European Review for Medical and Pharmacological Sciences 2017; 21: 4124-4128

Axillary ectopic lobular carcinoma of breast: two rare case reports

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Abstract. – OBJECTIVE: The presence of ectopic or supernumerary breast tissue is a rare event, related to a not complete regression of breast tissue along the milk line. Primary ectopic breast cancer of the axilla can create many difficulties in differential diagnosis with subsequent delayed specific treatments.

The incidence of ectopic breast tissue is 0.2-6%, and the axilla is the most common site involved. In this tissue, the same physiologic and pathologic changes as seen in ectopic breast tissue may occur, including carcinoma formation.

PATIENTS AND METHODS: Two patients (a 56 years old and 70 years old women) came to our attention for the recent development painless nodular axillary lesions, clinically characterized by an increased thickness, irregular margins and adherence to the floors below.

RESULTS: Patients underwent ultrasonography (US) and mammography (MMG) revealing non-specific features of the lesions. Magnetic resonance imaging (MRI), demonstrated margins slightly irregular and a non-specific appearance of each lesion. Both patients underwent wide local excision with axillary lymph node dissection. Histological examination showed infiltrating lobular carcinomas of the breasts.

CONCLUSIONS: We describe two unusual cases of ectopic axillary breast carcinoma localization. It is important a correct and fast diagnosis with a local examination, diagnostic instruments, surgical excision and histological examination.

Key Words:
Lobular carcinoma, Ectopic, Axillary, Breast.

Introduction

The possible development of breast cancer in peripheral and/or atypical locations produces a range of issues both diagnostic and surgical procedures. The presence of ectopic or supernumerary breast tissue is a rare event. In almost all cases we may find this breast tissue along the *milk line*. These structures are bilateral ectodermal ridges extending from anterior axillary folds to inguinal folds. During embryogenesis, they regress, except for the thoracic region, where they form the breasts. When the regression fails, ectopic breast tissue (EBT) develops, and axilla is the most common site of localization[1,2]. The incidence of EBT is 0.2-6%, being higher in Asians than in Caucasians[3,4].

The axilla is most frequently involved (70%), and the glandular tissue is located in the subcutaneous tissue and deep dermis. This condition can become clinically evident mainly under hormonal stimulation, such as occurs at puberty, during pregnancy and lactation. Its presence may cause pain, restriction of arm movement whenever located in the axilla, cosmetic problems, and anxiety. Symptoms such as swelling, tenderness and, sometimes, secretion often appear during puberty, pregnancy or lactation[5]. In this tissue, the same physiologic and pathologic changes as seen in eutopic breast tissue may occur, including carcinoma formation[5,6]. Ectopic breast carcinoma is well-documented in the literature, but is still a rare malignancy worldwide, and diagnosis is commonly delayed. We describe two cases of ectopic axillary breast carcinoma diagnosed on excisional biopsy and axillary dissection. Especially in the first case, the lesion was not localized along the milk line; it was at the center of the axillary pyramid, a rarely reported location that creates many difficulties in differential diagnosis. The histopathological findings and surgical treatment are described below.

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Case Report

In January 2014, a woman of 56 years noticed a nodule in the right axilla some months before. The patient was examined at another hospital where she underwent local examination and bilateral ultrasound examination. The US revealed a hypoechoic homogenous mass (0.4 x 0.6 x 0.9 cm) with irregular margins in the right axilla. No mass was found in either breast. The tentative diagnosis was a benign mass in the right axilla. A wait-and-see policy was taken. This injury aroused concern in the patient who has come to our attention for further specialist examination. The lesion was at the level of the right axilla, appeared with increased thickness, irregular margins, not painful, and it was fixed to the floors below. The US examination was substantially similar to that executed a few weeks prima. The patient underwent mammography (MMG) and magnetic resonance imaging (MRI). MMG showed no lesions or microcalcifications in either breast or axilla. The MRI showed the injury at the level of the right axilla, with slightly irregular margins, and a non-specific appearance is showed it to slightly hypointense mass on T1-weighed images, a hyperintense mass on T2-weighed images. The diagnostic delay, in this case, was 24 months due to the underestimation of the patient herself and of diagnostic error.

