

Neuroendocrine carcinoma of the breast: a case report and review of the literature

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ABSTRACT

Objectives: Neuroendocrine carcinoma (NEC) is a very rare condition among other types of invasive cancer of breast. Whole-body screening should be performed in order to detect any metastatic or primary disease localization. A 58-year-old patient admitted to hospital with palpable mass on the right retro areolar region and with bloody nipple discharge. Due to axillary positivity with a diagnosis of neuroendocrine carcinoma neoadjuvant chemotherapy was performed. The pathological stage was reported T2N2 with a 2 cm tumor and 5 of 11 lymph node positivity after modified radical mastectomy following neoadjuvant therapy. Tumor cells were stained with positive for neuroendocrine markers. She received adjuvant hormonal treatment with aromatase inhibitors and on regular follow-up with a free of disease to date. The neuroendocrine tumor of the breast is a diagnosis of exclusion. Primary or metastasis distinction is compulsory for the planning of appropriate treatment. There is still a debate on how neuroendocrine differentiation affects the clinical outcome. **Keywords:** Neuroendocrine carcinoma, breast cancer, immunohistochemistry

The term neuroendocrine tumor was first described by Cubilla *et al.* [1] in the late 70's which reports 'neurosecretory' granules were seen under electron microscopy. Neuroendocrine tumors (NET) arise from the neuroendocrine cells. The gastrointestinal tract and the lungs are the most commonly observed locations of neuroendocrine tumors [2]. Pure neuroendocrine tumors of breast are very rare among all types of breast cancer (0.1% of all breast cancers), but neuroendocrine cells can be detected much more in other types of breast cancers [3, 4]. Here we would like to present a 58-year-old patient's management of treatment and review of the literature with a diagnosis of a neuroendocrine differentiating tumor of the breast.

CASE PRESENTATION

A 58-year-old generally in good health condition woman was admitted to polyclinic with a palpable mass on her right breast. The patient has only mild hypertension. A palpable 3×2 cm mass examined on the right upper retro areolar region. Ultrasonography and bilateral mammography performed. A BIRADS category 4c was reported by both sonographic and mammographic examination. Enlarged lymph nodes were detected in the axilla. A tru-cut biopsy was performed from the palpable mass under sonographic guidance. Pathology has resulted in a suspicious neuroendocrine tumor whether primary or metastatic. Immunohisto-

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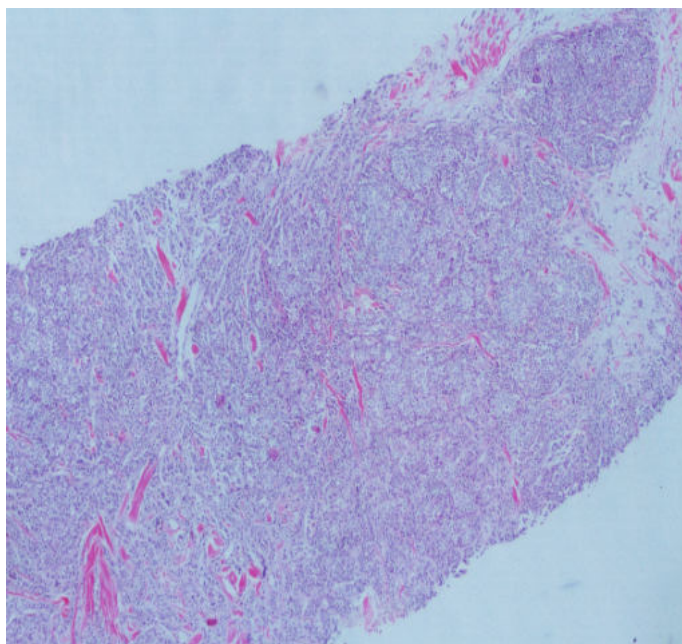


Fig. 1. Tumor as solid nests, H&E X40

chemical receptor status of the pathology was as follows: Estrogen receptor: (+), progesterone receptor (-), HER2 (human epidermal growth factor receptor): (-), Ki67 proliferation index: 40%. Fig. 1 shows tumor deposits as solid nests; positive synaptophysin and neuron-specific enolase staining of tumor cells were observed in Fig. 2 and Fig. 3, estrogen receptor expressivity was shown in Figure 4. Since primary NETs of the breast are very rare, systemic studies have been conducted for suspected primary focus or metastasis.

