

NEUROENDOCRINE DIFFERENTIATED BREAST CARCINOMA: A CASE REPORT

Mücteba Gündüz, Yalın İşcan, Yeşim Erbil, Mahmut Müslümanođlu

İstanbul Üniversitesi İstanbul Tıp fakültesi, Genel Cerrahi, İstanbul, Türkiye

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ABSTRACT

Neuroendocrine tumors are rarely seen in the breast. They are commonly located in the gastrointestinal tract and the lungs. These tumors of the breast may be purely neuroendocrine or neuroendocrine differentiated. Some breast tumors may have neuroendocrine foci. The clinical significance of these tumors are unclear. However, they are thought to have no relation with the prognosis and patient outcome. This is the report of a patient with neuroendocrine differentiated invasive breast carcinoma treated surgically in the classical manner.

Keywords: neuroendocrine, breast cancer, neuroendocrine differentiated

NÖROENDOKRİN FARKLIŞMA GÖSTEREN MEME KANSERİ: OLGU SUNUMU

ÖZET

Nöroendokrin tümörler memede nadiren görülürler. Sıklıkla gastrointestinal sistem ve akciğerlerde yerleşirler. Memenin bu tümörleri saf nöroendokrin tümörler ya da nöroendokrin farklılaşmış şekilde olabilirler. Bazı meme tümörlerinde de nöroendokrin odaklar görülebilir. Nöroendokrin farklılaşma hem invaziv hem de in situ meme kanserlerinde bildirilmiştir. Müsinöz kanserler nöroendokrin farklılaşmayla en çok ilişkili görünen kanserlerdir. Kromogranin ve sinaptofizin nöroendokrin farklılaşmanın en çok kabul gören özgül belirteçleridir. Bu tümörler histokimyasal olarak argentafin ile boyanırlar ve elektron mikroskopunda nörosekretuar granülleri görülür. Bu tümörlerin klinik önemi hala belirsizdir. Fakat prognoz ve sağkalım ile ilişkiz oldukları sanılmaktadır. Burada klasik şekilde cerrahi olarak tedavi edilmiş nöroendokrin farklılaşma gösteren bir invaziv meme kanseri olgusu sunulmuştur.

Anahtar sözcükler: nöroendokrin, meme kanseri, nöroendokrin farklılaşma

Introduction

The breast is a rare site for neuroendocrine tumors. Most neuroendocrine tumors are located in the gastrointestinal tract and the lung (1). While pure neuroendocrine carcinoma of the breast is very rare, scattered neuroendocrine cells can be detected in up to 50% of breast tumors. Recently, an additional subset of breast tumors have been described as neuroendocrine differentiated breast tumors (2). Neuroendocrine differentiation has been reported in both in situ and infiltrating breast cancers. Mucinous carcinomas of the breast appear to have the greatest association with neuroendocrine differentiation (3). Chromogranin and synaptophysin are widely accepted as specific immunohistochemical markers of neuroendocrine differentiation. These tumors are stained with argentaffin histochemically and

neurosecretory granules are seen under electron microscopy (4). The significance of neuroendocrine differentiation in carcinomas of the breast remains unclear. However, it does not seem to carry a special prognostic or therapeutic significance (3). Prognosis

seems to correlate with the stage of the disease at the time of presentation (5). The following case report is on a 73 year-old female patient with neuroendocrine differentiated invasive ductal breast carcinoma.

Patient

A 73-year-old woman with no significant medical history was admitted to our clinic in April 2007 with a history of left nipple discharge for 2 years. At physical examination, there was no palpable mass. Ultrasonography revealed intraductal papilloma beneath the left areola. Surgical intervention was planned and a left retroareolar excision was performed. The histopathology after surgery showed invasive ductal carcinoma with morphological and histochemical

neuroendocrine features. The tumor was 4 mm in diameter. The nearest surgical margin measured 1mm. An intraductal component constituted 20% of the tumor volume. No mucinous component was present. The tumor did not have necrosis and no vascu-

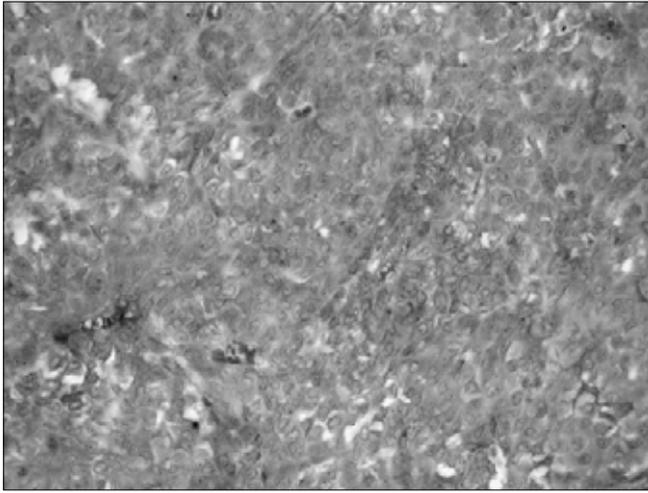


Figure 1.

lar space invasion was seen. The specimen stained weakly with synaptophysin (Figure1) and was positive for both estrogen and progesterone receptors. Due to the margin positivity, a re-excision with a sentinel lymph node biopsy (SLNB) was performed. The SLNB specimen was reported to be negative with frozen-section examination and the operation was terminated at this level. There was no tumor in the re-excision specimen and sentinel lymph nodes were negative for metastasis. No chemoradiotherapy was planned and the patient was began the follow up program.

