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How do I diagnose *Primary neuroendocrine tumor of the breast*

László Fónyad

Affiliation: 1st Department of Pathology and Experimental Cancer Research, Semmelweis University

László Piros, Gabriella Arató

Differential diagnoses: Primary breast carcinoma with neuroendocrine differentiation, Metastatic neuroendocrine tumor to the breast.

Abstract

Primary neuroendocrine tumor of the breast is a rare condition. Although 20-30% of primary breast cancers show neuroendocrine differentiation to some degree, according to the WHO classification, at least 50% of the tumor cells have to be positive with at least one neuroendocrine immunohistochemical marker to establish a diagnosis of neuroendocrine tumor of the breast while clinically excluding other primary sites and a metastatic nature. Due to the low prevalence of this disease our understanding of its development, prognosis and effective therapy is limited. Up to date there are 125 cases reported in the English and non-English literature, now including our own case as well. We report a case of a 75 years old female. The patient presented with a 2 cm large mobile nodule in the upper outer quadrant of the left breast. Lumpectomy was performed based on fine needle aspiration cytology with a positive result showing malignant proliferation. Examination of the surgical specimens revealed neuroendocrine differentiation in approximately 90% of the tumor cells. Immunohistochemical studies and additional imaging studies revealed no other primary.

Virtual Slides: www.diagnosticpathology.eu/vs/2016_2_101/

Anamnesis / History

A ~2 cm large nodule was found during regular breast cancer screening of a 75 years old female. FNAB was performed. Cytology showed atypical cells with moderate nuclear polymorphism, eccentric nuclei and occasinal nucleoli (Figure 1.).

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Gross - microscopic findings

A 20 mm large, whitish, firm, lobulated, relatively sharply demarcated nodule was found in the submitted surgical specimen.

Microscopy

After surgical resection histology showed a lobulated tumor growth and nests of monomorph cells with loose chromatin and finely granulated cytoplasm and occasional mitotic figures (Figure 2.). Immunohistochemical stains for synaptophysin (Figure 3.) showed ~90 % strong positivity. Cells with similar morphology were also found in smaller ductal structures, surrounded by an intact layer of p63 positive myoepithelial cells (Figure 4/5.). ER/PR were strongly positive, HER2 receptor was negative, approximately 15% of the tumor cells were positive with ki67 reaction. TTF-1 and CDX2 reactions were both negative. The sentinel lymph node was tumor-free. A final diagnosis of Well-differentiated neuroendocrine tumor of the breast was established. The patient receives aromatase inhibitor therapy. The octreoscan examination and other imaging studies revealed no tumor at other body sites.

Expression of markers

Synaptophysin - positive; Estrogen - positive; Progesteron - positive; HER2 - negative; TTF-1 - negative; CDX2 - negative.

Discussion

The first case of primary neuroendocrine carcinoma of the breast was described by Feyrter, in 1963. Although 20-30% of primary breast cancers show neuroendocrine differentiation to some degree, true primary neuroendocrine tumor of the breast is a rare condition. The WHO has strict criterias to establish a diagnosis of such tumor. At least 50% of the tumor cells have to be positive with at least one neuroendocrine immunohistochemical marker and other primary sites and a metastatic nature of the lesion must be excluded before making the diagnosis. To establish the correct diagnosis, characteristic growing patterns and cytological features of neuroendocrine differentiation should be carefully evaluated. In questionable cases the presence of a ductal in situ component with similar cytological appearance and immunophenotype could be helpful. In our case finding the in-situ component lead to the final diagnosis. Estrogen and/or progesterone positivity are not useful to prove the primary nature of the tumor as these markers could be positive in other primaries as well. Other markers, such as CDX2 or TTF1 could be applied aiming to exclude metastasis. Communication to the clinician about any controversies is important to facilitate thorough imaging and patient follow-up, to choose the best treatment for the patient.

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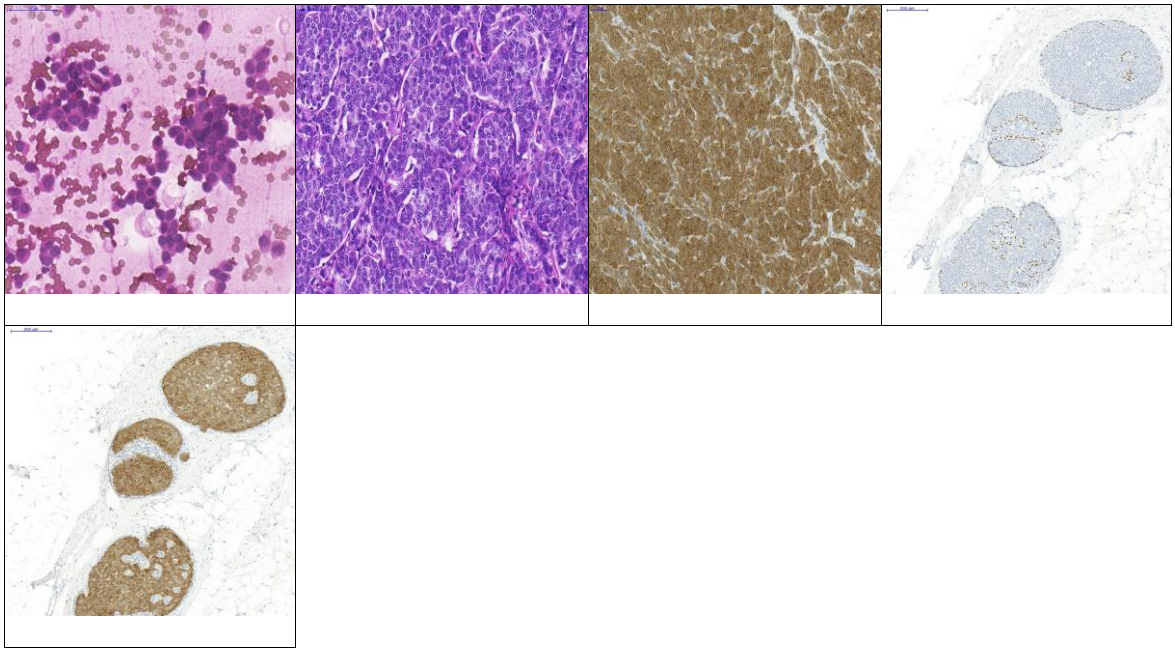
Hallmarks of Diagnosis

Recognizing neuroendocrine features on H&E slides. Prove neuroendocrine nature with immunohystochemical markers - sometimes a panel of markers is required. Exlude metastatic tumor to the breast. Search for in situ component.

Images (for full size images see supplements)



Keyword - Diagnosis: Primary neuroendocrine tumor of the breast

Keyword - differential diagnosis: Metastatic neuroendocrine tumor

Keyword - side findings:

Keyword - organ: breast

Keyword - methods: Immunohystochemistry

Keyword - others:

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