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Neuroendocrine carcinoma of the breast: a case presenting with Octreoscan™ positive skin metastases

Memenin nöroendokrin karsinomu: Cilt metastazı Octreoscan™ pozitif olgu

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Primary neuroendocrine carcinoma of the breast is very rare and has been revealed as a result of the widespread use of sensitive techniques for the detection of neuroendocrine markers. Published cases number less than 30, all presenting with a lump in the breast as the first sign. We report a case of neuroendocrine carcinoma of the breast that presented first with skin metastases. A 60-year-old woman with coin skin lesions, 2-3 cm, on the back, belly, and side of the hip was admitted to Istanbul University Oncology Institute. Histopathological results of a punch biopsy revealed lymphangitis carcinomatosa. Mammography and sonography performed as part of the systemic evaluation demonstrated a 6 mm solid lesion. Subsequent evaluation of the biopsy specimen revealed primary neuroendocrine carcinoma. First-line hormonotherapy with letrozole, to inhibit the estrogen receptor, together with monthly injections of long-acting 30 mg octreotide, for the skin lesions, were initiated. The patient was followed-up for 20 months, during which time no progression was observed. Then relaps was seen in the lungs and died six months later. Diagnosis, therapy, and follow-up of the case are presented.

Key words: Octreoscan; neuroendocrine carcinoma of breast.

Memenin primer nöroendokrin karsinomu, az görülen ve tanıya nöroendokrin markerlerin tespiti için duyarlı testlerin kullanılması sonucu ancak ulaşılabilen bir hastalıktır. Yayınlanan 30'dan az olguda hastanın ilk bulgusu memede kitle ile başvurmaktadır. Bu olgumuzda ilk defa memenin nöroendokrin karsinomunu, cilt metastazı olarak karşımıza çıkmıştır. Altmış yaşında kadın olgu bel, sırt, kalça bölgesindeki deride 2-3 cm'lik yuvarlak lezyonları ile İstanbul Üniversitesi Onkoloji Enstitüsü'ne başvurmuştur. Ciltten yapılan biyopside lenfanjitis karsinomatoza olarak gelmiştir. Sistemik değerlendirmenin bir parçası olarak yapılan mamografi ve ultrasonografiyle sağ memede 6 mm'lik solid lezyon tespit edilmiştir. Ardından yapılan biyopside primer meme nöroendokrin karsinomu olarak gelmiştir. İlk tedavi letrozol ile hormonoterapi olarak başlamış ve aylık uzun etkili octreotide 30 mg cilt lezyonları Octreoscan tuttuğu için başlanmıştır. Hastanın 20 ay süreyle takibi boyunca progresyon gözlenmemiştir; daha sonra akciğerlerde nüks görülmüş ve 6 ay içinde exitus olmuştur. Bu olgu tanı, tedavi ve takip özellikleriyle sunulmuştur.

Anahtar sözcükler: Octreoscan; memenin nöroendokrin karsinomu.

Neuroendocrine tumors can originate from various parts of the body and present with well-defined clinical entities, mostly in the gastrointestinal system, but primary neuroendocrine carcinoma of the breast is very rare and it has been revealed only as the result of the widespread use of sensitive techniques for the detection of neuroendocrine markers.[1]

The term, neuroendocrine differentiated breast cancers, describes a subset of tumors with neuroendocrine morphology that diffusely express neuroendocrine markers in more than 50% of cells, with frequently expressed estrogen and progesterone receptors, and the frequent coexistence of mucinous and apocrine differentiation. These tumors often occur in elderly patients and often have

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Fig. 1. Coin skin lesions, 2-3 cm, on the back, belly, and side of the hip at initial presentation.

low levels of aggressiveness. Clinical prognosis of these patients is generally based on pathology reviews or case reports.[2-4]

Wade et al. described the first neuroendocrine carcinoma of the breast in 1983 and since then all published cases number less than 30, all presenting with a lump in the breast as the first sign.

We report a case of neuroendocrine carcinoma of the breast that presented first with skin metastases.

CASE REPORT

A 60-year-old woman presented to Istanbul University Oncology Institute on December 2005 with coin skin lesions, 2-3 cm, on the back, belly, and side of the hip (Fig. 1). Histopathology results following punch biopsy revealed lymphangitis carcinomatosa.

Mammography and sonography performed as part of the systemic evaluation revealed a 6 mm solid lesion in the upper-outer quadrant of the right breast, which was categorized as ACR BIRADS 4, and axillary lymphadenopathy (18 × 9 mm). A tru-cut biopsy was performed and immunohistochemical evaluation showed a solitary type neuroendocrine carcinoma with both in situ and invasive components of nuclear grade II and histological grade III, and with diffuse positive staining for synaptophysin, focal positive staining for chromogranin (20%), and CD56 negative results.

The estrogen receptor was positive in 80% (NeoMarkers clone SP1), progesterone receptor in 60% (NeoMarkers clone SP1), and there was no overexpression of Her2/neu (Novo Castra 1A6).