A wide local excision, 3 cm in each direction around the biopsy site, with axillary lymph node dissection was performed. Macroscopically, no tumor nests were found. The surgical specimen consisted of post-excision skin, subcutaneous tissue, and a portion of the right thoracic wall. Histological examination showed an infiltrating lobular carcinoma of the breast (Figure 1). Immunohistochemical staining for E-cadherin was negative, while that for human milk factor was positive. The positivity of the receptors for estrogen is 75% of the neoplastic cells. The progesterone receptors positivity is of 80%. The immunoreactivity for Her-2/neu is 15% of the neoplastic cells. The proliferation index evaluated by Ki-67 is equal to 2%. Among the two lymph nodes sent to the pathologist as sentinel lymph nodes, all were free of disease.

The cancer was completely excised. Postoperatively, the patient received hormonal therapy until today. The patient has remained free of disease for 1 years 4 months after the operation.

Currently, the patient is in both local and general good physical condition.

Our second case is a woman of 70 years of age who presented to us in July 2014. The patient was brought to our attention at the Department of Plastic Surgery of Umberto I Polyclinic of Rome, affected by two lesions in both the right and left axilla. The lesion on the right appeared about 13 months ago; the patient discovered this injury fingering in the shower. She underestimated it, thinking it was a mild and temporary problem, like an inflamed lymph node. In the months following the lesion increased in size and consistency.

This lesion was at the center of the axillary pyramid, its size of 1.5 x 1 cm, the skin covering it appeared retracted, at palpation is adherent to the underlying tissues.

The lesion in the left axillary, however, appeared pigmented, measuring 1.5 x 1 cm, along with the anterior axillary line, warty appearance, at palpation is movable in the above and below floors.

Ultrasonographic examination revealed a hypoechoic homogenous mass (1.5 x 1 x 0.7 cm) with irregular margins in the right axilla. No mass was found in either breast.

The patient underwent mammography (MMG) and magnetic resonance imaging (MRI). MMG showed no lesions or microcalcifications in either breast or axilla. The MRI showed the tumor at the level of the right axilla, with margins slightly irregular, and a non-specific appearance. It showed a slightly hypointense mass on T1-weighed images, a hyperintense mass on T2-weighed images.

Surgical excision was performed for both injuries. Histological examination of the right lesion showed an infiltrating lobular carcinoma of the breast, with marked desmoplastic reaction (Figure 1).

Immunohistochemical staining for E-cadherin was negative, while that for human milk factor was positive. The positivity of the receptors for estrogen is 90% of the neoplastic cells. The progesterone receptors positivity is of 85%. The immunoreactivity for Her-2/neu is 10% of the neoplastic cells. The proliferation index evaluated by Ki-67 is equal to 3%. Cancer came on one of the surgical margins. For this reason, the patient was subjected to surgery of enlargement to obtain a complete surgical radicality. A wide local excision, 3 cm in each direction around the biopsy site, with axillary lymph node dissection was performed. Macroscopically, no tumor nests were found. The surgical specimen consisted of post-excision skin, subcutaneous tissue, and a portion of the right thoracic wall, measuring 6x4x2 cm. There was no residual tumor with a clear-cut margin. Among the four lymph nodes

