Case report:

Neuroendocrine Tumour of the Breast in a Young Lady: A Case Report

Zainal Adwin Zainal Abidin[1], Firdaus Hayati[2], Nornazirah Azizan[3], Jasmin Jaszle Saladina[4]

Abstract:
Primary neuroendocrine tumours of the breast are rare. The WHO has classified them according to the tissue grading. The clinical presentation is similar to the usual infiltrating ductal carcinomas, however the histopathological assessment requires special staining to confirm the diagnosis of neuroendocrine tumour. We report a case of a primary neuroendocrine tumour of the breast in a 33-year-old lady who presented with a locally advanced breast tumour with multicentric disease.

Keywords: Neuroendocrine; breast; mastectomy; multicentric; immunohistochemistry

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Introduction

Neuroendocrine tumour is rare; however primary neuroendocrine tumour (NET) of the breast is even rarer. It was only categorized by the World Health Organization (WHO) in its tumour classification back in 2003[1]. Morphologically, primary NET of the breast has features similar to NET of the gastrointestinal tract and lung. They present clinically with a breast mass and is often wrongly diagnosed as infiltrating ductal carcinoma (IDC) from a core biopsy resulting in less effective neoadjuvant or adjuvant treatment regime. Recent immunohistochemical studies revealed that some typical IDC of the breast also show areas of neuroendocrine differentiation, however primary neuroendocrine tumours with lymph node involvement are still extremely uncommon[2,3]. We describe a case of primary NET of the breast in a young lady and its subsequent management.

Case Report

A 33-year-old lady was referred to our clinic with a complaint of a left breast lump for one month duration. It initially started with a throbbing pain and yellowish nipple discharge. She was treated symptomatically by another center and was subsequently referred to us. Physical examination revealed three palpable lumps in the lower quadrants with a diameter of 2cm, 1.8cm and 2.5cm respectively. The lumps were mobile, not fixed to skin or muscle with no skin changes. The nipple discharge was not reproducible at examination. There was also a large mobile and non-tender single lymph node at the left axillary region. The right breast was normal. She otherwise denied flushing, diarrhoea or respiratory difficulties to suggest of any primary pathology of NET.

Ultrasonography of the left breast showed multiple well-defined hypoechoic solid lesions in the lower quadrants with the largest being 2cm in diameter. In the axilla, there was a 2cm enlarged lymph node with suspicious features. An ultrasound-guided core biopsy of the axillary mass and the suspicious breast lesion was performed. The biopsies were consistent with a neuroendocrine carcinoma of the breast.

In view of the multicentricity and positive axillary lymph nodes, the patient underwent a mastectomy

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and axillary lymph node dissection. Immediate breast reconstruction was offered initially but she refused. The tumour measured 1.5x1.5x0.5cm in dimension with 1 positive level I lymph node. Histopathological examination revealed a poorly-differentiated NET of the left breast displaying a densely packed solid nest of small round cells surrounded by desmoplastic stroma (Figure 1, 2).

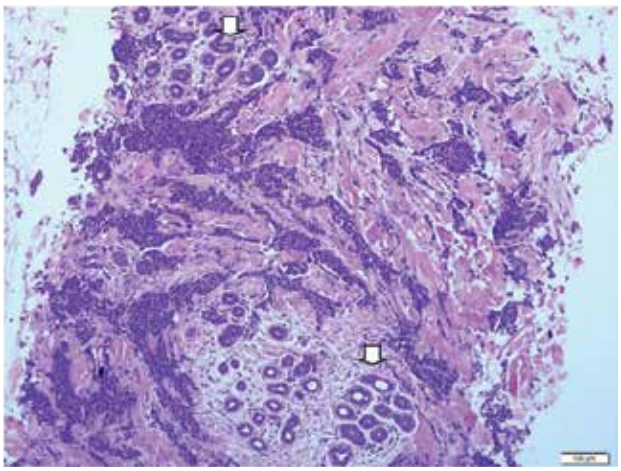

Figure 1: A breast tissue infiltrated by malignant cells composed of a densely packed solid nest of small round cells surrounded by desmoplasticstroma. Note the presence of benign breast acini (arrow). (Hematoxylin and Eosin, original magnification x10)