The tru-cut biopsy from the breast and punch biopsy from the skin lesions were compared. Although the receptor evaluations of the skin lesions were negative for chromogranin A and synaptophysin, they were considered metastases because of cellular immunohistochemical similarities. The negativity of the receptors was considered to be due to the differentiation in metastatic cells or to the insufficiency of the material for immunohistochemical evaluation.

As a part of the patient's clinical evaluation octreotide scintigraphy was performed. Octreotide scintigraphy showed increased activity on the thorax, belly, and side of the hip. In particular, the increased activity of the regions with the skin lesions supported the data that the lesions were metastases of neuroendocrine carcinoma (Fig. 2).

First-line hormonotherapy with letrozole, to inhibit the estrogen receptor, together with monthly intramuscular injection of long-acting octreotide (Sandostatin LAR 30 mg, Novartis), for the skin lesions, were initiated. Two months later the skin lesions paled (Fig. 3) and 20 months after diagnosis lung metastasis occurred. The patient was followed-up for 26 months. To the best of our knowledge this is the first case of neuroendocrine carcinoma of the breast involving the skin and demonstrated via octreotide scintigraphy.

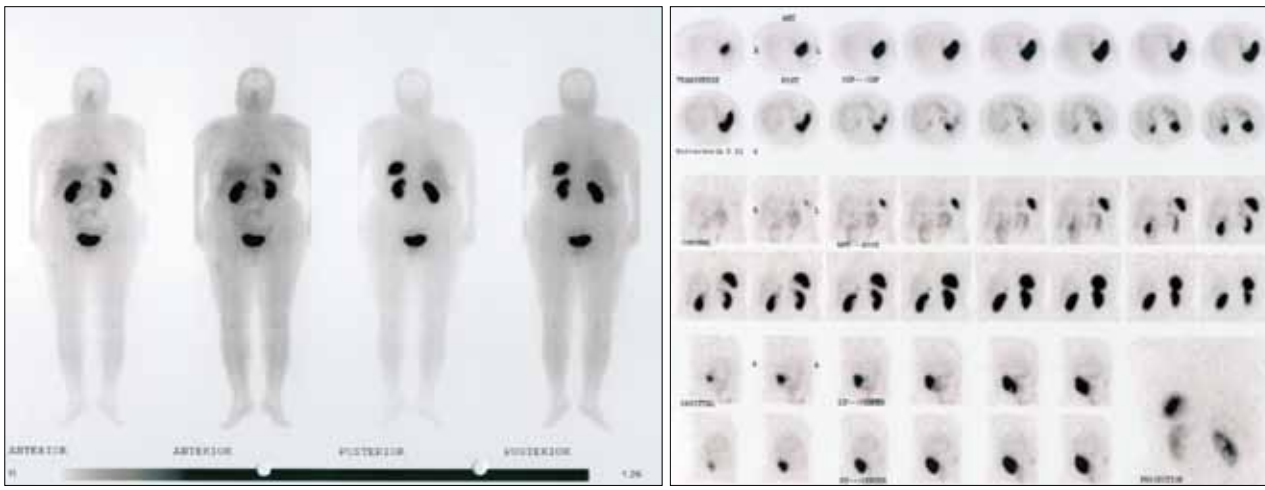

Fig. 2. Octreotide scintigraphy showing increased activity on the thorax, belly, and lateral right femur.

DISCUSSION

Neuroendocrine carcinoma of the breast exhibits different histology, clinical profile, and biological behavior comparing to breast carcinoma. Current knowledge of this carcinoma is insufficient.

Studies on neuroendocrine carcinoma of breast show diverse results on the prognostic factors. Importance of histological grading were proved in Sapino's study,[1] but van Krempen's study showed that tumor size, and lymph node involvement as well as grade effect survival.[4] These findings are similar to those for any type of breast cancer. The presented case was histological grade III, which demonstrated aggressiveness with skin metastases.

Fig. 3. Paled skin lesions.

There are no guidelines and little experience reported concerning the treatment of neuroendocrine carcinoma of the breast. Most publications are based on gastrointestinal neuroendocrine tumors.[2]

Somatostatin receptors (SSTRs) can be found in breast cancer cells, making the use of somatostatin analogs possible.[4] Somatostatin receptor scintigraphy (Octreoscan™) detects octreotide distribution in the body and evaluates octreotide utility in patients.[2] The standard dose is generally 30 mg with intramuscular application in monthly. Treatment response was observed on skin lesions for this patient.

Systemic chemotherapy is not planned until progression occurs. Interferon treatment is very complicated in neuroendocrine tumors and has no significant effect on survival.[6]

Additional studies on neuroendocrine carcinoma of the breast are necessary to further clarify its biological behavior and to define an appropriate treatment protocol. The presented case highlighted various aspects of neuroendocrine carcinoma based on its presentation, diagnosis, and treatment.

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