound may not have healed which may have precluded the ability to treat this patient with chemotherapy.

Image guided biopsy of the left neck mass was performed that was inconclusive. Immunohistochemistry (IHC) was also performed which showed positive CK7+ and Pancytokeratin tests, and negative CK20, S-100, Mart-1, HMB45, TTF-1, p40 and synaptophysin tests. Flow cytometry was non-diagnostic. Since the patient never smoked and was P63 and P40 negative, squamous cell carcinoma of the head and neck was felt to be less likely. On repeat physical exam to look for the primary malignancy, an indurated left subareolar breast mass was noted. On further questioning, the patient claimed that the mass started to appear few days earlier. Meanwhile tissue biopsy of cervical lymph node was sent to undergo further staining given that differential was broad, with breast and salivary, or other ENT-related cancer, as the mostly likely primary malignancy. The second pathology read was; grossly, tissue appearing most similar to breast tissue. GATA3 was positive 1/20, further suggesting breast as primary origin. Hormone receptors were pending. However, given the aggressive nature of presentation and tumor burden, the patient was started on chemotherapy as an inpatient to more quickly address patient's primary symptoms with weekly paclitaxel and with possible endocrine therapy subsequently, pending further studies. Re-evaluation of pathology showed positive GATA3 and HER-2/neu (FISH for HER2 ratio; 4.2, average copy number 9.7), negative CK5/6, CDX2, PAX8, and E-cadherin.

Mammography of left breast showed and irregular asymmetry in the left breast central to the nipple in the anterior depth as well as skin and trabecular thickening. Left breast ultrasound showed multiple cysts and a 1.7 cm hypochoicretroareolar mass with associated nipple retraction. Ultrasound guided biopsy of the mass was subsequently performed, with pathology showing invasive lobular carcinoma with positive lymphatic invasion.

CT of the chest and abdomen was negative for malignancy or metastasis. MRI of the brain was performed that showed; at least 3 nodular foci of enhancement in the cerebellum in the following locations: right superior cerebellum (measuring 4.6 mm), left superior cerebellum (measuring 5 mm), and left inferior cerebellum (measuring 6.6 mm). FLAIR imaging showed T2 hyper intensities surrounding the aforementioned cerebellar lesions. The findings were consistent with development of bilateral cerebellar metastases, with surrounding vasogenic edema.

Computed tomography (CT) scan of the neck showed extensive left neck inflammation and necrotic lymphadenitis with phlegmon development in the lateral mid neck soft tissue.

Repeated neck CT showed interval development of a retropharyngeal fluid collection/abscess with possible involvement of the prevertebral space at the C4-C5 level, and new severe effacement of the airway at the level of C2-C3. In addition, the CT showed a likely neoplastic process involving lymph nodes in the left masticator space, parotid space (superficially and deep), and post styloidparapharyngeal space, as well the deep cervical musculature (left longuscolli), left lateral paraspinous musculature, and left prevertebral musculature, which appeared to enhance more avidly than on prior exam.

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Differential Diagnosis

Metastatic squamous cell cancer of head and neck.

Lymphoma.

Intrathoracic or intraabdominal malignancy with metastasis to the cervical lymph nodes.

Breast malignancy.

Given the aggressive nature of presentation and tumor burden, the patient was started on chemotherapy as an inpatient to more quickly address patient's primary symptoms with weekly paclitaxel and with possible endocrine therapy subsequently, pending further studies.

Discussion

Breast cancer in the male is rare, constituting only 1% of cancers. Invasive lobular carcinoma is also rare among breast cancers with a 0.8% incidence. This is likely because males normally do not have acini and lobular units in their breast tissue. Based on a meta analysis of seven case-control studies the risk factors associated with male breast cancers were; Jewish race, previous breast pathology, those that never married, gynecomastia, previous testicular pathology, liver disease and family history of breast cancer [6]. However, all these studies did not include other potential risk factors and no conclusion could be drawn based on other risk factors. Other risk factors reported in the literature include: Positive mutation for BRCA (especially BRCA2), obesity, use of medications (Methyldopa, digoxin and cimetidine), Klinefelter syndrome, previous thoracic radiotherapy, alterations of the estrogen-testosterone balance, and testicular disease [6-9]. Of note, BRCA2 mutations have been found to predispose men to breast cancer and may account for 4% to 14% of all cases [2] and Klinefelter syndrome is considered the strongest risk factor for male breast carcinoma. [10] The rate of cancer is slightly higher in the left breast, which happened to be the case in this patient [2]. Unless misdiagnosed with gynecomastia, male breast cancer presents earlier than in the female, [11] likely due to the scarcity of breast tissue and the retroareolar location of most cancers. Although there are some studies linking gynecomastia to increased risk of breast cancer, based