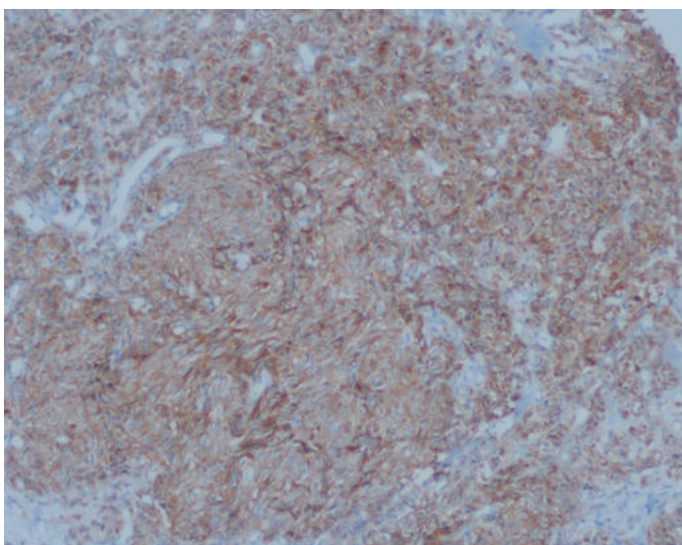


Fig. 2. Immunohistochemical positivity in the tumour cells, Synaptophysin, - Immunohistochemical staining X100

There was no additional focus observed except axillary involvement. Due to the locally advanced stage, neoadjuvant chemotherapy was planned by the oncological tumor board.

After neoadjuvant therapy control positron emission tomography revealed partial response and persistent axillary status. Modified radical mastectomy performed to avoid locoregional relapse. The final pathology result was invasive carcinoma of the breast with neuroendocrine differentiation. Five positive lymph nodes out of 15 were detected. Pathologic grade was T1N2Mx. Adjuvant hormone therapy with aromatase inhibitors and taxane based treatment was given. She is still on regular follow-up at our clinic.

DISCUSSION

Neuroendocrine carcinoma (NEC) of the breast is a rare condition that represents 0.1 % of breast cancers and less than 1% of other neuroendocrine tumors. Mainly, neuroendocrine tumors observed in the gastrointestinal system and pulmonary system [3]. It was also reported in a retrospective study reported by Wang *et al.* [5] a total of more than 380 thousand invasive carcinomas of the breast only 142 of them were diagnosed as neuroendocrine carcinoma which refers to 0,1 % of invasive carcinoma of the breast, and also was observed relatively older ages (mean age was 64). NEC of breast could also be observed younger ages and among men [6, 7]. Palpable mass, bloody nipple discharge can be the s first signs observed on admission to hospital [7]. Almost there were no specific or pathognomonic sign presents in breast ultrasonography and mammography but Park *et al.* mentioned that some radiological characteristics such as high-density round, oval, or lobular noncalcified mass with non-spiculated margins suggest neuroendocrine tumor of the breast [8, 9]. Chromogranin and synaptophysin and neuron-specific enolase are known as specific immunohistochemical markers of neuroendocrine differentiation. They could be stained with argentaffin histochemically and neurosecretory granules of the tumor could be observed under electron microscopy. NEC diagnosis could be made whether these marker occupy more than 50% of tumor cells [10-12].

Estrogen receptor (ER) and progesterone receptor (PR) positivity and human epidermal growth factor re-

