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Primary Male Neuroendocrine Breast Carcinoma: A Case Report and Review of Literature

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Abstract

Primary neuroendocrine carcinoma of the male breast is an exceptionally rare entity, with fewer than 50 cases documented in the literature. We present a case of a 71-year-old male with a rapidly growing retro-areolar mass. The histopathological and immunohistochemical evaluation confirmed a diagnosis of primary neuroendocrine carcinoma of the breast, with positivity for chromogranin A, synaptophysin, and CD56 and a Ki-67 proliferative index of 30%. The patient underwent total mastectomy with axillary lymph node dissection followed by adjuvant tamoxifen. At 24-month follow-up, he remains disease-free. This case highlights the diagnostic challenges of male neuroendocrine breast carcinoma (NEBC) and emphasizes the critical role of histopathology and immunohistochemistry in achieving an accurate diagnosis. We provide a comprehensive review of the literature, propose a management algorithm, and suggest future research directions to address knowledge gaps in this rare malignancy. This report adheres to the SCARE 2020 criteria for surgical case reports.

Keywords

Male Breast Cancer, Neuroendocrine Carcinoma, Chromogranin A, Synaptophysin, Immunohistochemistry, Tamoxifen

1. Introduction

Male breast cancer is a rare malignancy, constituting less than 1% of all breast cancer diagnoses, with distinct clinical and biological characteristics compared to its female counterpart [1]. Among its subtypes, neuroendocrine tumors (NETs)

of the breast are exceptionally uncommon, accounting for fewer than 2% of male breast cancers [2]. These tumors pose significant diagnostic challenges, particularly in distinguishing primary breast NETs from metastatic lesions originating elsewhere in the body, as no definitive clinical or radiological features reliably differentiate the two [3].

Recent studies emphasize the indispensable role of immunohistochemistry (IHC) in confirming neuroendocrine differentiation, with markers such as chromogranin A, synaptophysin, and CD56 serving as critical diagnostic tools [4] [5]. However, despite these advancements, comprehensive case reports detailing the clinical, radiological, and histopathological nuances of primary male breast NETs remain sparse. Existing literature often focuses on female cases or lacks granular diagnostic insights, leaving a gap in understanding the unique presentation and management of these tumors in male patients [6].

This case report describes a 71-year-old male with primary neuroendocrine carcinoma of the breast, underscoring the diagnostic complexities and the pivotal role of IHC in achieving accurate classification. By detailing the clinical course, imaging findings, and histopathological evaluation, this report addresses the paucity of data on male breast NETs and highlights the need for heightened awareness and standardized diagnostic protocols. The findings reinforce the importance of integrating IHC into routine pathological assessment to guide tailored treatment strategies, particularly given the potential for divergent therapeutic responses in NETs compared to other breast malignancies. This work adheres to the SCARE 2020 criteria, ensuring transparency and rigor in reporting surgical case studies [7].

2. Case Report

2.1. Patient History and Clinical Presentation

Our case involves a 71-year-old male patient with no significant medical history, including no known chronic conditions such as diabetes, hypertension, cardiovascular disease, prior neoplasia, or metabolic disorders. The patient had no history of major surgery, prolonged hospitalizations, or long-term chronic medication use. There was no family history of breast cancer or known genetic predisposition (e.g., BRCA mutations). Additionally, he had no history of hormonal therapy exposure, excessive alcohol consumption, or use of substances linked to gynecomastia (e.g., anti-androgens, steroids). His lifestyle was described as not sedentary, with no current or past smoking.

The patient presented with a rapidly evolving left breast mass over the past month. Clinical examination revealed stable general health with non-tender bilateral gynecomastia. On the left breast, a firm, mobile mass measuring 3 cm × 3 cm was located retro-areolar in the external quadrants, with no signs of inflammation (erythema, warmth, edema) or associated lymphadenopathy. The right breast showed no nodules or lymphadenopathy.

