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Memenin primer nöroendokrin karsinomu: Vaka sunumu.

PRIMARY NEUROENDOCRINE CARCINOMA OF THE BREAST: Case report.

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ABSTRACT

Primary neuroendocrine carcinoma of the breast is an extremely rare tumor. Tumours can only be considered small cell neuroendocrine tumour of the breast if nonmammary sites are excluded. We present our experience of primary neuroendocrine carcinoma of the breast in a 76-year-old woman and 87-year-old woman. First patient has presented with just about 4 cm palpable mass in her left breast. Tru cut biopsy from left breast showed a invasive carcinoma. Wide surgical excision and sentinel lymph node biopsy were performed. The second patient admitted our clinic complaints of a mass in her left breast. Because of limitted cardiac failure, only lumpectomy was performed with local anestesia. Also in two patients, immunohistochemical staining showed primary neuroendocrine carcinoma of the breast. Computed tomography scans of the chest and abdomen showed no lesion for metastasis or another primary origin. Adjuvant hormone therapy was given, since the tumor was immunohistochemically receptor positive.

Key words: Breast neoplasm, neuroendocrine tumor.

ÖZET

Memenin primer nöroendokrin karsinomu, oldukça nadir görülen bir tümördür. Tümörün primer olarak meme kaynaklı olduğunu söylemek için meme dışı organlarda olmadığı kanıtlanmalıdır. Bu çalışmada, memenin primer nöroendokrin tümörü tanısı koyduğumuz 76 ve 87 yaşındaki iki kadın hastamıza ait tecrübemizi sunduk. İlk hastamız sol memede yaklaşık 4 cmlik kitle şikayeti ile başvurdu. Yapılan tru cut biyopsi sonucu invazif karsinom olarak sonuçlandı. Hastaya sentinel lenf nodu biyopsisi ve geniş cerrahi eksizyon uygulandı. İkinci hastamız sol memede kitle ile klniğimize başvurdu. İleri kardiyak yetersizliği olan hastaya lokal anestezi altında yalnızca lumpektomi uygulandı. Her iki hastada immunhistokimyasal boyamalar sonucunda memenin primer nöroendokrin karsinomu saptandı. Toraks ve batına yönelik bilgisayarlı tomografi incelemelerinde metastaz saptanmadı. Reseptörleri pozitif olan hastalara sonraki dönemde hormonoterapi verildi.

Anahtar kelimeler: Meme tümörü, nöroendokrin tümör.

INTRODUCTION

Neuroendocrine tumors are rare, slow-growing tumors derived from neuroendocrine cells, which are present throughout the body; they arise most commonly in the bronchopulmonary system and gastrointestinal tract (1). Neuroendocrine tumors in the breast are rare, accounting for less than 0.1% of all breast cancers and less than 1% of all neuroendocrine tumors (2). The diagnosis can only be made if non-mammary sites are excluded or if an in situ component can be found. According to the World Health Organization (WHO) classification of tumors, neuroendocrine tumor in the breast is a category that includes solid neuroendocrine carcinoma, small cell / oat cell carcinoma, and large-cell neuroendocrine carcinoma (3). The characteristics of similar cases in the literature, the differential diagnosis, cell origin, and ways to distinguish primary and secondary tumors of this kind are discussed.

Case 1

A 76-year-old woman referred our clinic with a pain, and a mass in her left breast, which she had noticed 2 weeks previously. Physical examination revealed an elastic, hard, indistinct mass with a diameter of 4 cm in the upper inner quadrant of left breast, suggesting malignancy. The breast skin was normal. The contralateral breast was normal, and there was no palpable adenopathy in the bilateral axillae and supraclavicular region. Preoperative laboratory values were all within normal limits. Ultrasonography showed an irregular mass with a diameter of 3,5 cm having both hypoechoic and hyperechoic components in left breast and having increased vascularity. The mammographic findings were irregular shape, spiculer margine and high dens BIRADS-5 lesion (Figure 1). Computed tomography scans of the chest and abdomen showed no lesion for metastasis or another primary origin. A true cut biopsy of the mass was performed and showed an invasive carcinoma. The patient underwent wide surgical excision and sentinel lymph node biopsy (SLNB) with general anesthesia. It was no determined 3 sentinel lymph nodes metastasis with frozen section examination. Solid tumor mass measuring 35x25x25 mm diameter located in the upper inner quadrant of left breast. Microscopic examination with immunohistochemical staining revealed high grade neuroendocrine small cell carcinoma. Positivity for neuron spesific enolase (NSE), chromogranin and synaptophysin was found 70%, 70%, 80% of tumor cells respectively. The patient received postoperative chemotherapy and adjuvant radiation treatment The patient was discharged seventh postoperative day. There is no problem in 13 months follow up.