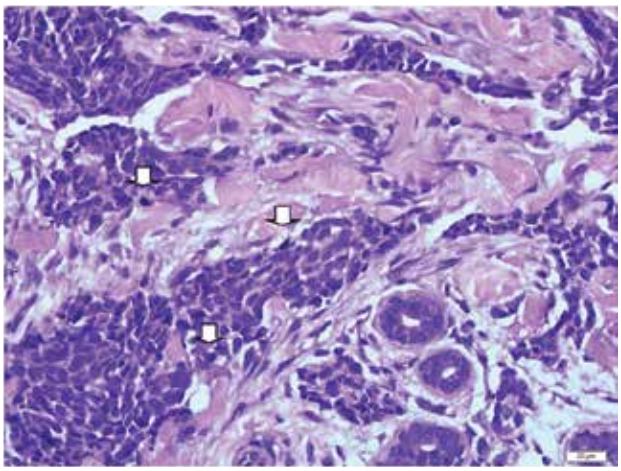

Figure 2: Higher magnification of tumor cells displaying round hyperchromatic nuclei with inconspicuous nucleoli and scanty cytoplasm. Mitotic figures are seen (arrow). (Hematoxylin& Eosin, original magnification x40)

Breast ducts and acini were seen lined by double layered epithelium and myoepithelium. No evidence of IDC or ductal carcinoma in situ seen. The tumor cells showed immunoreactivity towards synaptophysin and chromogranin A (Figure 3a, 3b). Other positive markers include progesterone and estrogen receptor (Fig. 3c, 3d). Ki67 markers revealed a high proliferating rate of 25% [Figure 4].

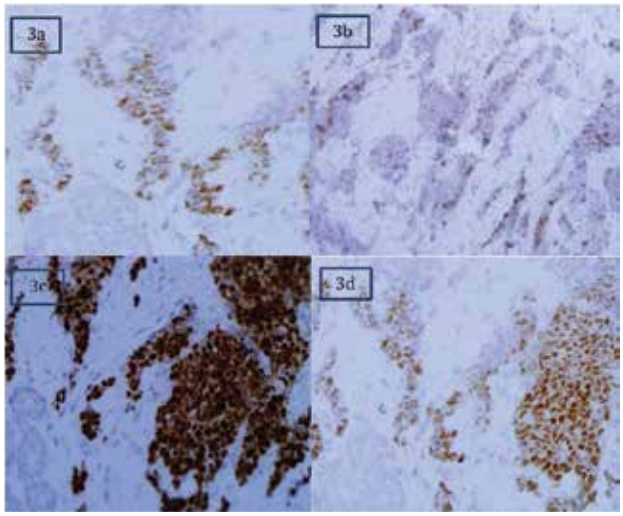

Figure 3: Immunohistochemical studies show the malignant cells are positive for (a)chromogranin A, (b) synaptophysin, (c) progesterone receptor and (d) estrogen receptor.

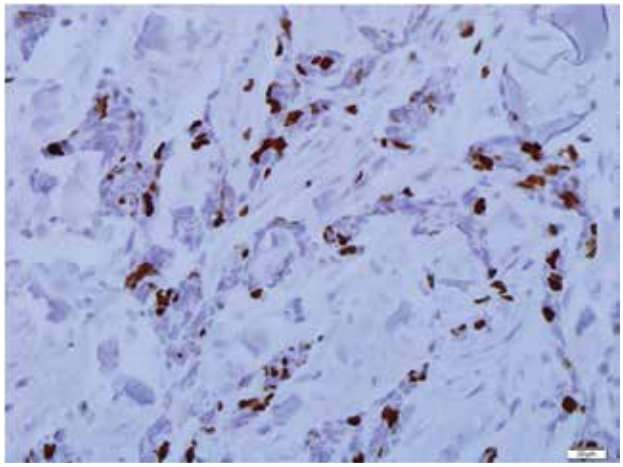

Figure 4: Note that the tumor cells are highly proliferating with ki67 proliferation rate of 25%.