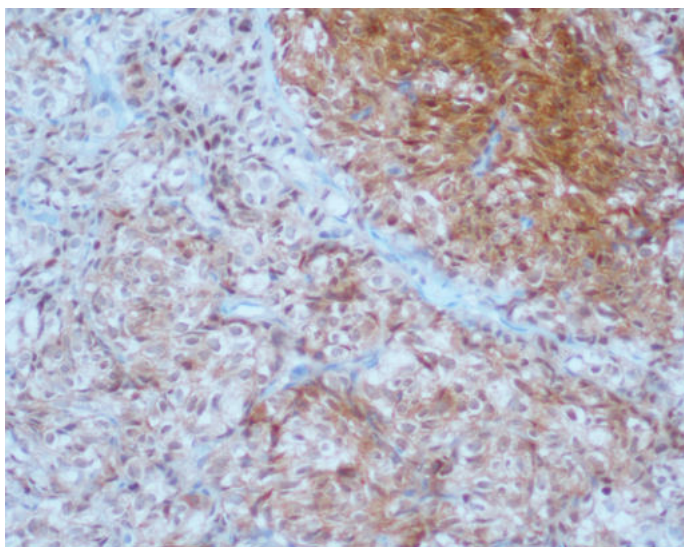


Fig. 3. Immunohistochemical positivity in the tumour cells, Neuron Specific Enolase (NSE)- Immunohistochemical staining X 200

ceptor 2 (HER-2) negativity mostly observed in neuroendocrine tumors of breast [13-15]. Positive ER status may not contribute positive prognostic benefit as it does in other types of invasive carcinomas of breast [5].

Ki 67 protein is a proliferation antigen, which is present in the different phases of the cell cycle and accepted as a poor prognostic factor and high Ki 67 index observed in poorly differentiated tumors [15,

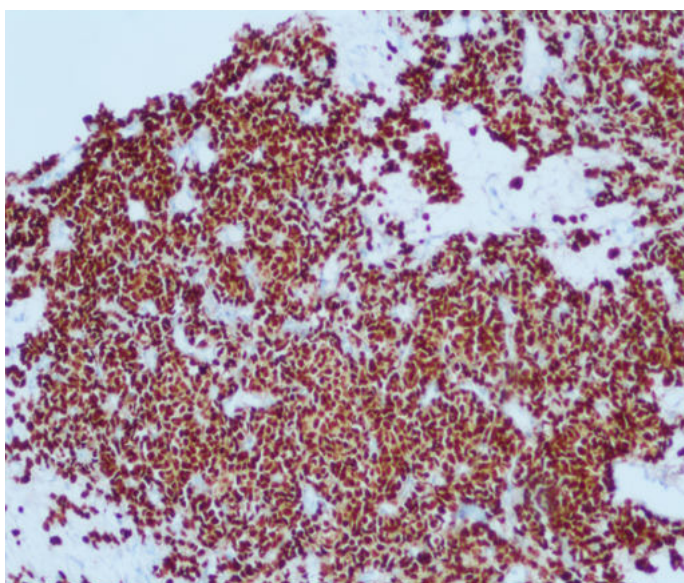


Fig. 4. Immunohistochemical positivity in the tumour cells, Estrogen receptor (ER) – Immunohistochemical staining X 100

16]. Although neuroendocrine carcinoma is a rare condition observed in the breast, routine systemic work-up should be performed to rule out any other primary or metastatic focus with positron emission tomography and bone scintigraphy [17, 18].

Surgical approach to neuroendocrine carcinoma of the breast is not different in any other type of invasive carcinoma of breast. The location of the tumor and the clinical stage are the main determinants of the surgical procedure [19, 20]. Neo-adjuvant chemotherapy is indicated in case of locally advanced disease or malignancy which is not suitable for surgery. Adjuvant therapy regimens including anthracyclines and/or taxanes, hormonal and HER-2 status should be evaluated for endocrine and anti HER-2 treatment [19].

CONCLUSION

In conclusion, the neuroendocrine tumor of the breast is a diagnosis of exclusion. A biopsy followed by appropriate immunohistochemical staining could help for diagnosis. Primary or metastasis distinction is compulsory for the planning of appropriate treatment. There is still a debate on how neuroendocrine differentiation affects the clinical outcome.

Authors' Contribution

Study Conception: KG; Study Design: KG; Supervision: KG; Funding: KG; Materials: KG; Data Collection and/or Processing: KG; Statistical Analysis and/or Data Interpretation: KG; Literature Review: KG; Manuscript Preparation: KG and Critical Review: KG.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

Informed Consent

Written informed consent was obtained from the patient for publication of this case and any accompanying images or data.