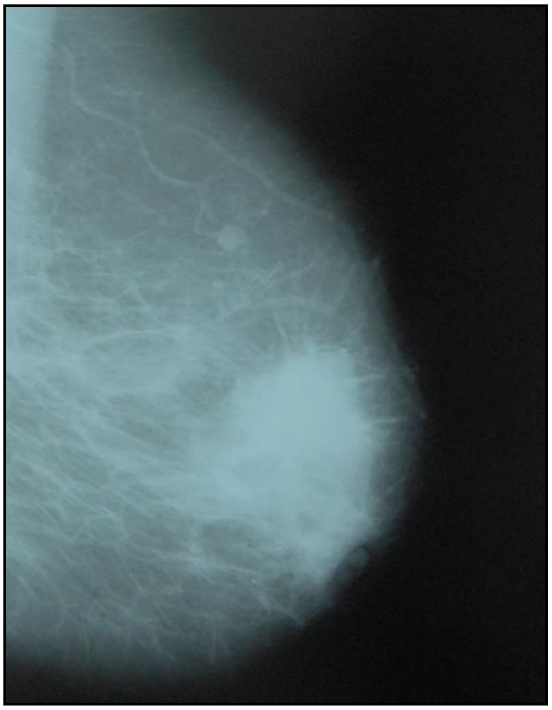

Figure 1: Mammographic view.

Case 2

A 87-year-old woman presented with a pain, and a mass in her left breast. Physical examination revealed an elastic mass with a diameter of 3 cm in the upper outer quadrant of left breast. There was no palpable adenopathy in the bilateral axillae and supraclavicular region. The complete blood count (CBC) and biochemical values were normal. Mammography and ultrasonographic examination revealed a lobulated, circumscribed, high-density mass in the upper outer quadrant of the left breast without microcalcifications. Because of her age and cardiac failure, wide surgical excision was performed with local anesthe-

sia. Immunohistochemical staining showed measuring 3 cm diameter high grade neuroendocrine small cell carcinoma microscopically. Synaptophysin, E-Chaderin, and cytokeratin stainings were positive (Figure 2 and 3). Estrogen and progesteron receptors were positive. The patient discharged third postoperative day. She received postoperative hormonotherapy. There is no problem in 24 months follow up.

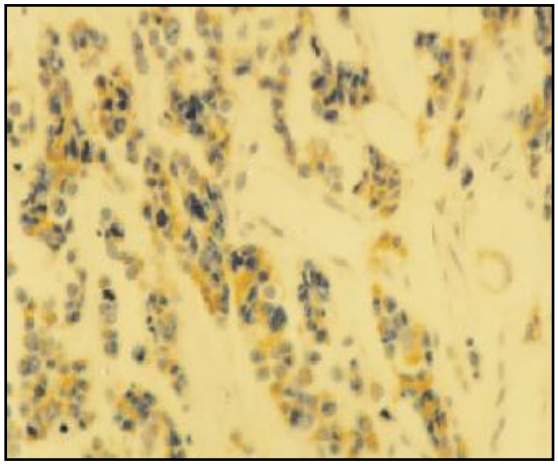

Figure 2: Cytokeratin staining X400.

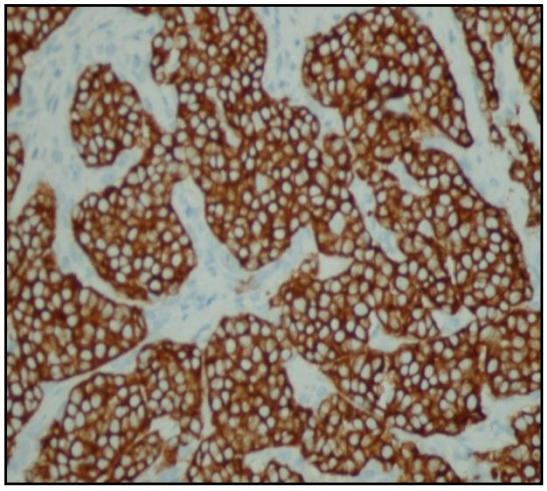

Figure 3: Cynaptophysin staining x400.

DISCUSSION

Neuroendocrine tumors are rare, slow-growing tumors that are derived from neuroendocrine cells throughout the body. They mainly occur in the bronchopulmonary system and gastrointestinal tract. The overall prevalence is estimated to be 1–2 cases per 100 000 persons (4). Neuroendocrine tumors are associated with multiple endocrine neoplasia syndrome type I (MEN-I), but this patient had neither such a family history nor an abnormality of the endocrine system (5). Our cases represents a good example of primary neuroendocrine carcinoma of the breast. Primary neuroendocrine small cell carcinoma of the breast is one of the least common types of breast cancer; fewer than a dozen cases have been reported in the literature, some of which involved the male breast (6).