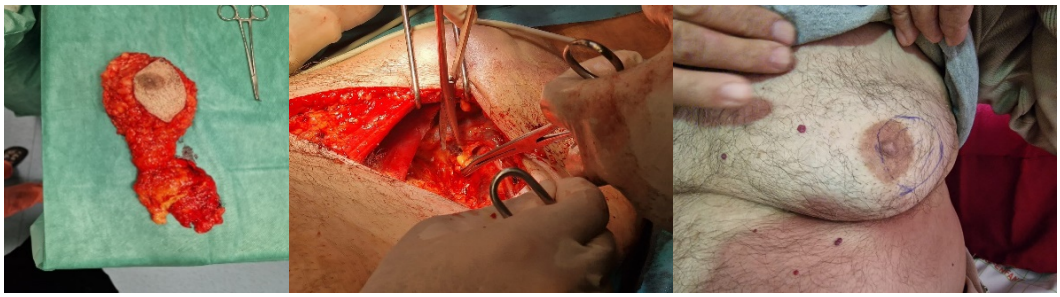
2.2. Imaging Findings

Ultrasound imaging identified a very hypoechoic, lobulated mass with a long axis perpendicular to the skin, slightly attenuated, measuring 15 mm × 13 mm. This mass had a rounded retro-areolar opacity extending into the right external quadrants, with lobulated contours and peripheral spicules. An ultrasound-guided biopsy suggested either extensive lobular carcinoma in situ or a neuroendocrine tumor. The biopsy demonstrated neuroendocrine differentiation with positive staining for chromogranin A, synaptophysin, and CD56. Histological examination revealed a largely necrotic tumor with small pleomorphic cells.

MRI further revealed a retro-areolar mass measuring 15 mm × 9.4 mm with irregular, spiculated contours, heterogeneous intermediate signal on T2-weighted images, and enhancement after gadolinium injection. No axillary adenopathy or bilateral/multifocal lesions were detected, and the lesion was classified as BI-RADS 6.

2.3. Surgical Intervention and Anatomopathological Analysis

The patient underwent a left mastectomy with bloc axillary lymph node dissection (Figure 1). The surgical specimen revealed a well-circumscribed carcinoma with solid proliferation and significant necrosis. Tumor cells were organized in nests and clusters, with small, pleomorphic, and spindle-shaped cells showing moderate atypia, granular chromatin, and eosinophilic cytoplasm. Fine vascularization with necrotic and hemorrhagic areas was noted. The morphology indicated a well-differentiated neuroendocrine tumor, with definitive grading requiring additional immunohistochemical confirmation. There were no ductal carcinoma in situ components, and the surgical margins were clear. The nipple was free of tumor infiltration or Paget's disease. The axillary lymph node dissection revealed reactive granulomatous inflammation without caseous necrosis (16/16 nodes negative).



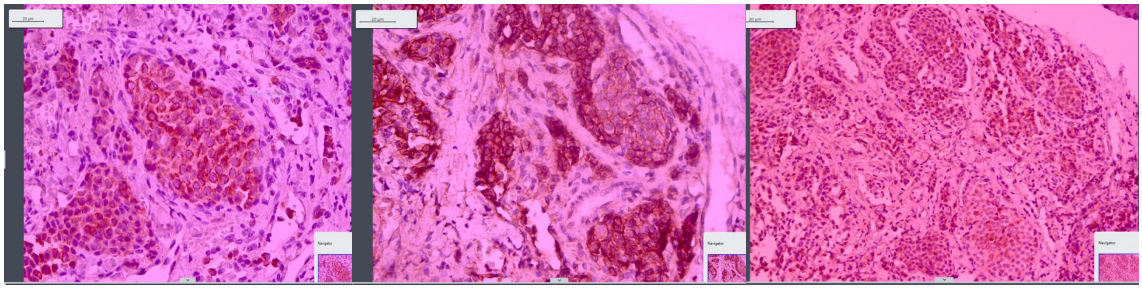
(A) (B) (C)

Figure 1. Preoperative clinical photograph of the left breast demonstrating a retro-areolar mass and gynecomastia. (A) Intraoperative image of the mastectomy (Patey monobloc). (B) Preoperative image of axillary lymph node dissection. (C) Clinical presentation of the 3 cm × 3 cm retro-areolar mass in the left breast.