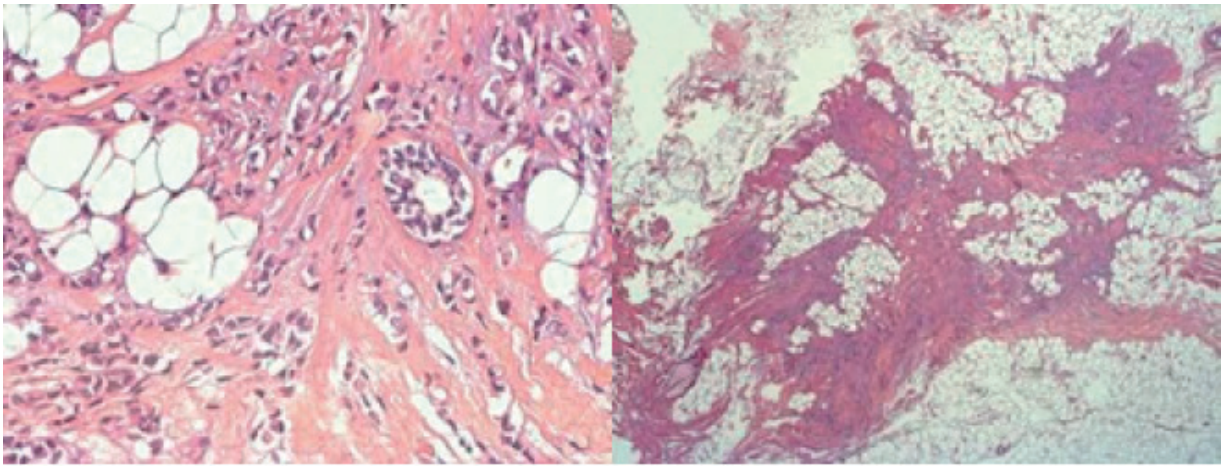

Figure 1. Histological examination. At the histological examination is observed within the breast parenchyma infiltration by neoplastic cells, now isolated, now in the supply chain, with eccentric nuclei, irregularly shaped, with the occasional presence of perinuclear vacuoles, and eosinophilic cytoplasm (300 ×).

sent to the pathologist as sentinel lymph nodes, one with a diameter of 0.9 cm is the site of metastases (pN1a). Additional lymph nodes, however, appear free from repetition tumor. The left lesion was a type of hyperkeratotic seborrheic keratosis, and it was completely excised. The patient has no family history of breast cancer. The only important note of her medical history was an adenocarcinoma of descending colon surgically treated in 2010. Postoperatively, the patient underwent adjuvant radiotherapy and hormonal therapy. She has remained free of disease for 11 months after the operation. Currently, the patient is in both local and general good physical condition.

Discussion

Accessory breast tissue is a relatively common occurrence that a high incidence of being misdiagnosed. Potential accessory breast tissue in a patient merits further investigation by the clinician, as this tissue has the ability to undergo all the pathological changes of the normal breast and the presence of ectopic breast tissue may indicate underlying congenital anomalies.

Primary ectopic breast cancer (PEBT) arises from aberrant tissue or supernumerary breasts. Its rarity also contributes to a low index of suspicion for the physician. PEBT is rare and estimated at 0.3% of all breast cancers[7]. For the pathologist, the diagnosis of mammary carcinoma arising in ectopic breast tissue can be difficult, especially in the axilla, where carcinoma of adnexal origin must be excluded. Evans et al[8] reported that 71% of ectopic breast cancers occurred in the axilla. Marshall et al[9] reported that 58% were located in the axilla, 18.5% were parasternal, 8.6% were subclavicular, 8.6% were submammary, and 4% were vulvar. Because ectopic breasts are located most frequently in the axilla, ectopic breast cancer must be distinguished from other subcutaneous masses arising in this location. The most common axillary abnormality was lymphadenopathy associated with benign or malignant disease[10,15]. Moreover, PEBC in the axilla may be misdiagnosed as a lipoma, enlarged lymph node, sebaceous cyst or as hidradenitis suppurative.

The diagnosis of PEBT of the axilla is not always thought of and is, therefore, often delayed. From the available data, the calculated delay was 40.5 months on average[15].