Differential diagnosis should include direct invasion of the breast by Merkel cell carcinoma, malignant lymphoma (either primary or as a manifestation of systemic disease), carcinoid tumor, and malignant melanoma, which should be excluded by the exact location and extension of the tumor and by immunohistochemical stains, such as leukocyte common antigen, neuroendocrine markers, S100 protein, and HMB-45, respectively (7) In neuroendocrine carcinomas, immunohistochemical studies for neuroendocrine markers have been reported. NSE, cytokeratins (AE1 / AE3, CAM 5.2 or CK7) and neuroendocrine differentiation indicators such as Grimelius stain, snaptophysin, Leu 7, serotonin, bombesin and chromogranin A or B are most commonly used (8,9). The expression of the protooncogene bcl-2, which has a role in the anti-apoptotic pathway, has been present in some cases (9). Estrogen and progesterone receptors are rarely positive in neuroendocrine carcinoma of the breast (8,9,10). These tumors can secrete hormones and rarely cause particular clinical manifestations (11). Metastatic neuroendocrine tumors to the breast have also been reported (12,13). Although a very rare tumor, neuroendocrine differentiated breast carcinoma should be included in the differential diagnosis of mammographically dense, round masses with predominantly spiculated or lobulated margins. Sonographically, they mostly present as irregular or microlobulated, homogeneously hypoechoic masses with normal sound transmission. Screening by computerized tomography is thus important to detect primary locations. Computerized tomography of the thorax and abdomen should be performed to exclude a primary lung and alimentary tract tumor. In our

case, computed tomography scans of the chest and abdomen showed no lesion for metastasis or another primary origin Furthermore, an octreotide scan is helpful to identify other sites of endocrine tumors. Sandostatin analogs can be used for patients who have a positive octreotide scan. Mammography or ultrasound examinations are equivalent in adenocarcinomas of the breast. For this reason, magnetic resonance imaging can be useful to detect a multicentric tumor (10).

The standard therapy for this rare tumor remains controversial. Modified radical mastectomy with axillary lymph node dissection seems to be the treatment of choice with adjuvant radiation, chemotherapy, or both, based on the clinical stage and presence of metastasis (14). We preferred to perform a wide surgical excision in our cases. The role of adjuvant radiotherapy and chemotherapy is unknown (15,16). Adjuvant chemotherapy was given the first case due to tumor diameter. Owing to the estrogen and progesterone receptor positivity, adjuvant hormone therapy was given. New studies encompassing a larger patient population are needed to standardize a treatment regimen for this very rare tumor.

REFERENCES

1. Papotti M, Gherardi G, Eusebi V, Pagani A, Bussolati G: Primary oat cell (neuroendocrine) carcinoma of the breast. Report of four cases. Virchows Arch A Pathol Anat Histopathol 1992;420:103-108

2. Ando H, Maeda S, Kameoka N, Fujimoto K, Tsuboi S. A case of primary carcinoid tumor of the breast. J Jpn Surg Assoc 2006;67:763–7 (in Japanese with English abstract).

3. Anonymous. Tumours of the breast: neuroendocrine tumours. In: Tavassoli FA, Devilee P (eds) World Health Organization classification of tumours, pathology and genetics of tumours of the breast and female genital organs. Lyon: IARC press; 2003. P:32–4

4. Robertson RG, Geiger WJ, Davis NB. Carcinoid tumors. Am Fam Physician 2006;74:429-34

5. H. Ogawa, A. Nishio, H. Satake, and at al. Neuroendocrine tumor in the breast. Radiat Med 2008;26:28–32

6. Jundt G, Schulz A, Heitz PU, Osborn M. Small cell neuroendocrine (oat cell) carcinoma of the male breast. Virchows Arch A Pathol Anat Histopathol 1984;404:213–221

7. Samli B, Celik S, Evrensel T, Orhan B, Tasdelen İ. Primary Neuroendocrine Small Cell Carcinoma of the Breast. Arch Pathol Lab Med 2000;124

8. Shin SJ, DeLellis RA, Rosen P: Small cell carcinoma of the breast: a additional immunohistochemical studies. Am J Surg Pathol 2001;25:831-832

9. Francois A, Chatikhine VA, Chevallier B, Ren GS, Bery M, Chevrier A, Delpech B: Neuroendocrine primary small cell carcinoma of the breast: report of case and review of the literature. Am J Clin Oncol 1995;18:133-138

10. Shin SJ, DeLellis RA, Ying L, Rosen P: Small cell carcinoma of the breast: a clinicopathologic and immunohistochemical study of nine patients. Am J Surg Pathol 2000;24:1231-1238

11. Yaren A, Kelten C, Akbulut M, Teke Z, Duzcan E, Erdem. E Primary Neuroendocrine Carcinoma of the breast: A case report. Tumori 2007;93:496-498

12. Kelly C, Henderson D, Corris P: Breast lumps: rare presentationof oat cell carcinoma of lung. J Clin Pathol 1988;41: 171-172

13. Jochems L, Tjalma WAA: Primary small cell neuroendocrinetumour of the breast. Eur J Obstetr Gynecol Rep Biol 2004;115:231-233

14. Francois A, Chatikhine VA, Chevallier B, et al. Neuroendocrine primary small cell carcinoma of the breast: report of a case and review of the literature. Am J Clin Oncol 1995;18:133–138

15. Modlin IM, Shapiro MD, Kidd M: An analysis of rare carcinoid tumours: clarifing these clinical conundrums. World J Surg 2005;29:92-101

16. Tsai WC, Yu JC, Lin CK, Hsieh CT: Primary alveolar-type large cell neuroendocrine carcinoma of the breast. Breast J, 2005;11:487

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