2.4. Histopathological and Immunohistochemical Analysis

To further characterize the tumor, special staining techniques were employed (Figure 2):

- **Grimelius Staining:** This silver staining technique was used to highlight argyrophilic granules within the tumor cells, providing strong evidence of neuroendocrine differentiation [8].
- **Silver Staining:** Additional silver staining methods were utilized to visualize neuroendocrine granules, offering further insights into the tumor's characteristics [9].



(A) (B) (C)

Figure 2. Immunohistochemical staining results. (A) Positive cytokeratin staining in the heterogeneous cytoplasm. (B) Positive E-cadherin staining, excluding lobular carcinoma. (C) Positive chromogranin A staining in the cytoplasm.

Immunohistochemical profiling demonstrated neuroendocrine markers with positive staining for chromogranin A (80% of cells), synaptophysin (70% of cells), and CD56 (60% of cells). Ki-67 was high at 30%, indicating strong proliferative activity. Estrogen receptors (60% of cells) and progesterone receptors (50% of cells) were positive, potentially influenced by prior tamoxifen use. HER2/neu was negative, and E-cadherin was positive, excluding lobular carcinoma. Pan-cytokeratin was positive (80% - 90% of cells), while CK7 was positive (90% of cells), and CK20 was negative.

2.5. Postoperative Course

An evaluation of gynecomastia, including TSH, T4, FSH, LH, and renal function tests, was normal, leading to a diagnosis of idiopathic gynecomastia. The patient was discharged on postoperative day three with an uneventful immediate follow-up. Postoperative evolution included the development of an axillary seroma one week after surgery, requiring weekly drainage for one month. The patient subsequently received adjuvant hormonal therapy with tamoxifen and is currently in remission with regular follow-up at our center.

3. Discussion

3.1. Rarity and Diagnostic Challenges of Male Neuroendocrine Breast Carcinoma (NEBC)

Neuroendocrine breast carcinoma (NEBC) is an exceptionally rare entity, particularly in males, with fewer than 50 cases documented in the literature [10]. This rarity poses significant diagnostic challenges, especially in distinguishing primary

NEBC from metastatic neuroendocrine tumors originating from other sites, such as the gastrointestinal tract or lungs [11]. In our case, the patient presented with a rapidly growing retro-areolar mass, which initially raised suspicion for a more common breast malignancy. However, histopathological and immunohistochemical (IHC) evaluation confirmed the diagnosis of primary NEBC, highlighting the critical role of IHC in differentiating this rare tumor from other breast cancers.

The diagnosis of NEBC relies heavily on the expression of neuroendocrine markers such as chromogranin A, synaptophysin, and CD56, as seen in our patient [12] [13]. These markers, along with the characteristic histological patterns (solid, trabecular, or nested arrangements), are essential for accurate diagnosis [14]. However, the variability in hormone receptor expression (ER and PR) adds another layer of complexity. Contrary to some misconceptions, NEBC can express hormone receptors, as demonstrated in our case, where the tumor was ER+ (60%) and PR+ (50%) [15]. This finding underscores the importance of integrating hormone receptor status into the diagnostic workup, as it influences treatment decisions.

3.2. Histopathological and Immunohistochemical Features

Histologically, NEBC exhibits distinct architectural patterns, including solid, trabecular, or nested arrangements of tumor cells [16]. The tumor cells are typically small to medium-sized, with moderate to abundant cytoplasm and finely granular chromatin. Necrosis and hemorrhage are common features, as observed in our case [17]. Immunohistochemistry (IHC) plays a pivotal role in confirming neuroendocrine differentiation. Key markers include chromogranin A, synaptophysin, and CD56, which were all positive in our patient [18]. Chromogranin A, a glycoprotein found in neurosecretory granules, is a highly specific marker for neuroendocrine tumors [19]. Synaptophysin, a synaptic vesicle protein, is another reliable marker, while CD56, a neural cell adhesion molecule, is frequently expressed in neuroendocrine tumors [20].

The Ki-67 proliferation index is a valuable prognostic marker in NEBC. A high Ki-67 index (≥20%) is associated with more aggressive tumor behavior and poorer outcomes [21]. In our patient, the Ki-67 index was 30%, indicating a high proliferative rate and underscoring the need for aggressive treatment.