REFERENCES

- Cubilla AL, Woodruff JM. Primary carcinoid tumor of breast: a report of eight patients. *Am J Sur Pathol* 1977;1:283-92.
- Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. *Cancer* 2003;97:934-59.
- Singh S, Aggarwal G, Kataria SP, Kalra R, Duhan A, Sen R. Primary neuroendocrine carcinoma of breast. *J Cytol* 2011;28:91-2.
- Sapino A, Bussolati G. Is detection of endocrine cells in breast adenocarcinoma of diagnostic and clinical significance? *Histopathology* 2002;40:211-4.
- Wang J, Wei B, Albarracin CT, Hu J, Abraham SC, Wu Y. Invasive neuroendocrine carcinoma of the breast: a population-based study from the surveillance, epidemiology and end results (SEER) database. *BMC Cancer* 2014;14:147.
- Sapino A, Righi L, Cassoni P, Papotti M, Gugliotta P, Bussolati G. Expression of apocrine differentiation markers in neuroendocrine breast carcinomas of aged women. *Mod Pathol* 2001;14:768-76.
- Righi L, Sapino A, Marchiò C, Papotti M, Bussolati G. Neuroendocrine differentiation in breast cancer: established facts and unresolved problems. *Semin Diagn Pathol* 2010;27:69-76.
- Adams RF, Parulekar V, Hughes C, Kadour MJ, Talbot D. Radiologic characteristics and management of screen-detected metastatic carcinoid tumor of the breast: a case report. *Clin Breast Cancer* 2009;9:189-92.
- Park YM, Wu Y, Wei W, Yang WT. Primary neuroendocrine carcinoma of the breast: clinical, imaging, and histologic features. *Am J Roentgenol* 2014;203:W221-30.
- Tang F, Wei B, Tian Z, Gilcrease MZ, Huo L, Albarracin CT, et al. Invasive mammary carcinoma with neuroendocrine differentiation: histological features and diagnostic challenges: histological features of mammary NEC. *Histopathology* 2011;59:106-15.
- Gould VE, Lee I, Wiedenmann B, Moll R, Chejfec G, Franke WW. Synaptophysin: a novel marker for neurons, certain neuroendocrine cells, and their neoplasms. *Human Pathol* 1986;17:979-83.
- Tapia FJ, Barbosa AJA, Marangos PJ, Polak JM, Bloom SR, Dermody C, et al. Neuron-specific enolase is produced by neuroendocrine tumors. *Lancet*. 1981;317:808-11.
- Mohanty SK, Kim SA, DeLair DF, Bose S, Laury AR, Chopra S, et al. Comparison of metastatic neuroendocrine neoplasms to the breast and primary invasive mammary carcinomas with neuroendocrine differentiation. *Mod Pathol* 2016;29:788-98.
- Wei B, Ding T, Xing Y, Wei W, Tian Z, Tang F, et al. Invasive neuroendocrine carcinoma of the breast: a distinctive subtype of aggressive mammary carcinoma. *Cancer* 2010;116:4463-73.
- Wolff AC, Hammond MEH, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *Arch Pathol Lab Med* 2007;131:18-43.
- La Rosa S, Capella C, Sessa F, Riva C, Leone BE, Klersy C, et al. Prognostic criteria in nonfunctioning pancreatic endocrine tumours. *Vichows Archiv A Pathol Anat*. 1996;429:323-33.
- Squires MH, Volkan Adsay N, Schuster DM, Russell MC, Cardona K, Delman KA, et al. Octreoscan versus FDG-PET for neuroendocrine tumor staging: a biological approach. *Ann Surg Oncol* 2015;22:2295-301.
- Putzer D, Gabriel M, Henninger B, Kendler D, Uprimny C, Dobrozemsky G, et al. Bone metastases in patients with neuroendocrine tumor: ⁶⁸Ga-DOTA-Tyr³-octreotide PET in comparison to CT and bone scintigraphy. *J Nucl Med* 2009;50:1214-21.
- Irelli A, Sirufo MM, Morelli L, D'Ugo C, Ginaldi L, De Martinis M. Neuroendocrine cancer of the breast: a rare entity. *J Clin Med* 2020;9:1452.
- Adams RW, Dyson P, Barthelmes L. Neuroendocrine breast tumours: breast cancer or neuroendocrine cancer presenting in the breast? *Breast* 2014;23:120-7.



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