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Case Study

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LARGE-CELL NEUROENDOCRINE MAMMARY CARCINOMA OF THE BREAST: CASE REPORT AND LITERATURE REVIEW OF A RARE ENTITY IN MOROCCO

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ABSTRACT

Large-cell neuroendocrine carcinomas of the breast are extremely rare entities, and very few cases have been reported in the literature to date. The incidence of this histological type varies between 2 and 5% of breast cancers, and it is often diagnosed in elderly patients and rarely in young ones. Diagnosis is based on immunohistochemistry, and treatment of localized stages is based on surgery, chemotherapy and radiotherapy. We report the case of a 38-year-old woman, with a review of the literature on histology and treatment.

KEYWORDS: Large Cell, Neuroendocrine Carcinoma, Breast.

INTRODUCTION

Neuroendocrine tumors (NETs) are a group of tumors that can arise anywhere in the body.[1] Neuroendocrine carcinomas mainly affect the respiratory and gastrointestinal tracts.[1] Mammary localization is rarer, accounting for 2-5% of breast tumors.[2] The diagnosis is confirmed by immunohistochemistry, and review by an expert center is recommended. Management is similar to that of other histological types, and consists of systemic treatment with anthracycline and taxane; surgery, radiotherapy and hormone therapy in localized situations. We report here a case of neuroendocrine carcinoma of the breast in our center, in a young, non-menopausal woman

CASE REPORT

Our patient is 38 years old, non-menopausal, with no particular history. She had self-cancelled a right breast nodule six months prior to her first consultation. Clinical examination revealed a 4 cm hard, painless nodule in the internal quadrant without axillary or supraclavicular adenopathy. Ultrasound mammography revealed a right breast lesion at the junction of the internal quadrants measuring 20 mm with suspicious homolateral axillary adenopathy classified as Birads.[5] A complementary bilateral axillary ultrasound found no axillary adenopathy. A microbiopsy revealed a breast carcinoma with SBR grade II neuroendocrine appearance (3+2+2) on anatomical pathological and immunohistochemical examination. A chest X-ray and abdominopelvic ultrasound revealed no secondary lesions. The tumor was classified cT1cN0M0. The patient underwent total right mastectomy + axillary curage.

Anatomopathological examination of the surgical resection specimen described a morphological appearance and immunohistological profile of a large-cell neuroendocrine carcinoma of the breast measuring 3.3 cm long with SBR grade III (3+2+3), with the presence of extensive intraductal carcinoma of intermediate nuclear grade; presence of vascular emboli; non-tumoral lateral and deep surgical margins.

Axillary lymph node dissection revealed one invaded lymph node out of 12 (1N+/12N) for a tumour classified as pT2N1aMx 80% estrogen receptor (ER) positive and 0% progesterone receptor (PR) with HER2- (score 0).

A thoracoabdominopelvic CT scan found no distant secondary lesion. The decision to initiate additional treatment with adjuvant chemotherapy combined with radiotherapy and hormone therapy was validated at a multidisciplinary consultation meeting. The patient underwent six sequential courses of adjuvant chemotherapy (3 courses of anthracyclines and 3 courses of taxanes), followed by curative radiotherapy to the wall, with irradiation of the sub- and supra-clavicular lymph nodes, with a total dose of 42 Gy at a rate of 2.8 Gy /fraction in 15 fractions. She has been undergoing adjuvant hormone therapy with Tamoxifen for 12 months, with no new lesions described on the evaluation thoracoabdominopelvic scan.

DISCUSSION

Neuroendocrine tumors (NETs) are a group of tumors that can arise anywhere in the body.[1] They have been described in other organs such as the thymus[4], stomach[5], cervix[6], colon and rectum[5], urinary tract[7], ovary[8], ampulla of Vater[9], salivary glands and corpus uteri.[10]

Primary neuroendocrine tumors of the breast are a rare histological form, representing less than 0.1% of all cancers. The incidence of these tumors is estimated by the World Health Organization (WHO) at between 2% and 5% of all breast cancers.[2] In the literature, incidence varies from 0.1% to 20%. One of the largest published series is that of Wang et al[11]: between 2003 and 2009, the authors identified 142 cases out of a total of 381,644 stage I to IV breast tumours in the US SIRE database, representing an incidence of less than 0.1% of invasive breast cancers over the same period. This tumour usually affects older women, between the sixth and seventh decades with a slightly higher mean age, but in rarer cases younger women.[12]

