

Is Imaging Helpful in the Diagnosis of the Primary Neuroendocrine Carcinoma of the Breast?

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Citation: Sheoran N. Is Imaging Helpful in the Diagnosis of the Primary Neuroendocrine Carcinoma of the Breast? J Rare Dis Diagn Ther. 2015, 2:1.

Abstract

Invasive carcinomas of breast constitute a heterogeneous group of lesions in terms of their clinical presentation, radiographic characteristics, pathological features and biological behaviour. The classification is mainly based upon character of growth pattern and cytological features. The radiological findings usually overlap with other invasive types resulting in the under diagnosis of these tumours. Hence, suspicion of primary NEC of breast should prompt immunohistochemical confirmation for appropriate diagnosis. Although appearance on mammography, sonography and MRI could help differentiate these tumours from other malignancies but still histological features with immunohistochemical markers remain the benchmark to confirm these tumours.

Keywords: Neuroendocrine carcinoma; Sonography; Mammography; MRI

Received: November 01, 2015; **Accepted:** December 10, 2015; **Published:** December 17, 2015

Background

Breast cancer is the most common cancer in women and second most common cause of cancer related death. Invasive carcinomas of breast constitute a heterogeneous group of lesions that differ with regard to their clinical presentation, radiographic characteristics, pathological features and biological behaviour. Initially, it was classified based on the morphological features on light microscopy. Currently, the classification is mainly based upon the character of growth pattern and cytological features. The primary neuroendocrine carcinoma of the breast is a rare histology which is yet to be understood., Invasive breast cancer expressing one or more neuroendocrine markers in >50% of cancer cells with evidence of an in situ component is the standard diagnostic criteria of the primary neuroendocrine carcinoma of the breast as per the WHO. It also requires that other primary sites have been ruled out [1].

Imaging of the Primary Neuroendocrine Carcinoma of the Breast

The biological behaviour, treatment approach and prognosis have still not been studied due to its rare presentation. Due to lack of adequate literature, the imaging characteristics were

described in many case reports and series [2, 3]. The influence of neuroendocrine differentiation to the radiologic features is not clear.

Ultrasonography

Primary NEC of breast presents on sonography as an irregular and ill-defined solid lesion with or without cystic component and with increased peripheral vascularity. It is a hypo-echoic mass without posterior enhancement [4]. These features seem to be similar to other invasive carcinoma breast. The other suspicious findings are angular margins, marked hypo-echogenicity, shadowing, calcifications, duct extension, branched patterns, and microlobulation [5]. On colour Doppler, the mass shows increased vascularity. However, if any lesion on ultrasound appears to be a benign lesion, NEC should be considered as a differential diagnosis.

Mammography

The typical invasive breast cancer on mammography has an irregular shape, spiculated margins, and associated micro calcifications, but NEC may have high-density round, oval, or lobular

non-calcified mass with non-spiculated margins (e.g., circumscribed, obscured, microlobulated, or indistinct margins) [4]. It is supposed that the hormone receptor also influence the mammographic features. The lesions with non-spiculated margins or hyperdense masses are associated more with ER-negative breast cancer as compared to the ER-positive lesions which are irregular in shape and have spiculated margin. The triple negative cancers are most frequently round, oval or lobular and have indistinct margins [6, 7]. The neuroendocrine tumour of the common organs such as gastrointestinal tract and lung also have features similar to breast NEC such as the lack of spiculated margins on mammography and the lack of posterior shadowing on sonography. There is no difference in the appearance of primary tumour and metastasis from extra-mammary malignancies to the breast [8]. NEC with sharply circumscribed margins might mimic fibroadenomas, cysts, or intramammary lymph nodes on mammography leading to under diagnosis in 1% to 3% of these cases [2, 9]. Interestingly, tumours with circumscribed margins are frequently high-grade [10].

Magnetic Resonance Image (MRI)

The primary neuroendocrine carcinoma breast may present with nipple discharge, mastalgia without any palpable lump and has higher incidence of bilateral, multifocal and multicentric disease. Typically, MRI shows mass lesions with initial rapid or medium enhancement followed by delayed wash-out on the kinetic curves of MR CAD imaging which suggests a malignant lesion [11, 12]. The synchronous contralateral cancer, multifocality, multicentricity, DCIS component, and skin invasion would be revealed and extent of primary lesion could be assessed better with the help of MRI.

Positron Emitting Tomography (PET) Scan

NEC breast has higher proliferative index compared to other

invasive carcinoma breast. Hence, these tumours can be identified by fluorodeoxyglucose (FDG) PET. The well-differentiated hormone-producing NE tumours are highly sensitive to PET tracer C11-5HTP which can identify tumour as small as 2 mm [13].

Somatostatin Receptor Scintigraphy (SRS)

The principle of somatostatin receptor scintigraphy (Octreoscan) is based upon the presence of the somatostatin receptors mainly subtypes 2 and 5 which are expressed on the surface of neoplastic cells. These tumours express these receptors in the range of 55–95%. SRS has diagnostic accuracy of 83% with 100% positive predictive value and has higher sensitivity than I-131-metaiodobenzylguanidine (MIBG) scan. It may be negative in highly proliferative poorly differentiated anaplastic NE tumours due to lack of somatostatin receptors. SRS has significantly improved the visualization of NE tumours at other sites especially for the well differentiated one [14].

Conclusion

The radiological findings usually overlap with other invasive types resulting in the under diagnosis of these tumours. Lack of the use of neuroendocrine marker in daily practice is yet another drawback. Hence, suspicion of primary NEC of breast should prompt immunohistochemical confirmation for appropriate diagnosis in each and every case. Although the radiologic findings on mammography, sonography and MRI could help differentiate these tumours from other malignancies but still histological features with immunohistochemical markers remain benchmark to confirm these tumours.

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