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Neuroendocrine breast carcinoma metastatic to the liver: Report of a case and review of the literature



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ABSTRACT

INTRODUCTION: Primary neuroendocrine breast carcinoma (NEBC) is a rare entity of breast cancer.

PRESENTATION OF CASE: We herein report a case of right hepatectomy for a NEBC liver metastasis.

DISCUSSION: Little is known about its evolution, biologic behavior and optimal treatment. Its malignant potential has been addressed in few reports, with cases of metachronous metastases in diverse sites, even years following treatment of the breast primarily.

CONCLUSION: Treating this kind of cancer implies both breast and hepatic surgery.

Primary neuroendocrine breast carcinoma (NEBC) is a rare entity of breast cancer. Little is known about its evolution, biologic behavior and optimal treatment. Its malignant potential has been addressed in few reports, with cases of metachronous metastases in diverse sites, even years following treatment of the breast primarily. We herein report a case of right hepatectomy for a NEBC liver metastasis.

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1. Introduction

Primary neuroendocrine breast carcinoma was first described by Cubilla and Woodruff.¹ Several reports defined the common features of NEBCs according to macroscopic, histological and immunohistochemical findings.^{2,3} However, due to lack of unambiguous diagnostic criteria, the actual incidence remained unknown. According to the most recent World Health Organization (WHO) classification of breast and gynecologic tumors,⁴ their incidence is estimated, approximately, to 1% of all breast carcinomas.

2. Case report

A 51-year-old Caucasian female presented with a multilobulated 8.4 cm mass lesion in the liver (segment VII). The lesion was discovered in the context of follow up of surgically excised breast carcinoma of neuroendocrine differentiation (NEBC) 8 years ago. At that time she had undergone quadrantectomy of the left breast and ipsilateral axillary lymph node dissection. The primary tumor was an invasive low-grade (Grade III), T2N0M0 adenocarcinoma of neuroendocrine differentiation, with positive estrogen receptors, negative progesterone receptors and negative c-erb-B2. Initially,

the patient was treated with 6 cycles of chemotherapy consisting of cyclophosphamide-epirubicin-5FU and local radiotherapy, followed by endocrine therapy of 3 years tamoxifen switched to 2 years aromatase inhibitor (AI) and LH-RH analogue.

A multidimensional computed tomography (MDCT) of the abdomen was undertaken in the course of the annual follow-up, 8 years after the initial surgical treatment. A metastatic lesion in the right liver, invading segments VI and VII was revealed and confirmed through an abdominal MRI with iv contrast (Fig. 1a). The preoperative tumor markers CA-125, CA15-3 and CA19-9 were within normal ranges. The patient underwent a right hepatectomy and the histologic examination confirmed its neuroendocrine origin, exhibiting morphological similarities to the breast primary tumor. In particular, the histological picture was compatible with a large cell, grade 3 neuroendocrine carcinoma (Figs. 2–4). The tumor showed moderate cellular atypia, increased mitotic figures (>16/100 visual fields), foci of necrosis, as well as neoplastic vascular emboli inside the main tumor mass. Satellite lesions were presented close to the main liver mass, invading the portal tracts. Tumor cells were NSE (++) , synaptophysin (++) , CD56(++) , chromogranin (+) , CK(++) , ER(+) , PR(-) , cerbB2(-) , HepPar-1(-) , and TTF1(-) . The residual non neoplastic hepatic parenchyma showed focal mild sinusoidal dilatation, with mild focal cholestasis, moderate fibrosis and chronic inflammatory cellular infiltration of the portal tracts. Both histology and immunohistochemistry indicated that the liver mass represented a metastasis of the known breast carcinoma. The patient remains free of disease, 18 months postoperatively (Fig. 1b).

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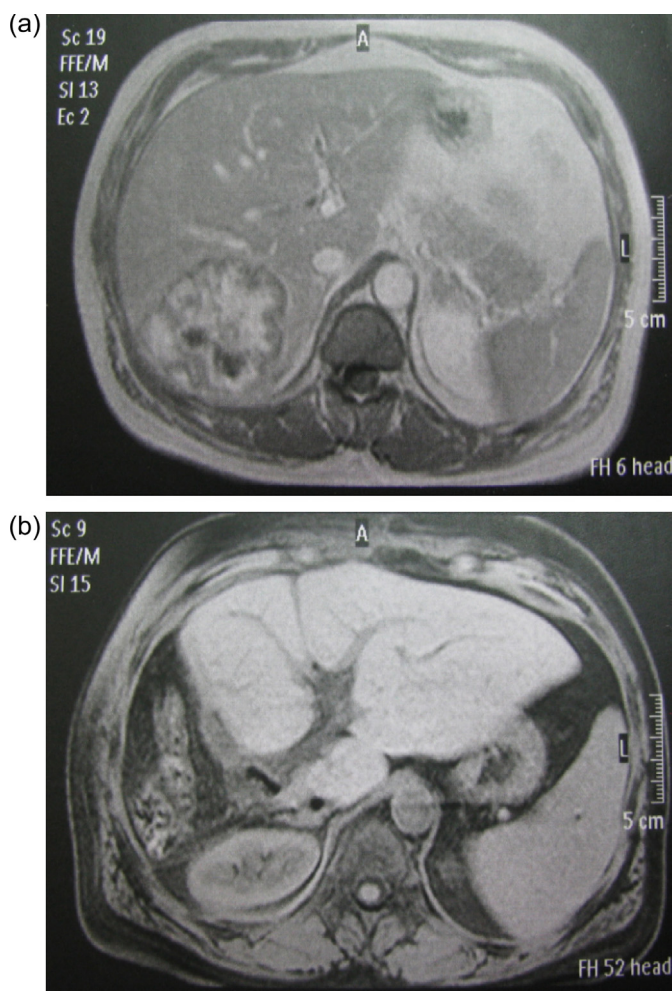


Fig. 1. (a) MRI abdomen–pelvis. (b) Post resection MRI.