on one study, the possibility that many patients with breast cancer may relate their breast mass to gynecomastia is what falsely makes the gynecomastia a risk factor [7] and to date there is no study to definitively establish the connection. Estrogen therapy for other reasons has also been documented as a risk factor for breast cancer [1]. Unlike estrogen, progesterone therapy is not associated with breast cancer and there is only one case report with breast cancer reported in a male patient undergoing palliative treatment of prostate cancer with progesterone [1].

The median age of breast cancer diagnosis in males is 60, with typical presentation being a breast mass or nipple discharge. The patient's presentation in this case was at age 63. The fact that gynecomastia is also most commonly seen in this age group (60-69) could lead to late diagnosis. Unlike invasive ductal carcinoma (IDC) that has mass growth, ILC normally infiltrates between the breast tissue and presents with focal asymmetry or a large area of architectural distortion with density similar to surrounding breast parenchyma and rarely presents with a mass unless in advanced cases. Like any other breast cancer, ILC is also diagnosed based on biopsy of suspicious mass or asymmetry on mammogram or ultrasound. E-Cadherins are class of cell transmembrane proteins that function in cell adhesion, which when negative due to loss of expression are specific markers of invasive lobular carcinoma [12,13].

The age and stage of cancer-adjusted breast cancer survival for female and male patients are usually similar. Given that breast cancer is very rare in males and ILC is even rarer, there are no guidelines based on prior studies as to how we should treat these patients and most are treated the same as their female counterparts with radiotherapy being more beneficial in males due to small breasts and concomitant nipple involvement in most cases, also males are more likely to be hormone receptor positive with better response to hormonal therapy [2,14]. Our patient was negative for estrogen and progesterone receptor but positive for HER-2/neu overexpression. There is no cure for metastatic lobular carcinoma and most treatments are only palliative.

Lung and breast are the most common tumors that metastasize to the Central nervous system (CNS). The incidence of CNS metastasis in these patients is 10 to 40% [15, 16]. They are normally present in the late stage and are multiple in 78% of the patients [16] Most of the data for brain metastasis in breast cancer are derived from female breast cancer studies. Ataxia can be seen as a symptom with cerebellar involvement, which is rare. [16] The risk factors or brain metastases include estrogen and progesterone receptor negative tumors, HER-2 positive tumors, tumor size, aggressiveness and young age [15,17]. There are two proposed reasons for high incidence of brain metastasis in patients with HER-2 positive breast cancers, either due to failure of anti HER-2 medications to block receptors in the brain or amplified cancers with high intrinsic propensity to metastasize to the CNS [16]. Our patient was also HER-2 positive and had three metastatic lesions in the cerebellum on diagnosis.

Although the rate of breast cancer is increasing in males, which might be due to better diagnostic modalities or higher suspicion, there is no guideline as to how we should screen high-risk males for breast cancer. The only guidelines for breast cancer screening in males are in those patients testing positive for BRCA that also have gynecomastia should have annual mammograms [18].

Based on a few recent studies, there is no difference in ILC and IDC with regards to metastases to the liver, skin, local areas, bone

or brain. The only difference is that ILC metastasizes more to the gastrointestinal tract and less to lung compared to IDC; [19] however, the exact pattern for ILC is not known due to lower prevalence [20]. Also despite metastatic predilection to the GI tract for ILC, the patient did not have any GI symptoms and chest and abdominal CTs were negative for metastatic disease.

In summary, this is a rare case of ILC presenting initially as necrotic cervical lymphadenopathy and brain metastases. According to a population based study, the prevalence of breast cancer, the age at diagnosis, and being lymph node positive at diagnosis have increased [21].

Learning Points/Take Home Messages

- 1- ILC is a very rare in male patients.
- 2- The initial presentation could be cervical lymphadenopathy.
- 3- Even though, extremely rare, the number of cases of breast cancer among older male population is increasing and in the ABSENCE of other findings, the breast should be part of the physical exam of male patients with unknown primary cancer metastatic to the cervical nodes

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