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Case Report

Primary neuroendocrine carcinoma of the breast with paraneoplastic thrombocytosis; a rare case report

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ABSTRACT

Introduction: primary neuroendocrine cancer of the breast (NECB) is a very rare entity, comprising less than 0,1% of all breast tumors. It was first reported in 1977 by cubilla et al.
Case presentation: we report the case of a 60-year-old rural Syrian female who admitted to our hospital due to a painless lump in her right breast. Radiological & clinical findings were highly indicative of breast carcinoma. Therefore, a partial biopsy was performed and microscopic examination suggested the diagnosis of neuroendocrine carcinoma of the breast, which was confirmed by immunohistochemical staining. Lab findings were also indicative for anemia & thrombocytosis.
Clinical discussion: neuroendocrine tumors are usually seen in the intestine & lungs. However, their presence as primary tumors in the breast is extremely rare.
Conclusion: our article demonstrates a challenging case of primary neuroendocrine breast carcinoma with paraneoplastic thrombocytosis, which clarifies the major diagnostic & therapeutic approaches used in its management.

1. Introduction

Primary neuroendocrine cancer of the breast (NECB) is a very rare entity, comprising less than 0,1% of all breast tumors [1]. It was first reported in 1977 by cubilla et al. [2].

In 2003, NEBCs were considered a distinct pathological pattern by world health organization (WHO) & defined as tumors in which at least 50% of cells are positive for neuroendocrine markers [3]. In 2012, the WHO reclassified this tumor into the following: poorly-differentiated, well-differentiated & Invasive breast carcinoma with neuroendocrine differentiation [1]. Herein, we report a challenging case of primary neuroendocrine breast carcinoma in a 60-year-old Syrian female.

2. Case presentation

We report the case of a 60-year-old rural Syrian female who admitted to our hospital due to a painless palpable mass in her right breast; that was first noticed in the outdoor oncology clinic of our hospital during a routine check-up. Her medical history was unremarkable. Physical examination showed a painless mass in the upper medial part of the right breast with notable nipple retraction, in addition to localized redness of the skin (Fig. 1A). Lab findings were significant for anemia (Hgb of 10,8g/dl) & thrombocytosis (537 $\times$ 10^9/l). Breast ultrasonography (U/S) revealed a hypoechoic mass with heterogeneous content & irregular borders (Fig. 1B), localized at the upper medial part of the right breast, measuring 55 $\times$ 48 mm, as well as ipsilateral axillary lymphadenopathy. The left breast U/S was normal. Chest computed-tomography (CT) showed a mass in the right breast with ipsilateral lymphadenopathy, whereas CT of brain, abdomen & pelvis were normal. Clinical & radiological findings were suggestive for breast carcinoma. Thus, the patient underwent a partial biopsy that demonstrated a firm white lump, surrounded by some yellow adipose tissue. Microscopic exam showed nests of large round cells with mild pleomorphism and hyperchromatic nuclei in addition to some mitotic activity (Fig. 2A) & some foci of necrosis (Fig. 2B). Immunohistochemistry staining (IHC) was positive for chromogranin-A (Fig. 3A), cytokeratin (CK) (Fig. 3B), estrogen receptors

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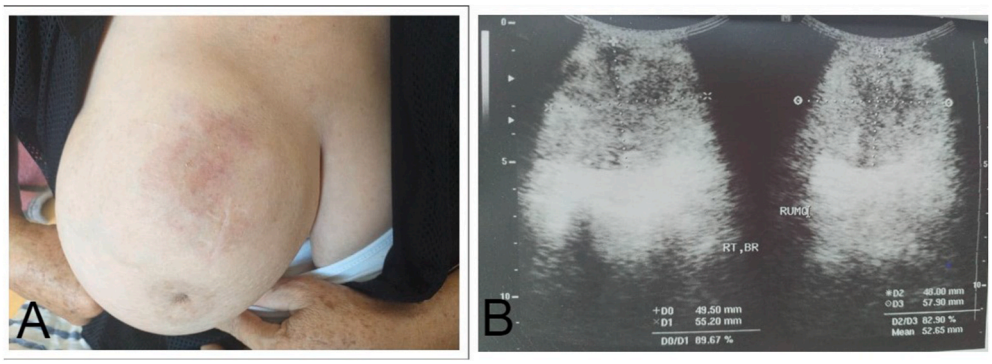

Fig. 1. (A) Gross image shows the nipple retraction & skin redness .(B) Right breast ultrasound shows hypoechoic mass with heterogeneous content, measuring 55x48mm.