Her recovery was uneventful as she underwent an adjuvant chemotherapy of cisplatin and etoposide and radiotherapy to the chest wall. At one year follow-up, she had no evidence of local recurrence and metastasis both clinically and radiologically.

Ethical Clearance:

This case report was submitted for publication after getting Ethical approval from the Ethics Committee of the Universiti Malaysia Sabah, Sabah, Malaysia

Discussion

Cubilla and Woodruff first reported 8 cases of neuroendocrine breast tumours back in 1977[4]. It was only until recently that the WHO recognized it as a distinct entity. It is defined as tumours that exhibit morphologic similarities as NET of the gastrointestinal tract and lung. To fulfill the diagnostic criteria, these tumours need to express

neuroendocrine markers which are chromogranin A and synaptophysin in more than 50% of the cell population[1].The WHO has classified NET of the breast into three categories: well-differentiated NET, poorly-differentiated/small cell carcinoma and invasive breast carcinoma with neuroendocrine differentiation[5].Solid neuroendocrine breast tumours are rare with an incidence of only 0.27% in series of 1845 histopathologically proven breast carcinomas as reported by Guenhan-Bilgen Iet al[6]. They occur most commonly in elderly women but rarely there are some reports of occurrence in male patients[7].

Well-differentiated neuroendocrine carcinomas typically consist of dense and solid nests of cells with large clear cells separated by a fibrovascularstroma. The cells are of uniform population displaying round nuclei with nuclear palisading and salt-and-pepper chromatin with eosinophilic cytoplasm. They may appear to grow in nests and resemble ductal breast carcinomas or to grow in strands and resemble lobular breast carcinomas[8]. It is crucial to rule out secondary NET from other primaries namely gastrointestinal and lung mostly as the morphologic similarities between them.

Any breast pathology needs to undergo triple assessments which include imaging modalities and cytology or histology. There are no specific clinical features or imaging appearances to confirm the diagnosis, but eventually surgery is the last resort. On ultrasound, it can appear as irregular hypoechoic solid masses with cystic components and some of them have posterior acoustic enhancement[6]. Upon mammography, it appears as sharply demarcated, non-spiculated margins with hyperdense mass[6]. These features are contrast with typical appearances of invasive ductal carcinoma on mammogram.

Neuroendocrine breast tumours are thought to arise from endocrine differentiation of breast carcinoma instead of preexisting endocrine cells with malignant transformation. However, the exact histogenesis remains dubious. As described earlier, neuroendocrine markers positivity are requisite to make the diagnosis. Other important aspect of histological analysis include Ki67 marker to prognosticate the patient histologically. Besides, cellular differentiation or grading, estrogen and progesterone receptor status are paramount indicators for subsequent choice of treatment.

Since there are only few published cases before, there is no established standard treatment protocol for breast NET. Primarily, the treatment is similar to the conventional infiltrating ductal carcinoma by following TNM classification and stage. Surgery undeniably is still the primary goal of treatment. Patients with poorly-differentiated NET have been treated with chemotherapy regimens of cisplatin-etoposide and paclitaxel-carboplatin[9]. There are commonly used in small cell lung cancer, gynecological cancers and melanoma[9]. Similarly, our patient used the same chemotherapy regimen as adjuvant therapy.

Since our patient has a poorly-differentiated NET of the breast, conspicuously it carries a guarded prognosis. The risk of local recurrence and metastasis are higher compared to other breast NET subtypes. Despite of having negative disease upon one year of follow up, the need for self-breast examination is extremely important. Counselling and motivation are essential as well for psychological support especially in breast cancer survivors.

In conclusion, the rarity of NET of breast is undeniable; there are no prospective cohorts or randomized controlled trials performed before. Its long-term prognosis and biologic behavior are still up for discussion. Larger number of cases should be collected and researched to determine a formal prognostication tool and outcome analysis to guide treatment regimes.

Conflict of interest: None declared

Authors' Contributions:

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Writing and submitting manuscript: Zainal Abidin ZA

Editing and approval of final draft: Zainal Abidin ZA, Hayati F

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