Discussion

The breast is a rare site for neuroendocrine tumors. Most neuroendocrine tumors are located in the gastrointestinal tract and the bronchopulmonary system. Among the rare locations are various digestive tract organs including the esophagus, Meckel's diverticulum, liver, pancreas, and biliary tract, as well as the pelvic and oto-laryngeal organs and the breast (1).

Widespread use of sensitive techniques for the detection of neuroendocrine markers has revealed the existence of neuroendocrine differentiation in breast cancer.

Neuroendocrine cells form a small, intrinsic component of normal breast epithelium and are also found in breast cancers. Though, there are some studies that failed to show the presence of neuroendocrine cells in human fetal and adult breasts by immunohistochemistry and electron microscopy. The role of breast neuroendocrine cells is unknown; however, according to their function in better studied organs like the lungs and the gastrointestinal tract, they probably function in the maintenance of ho-

meostasis and the regulation of secretion. Neuroendocrine cells secrete neuropeptides (serotonin, calcitonin, and others) and specific neuroendocrine products (chromogranins, neuron-specific enolase) (6).

Neuroendocrine tumors have particular characteristics that distinguish them from other solid malignancies. Pure neuroendocrine carcinoma of the breast is very rare. In 10–50% of breast tumors, scattered neuroendocrine cells can be detected depending on the definition and detection methods. A new type of breast tumor has recently been classified as neuroendocrine differentiated breast carcinoma whose features are common with both neuroendocrine and exocrine carcinomas (2). This indicates the ability of the same tumor cell to produce both exocrine and endocrine substances. Therefore, it should be discriminated from both pure neuroendocrine breast carcinoma and typical breast cancer with focal neuroendocrine differentiation. A classification scheme for neuroendocrine differentiation in carcinomas of the breast was proposed by Papotti et al. in 1989. Seven histological sub-types were defined: cohesive, mucoid, mixed, trabecular, atypical carcinoid-like, lobular carcinoma-like (confluent variant), and small cell/Merkel cell-like type (5). Mucinous carcinomas of the breast appear to have the greatest association with neuroendocrine differentiation (3).

The morphological features of the neuroendocrine carcinomas of the breast should be confirmed by immunohistochemical means or by electron microscopy. Chromogranin and synaptophysin have been widely accepted as specific markers of neuroendocrine differentiation. Demonstration of neurosecretory granules by electron microscopy and histochemical staining with argentaffin are also useful (4).

Although there is an intense investigation on neuroendocrine differentiation of the breast carcinoma there is still little knowledge about its clinical significance. David et al. found that diffuse neuroendocrine differentiation is not prognostically significant (3). On the other hand, prognosis seems to correlate with the stage of the disease at the time of presentation (5). Among patients who have neuroendocrine tumor metastases to the liver with an unknown primary site, it may be helpful to include breast as well as the other rare anatomic locations as a component of the comprehensive diagnostic workup (1). Since the significance of neuroendocrine differentiation in carcinomas of the breast remains unclear, they are treated in the classical manner (3).

Although the breast is a rare location for neuroendocrine tumors, it may be seen in the form of neuroendocrine differentiated carcinoma and its clinical importance still remains to be investigated.

References

1. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. *Cancer* 2003;97:934–959. (PMID: 12569593)
2. Sapino A, Bussolati G. Is detection of endocrine cells in breast adenocarcinoma of diagnostic and clinical significance? *Histopathology* 2002;40:211–4. (PMID: 11895485)
3. David O, Bhattacharjee M. Diffuse neuroendocrine differentiation in a morphologically composite mammary infiltrating ductal carcinoma: a case report and review of the literature. *Arch Pathol Lab Med.* 2003 Mar;127(3): e131-4. (PMID: 12653600)
4. Gould V E, Lee L, Wiedenmann B et al. Synaptophysin: a novel marker for neurons, certain neuroendocrine cells, and their neoplasms. *Hum Pathol* 1986; 17: 979–983. (PMID: 3093369)
5. Papotti M, Macri L, Finzi G, et al. Neuroendocrine differentiation in carcinomas of the breast: a study of 51 cases. *Semin Diagn Pathol.* 1989;6:174–188. (PMID: 2503862)
6. Sapino A, Righi L, Cassoni P, Papotti M, Pietribiasi F, Bussolati G. Expression of the neuroendocrine phenotype in carcinomas of the breast. *Semin Diagn Pathol* 2000;17(2):127–37. (PMID: 10839613)

Correspondence

Mücteba Gündüz
Tel : +90(212) 351 96 27
E-Posta : drmucteba@hotmail.com