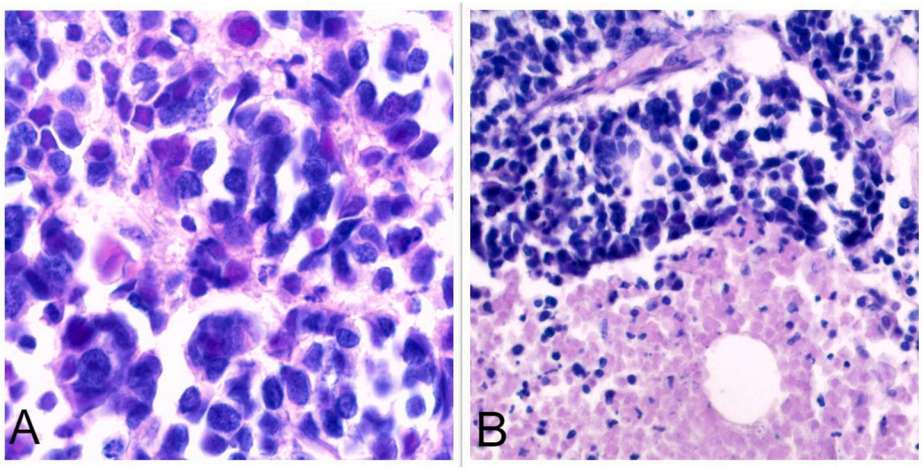

Fig. 2. (A) shows large round cells with mild pleomorphism and hyperchromatic nuclei in addition to some mitotic activity (H&E x400). (B) shows large round cells as well as foci of necrotic tissue (H&E x200).

(ER) (Fig. 3C), GATA-3 (Fig. 3D) & focally positive mammaglobin (Fig. 3E). Ki67~60% (Fig. 3F). On the other hand, IHC was negative for progesterone receptors (PR), Her2neu and LCA-CD45. This pattern confirmed our diagnosis of primary neuroendocrine carcinoma of the breast. Clinical TNM stage of T4N1M0 was given. The treatment plan was to start a neoadjuvant chemotherapy of etoposide & cisplatin, followed by radical mastectomy to be performed by a professional team of general surgeons in our hospital. The patient will be followed at periodic intervals of three months at the first two years. Then, at intervals of six months for the next three years.

3. Discussion

NEBC is a diverse group of malignancies, comprising of 2–5% of all invasive carcinomas of the breast [3]. According to 2012 world health organization (WHO) classification of breast tumors, the positivity of chromogranin A &/or synaptophysin is a unique feature of NEBCs. However, ER & PR receptors are positive in most well differentiated tumors as well as more than half of poor differentiated ones [4]. In Salemis, Nikolaos S article (2020), the differential diagnosis includes melanoma, lymphoma, Merkel cell carcinoma & metastatic neuroendocrine tumors to the breast [1]. It is essential to differentiate primary and metastatic neuroendocrine lesions of the breast, which can be achieved by positivity of GATA-3, mammaglobin & GCDFP15 in primary breast tumors [1]. Most cases of NEBC were among women in their sixth & seventh decades, especially among the whites [2]. The median size at presentation is 3.1 cm [1]. According to literature, 35% of patients with thrombocytosis (platelet count more than $400 \times 10^9/l$) have underlying malignancy [5]. This is due to excessive production of inflammatory cytokines such as IL-6, which implies a poor prognosis [5]. There are no special radiological or clinical features of this tumor (1 & 2). On U/S, this tumor presents as hypoechoic, irregular and non-demarcated mass [1]. The treatment of NEBCs is nonspecific and is similar to the treatment of ductal-type tumors. Therefore, surgery (partial/radical mastectomy) is the main treatment at early stages [6]. Chemotherapy formed of the combination of platinum agents and etoposide was recommended as a neoadjuvant therapy in non-operable or locally invasive tumors, or as an adjuvant therapy in tumors with high risk of recurrence [6]. Anti-hormonal therapy is useful in hormone receptor-positive tumors [6]. Most cases have a poor prognosis as they tend to be diagnosed at late stages [7]. Our work was reported according to the SCARE 2020 criteria [8].

4. Conclusion

Our article demonstrates a primary neuroendocrine breast carcinoma with paraneoplastic thrombocytosis & highlights the significant role of histological and immunohistochemical exams in confirming the diagnosis as well as the important role of neoadjuvant therapy to make the tumor operable as surgery remains the main treatment approach.

Ethical approval

Not applicable. It is a case report.