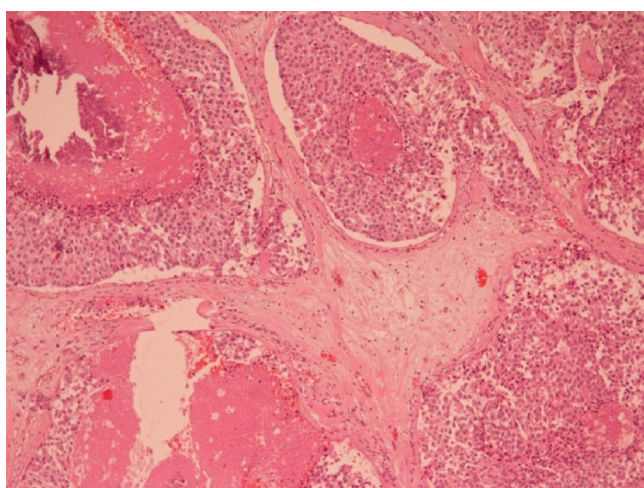


Fig. 2. Liver tumor with neuroendocrine differentiation and comedo-like necrosis, Hematoxylin–Eosin staining.

3. Discussion

The existence of neuroendocrine cells in normal breast epithelium is controversial.^{5–8} Since no hyperplastic or benign neoplastic neuroendocrine cell proliferations have been recorded in the breast, it has been suggested that NEBCs result from a divergent

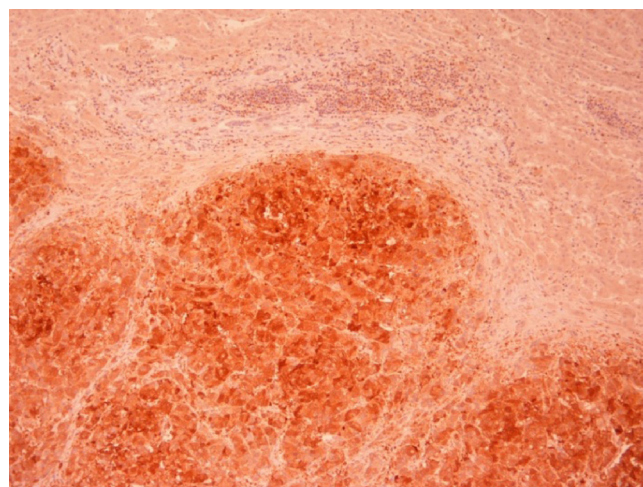


Fig. 3. Tumor cells are positive to NSE.

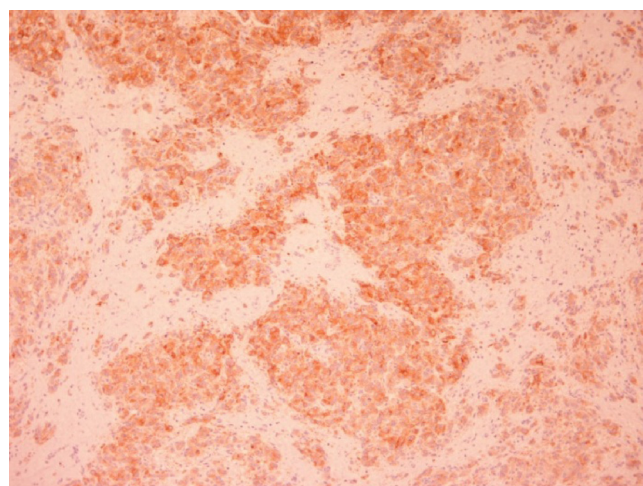


Fig. 4. Tumor cells are positive to synaptophysin.

differentiation event in breast cancer.⁹ The presence of an in situ component with NE characteristics, further supports this notion, suggesting possible progression to invasive forms.¹⁰ The in situ component along with the imaging modalities (excluding a non-mammary site) will further establish the primary nature of the NEBC.

The diagnosis of NEBC relies on the presence of morphologic neuroendocrine features and neuroendocrine markers expressed in more than 50% of tumor cells.⁴ The most sensitive and specific NE markers, are chromogranin A and B and synaptophysin. According to the above criteria, NEBCs constitute approximately 1% of all breast carcinomas. In 2012, the last edition of World Health Organization (WHO) classification of breast and gynecologic tumors, described 4 main histologic types: solid (usually of low to intermediate grade), small/oat cell and large cell, that are both poorly differentiated variants and lately added atypical carcinoid tumor.¹¹ In terms of prognostic and predictive factors, HER-2 is almost always absent in NEBCs, while the vast majority express estrogen and/or progesterone receptors. The prognostic relevance of neuroendocrine differentiation is controversial,^{12,13} though most studies report a relatively poor prognosis based on the extent of the neuroendocrine component and the degree of its differentiation.

In the literature, there have been reports about NEBCs metastasizing to multiple sites, even years following treatment of the primary breast tumor and despite the administration of systemic

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