In 2003, the WHO classification divided neuroendocrine tumors into three groups: solid neuroendocrine carcinomas, atypical carcinoids, small-cell carcinomas and large-cell neuroendocrine carcinomas.[13] Large-cell neuroendocrine carcinomas are poorly differentiated tumours of high malignant grade.[14,15] The majority of cases have been described in women. Only a few cases have been reported in men. According to the WHO in 2012, this tumor results from early divergent differentiation of breast cancer stem cells into epithelial and neuroendocrine lineages, respectively.[16]

Mammary neuroendocrine tumors have no specific clinical features compared with other breast tumors. Clinically, they present as a palpable breast mass, most frequently a single mass, often larger than 2 cm (mean of 32 mm in the series by Wang et al.)[11], with or without associated adenopathies. The histogenesis of neuroendocrine tumors of the breast is still controversial. The theory adopted by the WHO in 2012 is that the tumor results from early divergent differentiation of breast cancer stem cells into epithelial and neuroendocrine lineages. The diagnosis of neuroendocrine nature is evoked on morphology and confirmed after immunohistochemical study with neuroendocrine markers on the basis of the diagnostic criteria reported by the WHO classifications.[13] Neuroendocrine cells in fact synthesize common neuropeptides (serotonin, calcitonin) and other specific neuropeptides such as "Neurone Specific Enolase (NSE), chromogranin A, synaptophysin"; useful markers for demonstrating the neuroendocrine nature of the tumour[16] and CD56. However, the expression of neuroendocrine markers is inconsistent, and the absence of expression of any of these markers does not exclude the diagnosis of NEC of the breast.

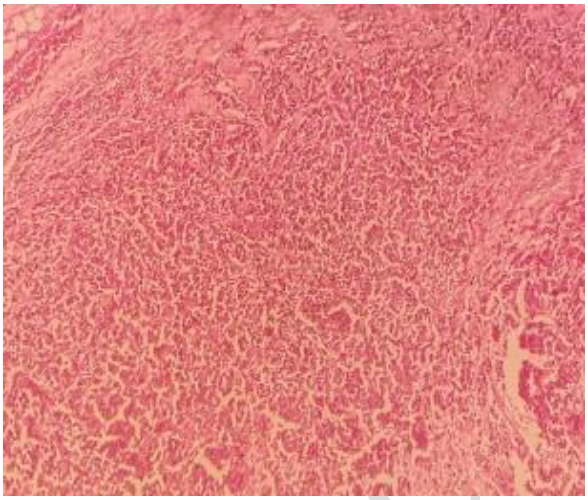

Figure 1: Microscopic pathology image showing neuroendocrine mammary carcinoma of breast.

According to the literature, however, the majority of neuroendocrine tumors do not express estrogen receptors (ER) and/or progesterone receptors (PR), but their presence makes the prognosis favorable, which may explain the patient's good evolution to date. Her-2 expression is rare.[17]

It should be noted that the expression of these receptors in the breast is not pathogenetic. The diagnosis of a primary large-cell NEC of the breast should only be made once another primary site has been ruled out, or if there is an associated ductal component in situ.[19] The expression of other markers may also be of diagnostic interest, such as CK7 and CK20. Coordinated expression of these two markers can also be used in breast NEC to rule out a non-mammary primary site.[18]

Due to the rarity of cases, there are no clear or codified recommendations concerning therapeutic modalities. From a therapeutic standpoint, there is no standard: neuroendocrine carcinomas of the breast are treated by some as classic breast carcinomas and by others as neuroendocrine carcinomas of the lung.[19] Treatment is essentially surgical[20] for localized stages. The indications for chemotherapy and radiotherapy are the same as for other breast cancers. There is no consensus on the choice of chemotherapy protocols. Etoposide and platinum salt are used in patients with high ki67 index or poorly differentiated small-cell carcinomas. Anthracycline- or taxane-based chemotherapy is mostly used when the ki67 proliferation index is low. Adjuvant hormone therapy is indicated in patients with a positive hormone receptor.[21]

CONCLUSION

Neuroendocrine tumors of the breast are rare and may be primary or secondary. Diagnosis of certainty is based on histological study, particularly immunohistochemistry. There is no standard treatment, and the prognosis may be difficult to determine in each situation.

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