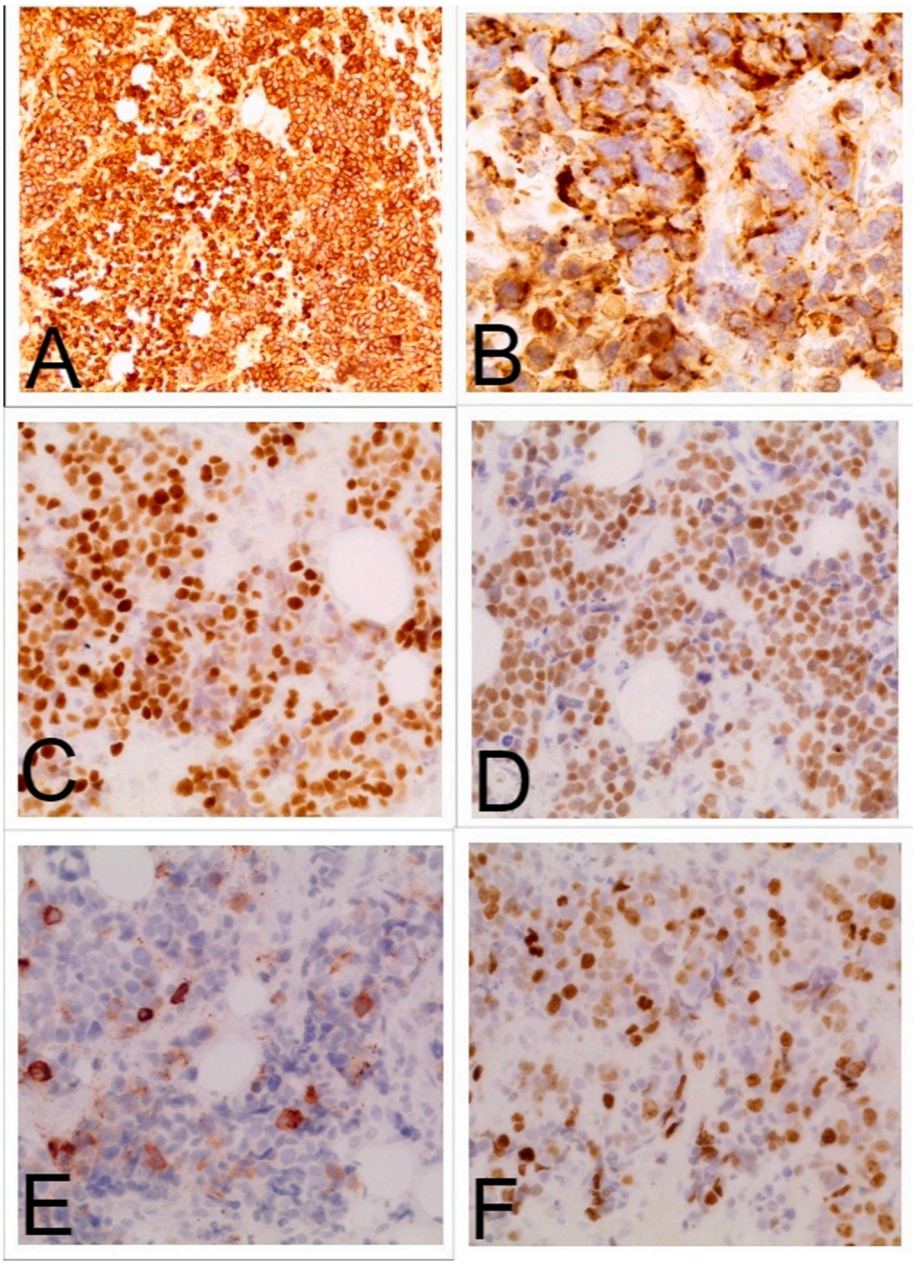

Fig. 3. Immunohistochemical staining shows positivity for chromogranin-A (A), CK (B), ER (C), GATA-3 (D), Mammaglobin (3E) & Ki67~ 60% (3F).

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Author contribution

HK: drafted the manuscript.

SA, SK & JS: collected the patient's data and participated in revising the article.

NZ: the oncologist: was in charge of the patient's treatment.

ZA: the guarantor and supervisor, performed and confirmed the pathological diagnosis and critically revised the article. All authors have read and approved the manuscript.

Research registration number

Not applicable. It's a case report.

Guarantor

Dr Zuheir Alshehabi.

Consent

We have obtained a written informed consent from the patient.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

No conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103664.

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