The patient normally consults the physician for the presence of an axillary mass with the following features: persistent unilateral growing subcutaneous/dermic nodule previously misdiagnosed, irregular, firm and not tender, red and painless, without any local symptoms associated. In most cases, the general condition of the patient is good. The presence of a subcutaneous mass along the milk line with the clinical features described above should provoke a high suspicion for PEBC, and this disease should be ruled out first[16]. It is more difficult to suspect this type of malignancy when it is apparently beyond the milk line, as in this case. Ultrasound is the first diagnostical step[17]. The presence of a hypoechoic, not well-defined heterogeneous mass (differential diagnosis: sebaceous cyst), without signs of inflammation such as in hidradenitis, is suspicious[18].

Mammography may add further information, for the evaluation of the axillae (microcalcifications) and both breasts[19]. In the case of a suspicious lesion, fine-needle aspiration biopsy (FNAB)/core biopsy of the axillary lump should be performed to harvest cells/tissue for histologic diagnosis[20].

If a PEBC in the axilla is diagnosed, the regular work-up guidelines for BC should be followed[21]. The contralateral axilla should be examined in detail as should be the eutopic breasts. A contrast-enhanced computed tomography (CT) scan and/or magnetic resonance imaging (MRI) might be useful in defining the dimension and the extension of the tumor before surgery.

Histologically, the lack of lymph node tissue and the presence of adjacent normal breast ducts and lobules are required to confirm the diagnosis of ectopic breast carcinoma and to exclude the possibility of a metastatic tumor arising from an occult primary lesion[12]. Mammary glandular tissue interspersed among adnexal glands anatomically suggests an origin other than pectoral breast tissue[13]. Most reported cases have involved invasive ductal carcinoma not otherwise specified (NOS) (72%), but other types, such as medullary, papillary, and lobular carcinomas, have been described. Our two patients have both been affected by lobular carcinoma, therefore, is a very rare clinical entity[22-24].

Regarding the surgical procedure, Cogswell and Czerny[14] reported the following findings: on autopsy of patients who had ectopic breast cancer and died of distant metastases, there was no evidence of infiltration or metastasis to the breast on the side of the primary tumor, even in the presence of extensive metastatic lesions to the skeletal system, pleura, and suprarenal bodies[22-26]. No breast involvement was seen even on radical mastectomy in patients with distant metastases. Early recurrence has been reported after radical mastectomy as well as wide local excision. For these reasons, they concluded that local excision combined with axillary dissection was the surgical procedure of choice. Evans and Guyton[8] suggested in their review that radical or modified radical surgery offered no advantage over local excision combined with axillary dissection or radiation with respect to outcomes[24-26]. They analyzed a total of 90 cases of carcinoma of ectopic breast tissue, 64 of which occurred in the axilla. The combined survival beyond the 4-year post-treatment period was 9.4%. The outcome was reported in 42 cases; 28 survived longer than 1 year, with 12 recurrences at the time of reporting, and 6 were alive with no evidence of disease at 4 years or longer.

Being cancer difficult to diagnose, often the local situation is at an advanced stage. The tumor may have metastasized elsewhere, thus reducing the survival rate.

The most recent review did not identify typical local issues or specific symptoms, so is the experience of the clinician to be able to guide the diagnostic process. Ectopic breast cancer does not appear to carry a poorer prognosis than usual breast cancer, given similar disease stages. However, further studies are needed to assess long-term survival.

Conclusions

The primary ectopic breast cancer of the axilla is a very rare clinical entity. It is very easy to underestimate this cancer, especially in women, their underarms are often affected by benign and transient problems, such as inflamed lymph nodes after shaving. We raccommend a careful examination of the local breast, axillary breast extensions, and both armpits. If the lesion has atypical features, the primary ectopic tumor should be immediately suspected.

We must quickly make a diagnosis, as the PECT of the axilla is a tumor with a low survival rate due to diagnostic delay.

Acknowledgments

Each author participated sufficiently in the work to take public responsibility for the content. Special thanks to Dr. Franco Bartolomei for his help in preparing this manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest.

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