3.3. Controversies and Knowledge Gaps in Male NEBC

One of the key controversies in male NEBC is the lack of standardized treatment protocols. Current management strategies are often extrapolated from those used for female breast cancer or other neuroendocrine tumors, which may not fully account for the unique biological behavior of male NEBC [22]. For instance, the role of axillary lymph node dissection (ALND) in male NEBC remains debated. In our case, ALND revealed reactive granulomatous inflammation without metastasis, supporting the decision to avoid aggressive systemic therapy. However, the optimal extent of surgical intervention in male NEBC, particularly in the

absence of lymph node involvement, warrants further investigation [23].

Another knowledge gap lies in the optimal chemotherapy regimen for male NEBC. While platinum-based regimens (e.g., cisplatin + etoposide) are commonly used for high-grade neuroendocrine tumors, their efficacy in male NEBC is not well-established [24]. In our patient, adjuvant chemotherapy was not administered due to the well-differentiated nature of the tumor and the absence of metastatic disease. However, in cases with high Ki-67 indices or poorly differentiated histology, chemotherapy may be warranted [25]. Future studies should aim to define the role of chemotherapy in male NEBC, particularly in the context of tumor grade and hormone receptor status.

3.4. Rationale for Tamoxifen and Hormonal Therapy

The decision to administer tamoxifen in our patient was based on the tumor's ER+ and PR+ status, which is consistent with the management of hormone receptor-positive breast cancers [26]. Tamoxifen, a selective estrogen receptor modulator, is a cornerstone of hormonal therapy for ER+ breast cancers, as it inhibits estrogen-driven tumor growth. In male NEBC, the use of tamoxifen is supported by the tumor's hormone receptor expression, as seen in our case. However, the efficacy of tamoxifen in male NEBC remains understudied, and its role in improving long-term outcomes requires further validation [27].

Alternative hormonal therapies, such as aromatase inhibitors, are typically reserved for postmenopausal women and are less commonly used in males. However, in cases where tamoxifen is contraindicated or poorly tolerated, aromatase inhibitors may be considered, particularly in older male patients [28]. The choice of hormonal therapy should be individualized based on the patient's hormone receptor status, age, and comorbidities.

3.5. Comparative Analysis and Treatment Strategies

A comparative analysis of our case with previously reported male NEBC cases reveals several similarities and differences (**Table 1**). Most cases involve elderly males presenting with a palpable breast mass, often with positive hormone receptor status and neuroendocrine marker expression [29]. However, the treatment strategies and outcomes vary, reflecting the lack of standardized protocols for this rare malignancy.

The management of NEBC is challenging due to the lack of standardized treatment protocols. Current practices often parallel those for invasive ductal carcinoma, with radical mastectomy and axillary lymph node dissection as the primary treatment modalities [30]. Adjuvant therapies, including chemotherapy and hormonal therapy, are tailored based on tumor characteristics.

In our case, the patient underwent total mastectomy with axillary lymph node dissection, followed by adjuvant tamoxifen therapy due to hormone receptor positivity. Tamoxifen, a selective estrogen receptor modulator, is commonly used in hormone receptor-positive breast cancers and has shown efficacy in NEBC [31].

Chemotherapy regimens for NEBC are not well-defined, but combinations such as cisplatin with etoposide or anthracycline-based regimens are frequently employed [32]. Radiation therapy is generally reserved for cases with high-risk features, such as lymph node involvement or positive margins [33].

Table 1. Comparative analysis of male neuroendocrine breast carcinoma (NEBC) cases. Includes data on markers (e.g., chromogranin A, synaptophysin), hormone receptor status (ER, PR), treatment modalities (e.g., surgery, chemotherapy), and outcome.

Case	Age	Presentation	Tumor Size	IHC Profile	Lymph Node Status	Treatment	Outcome
Current Case	71	Rapid-growing retro-areolar mass	3 cm	CgA+, Syn+, CD56+, ER+, PR+, HER2−	Negative (0/16)	Mastectomy + ALND + CT + Tamoxifen	Disease-free at 24 months
Gevorgyan *et al.* (2016)	62	Firm nodule	1.8 cm	CgA+, Syn+, ER+, PR−, HER2−	Negative	Mastectomy + SLNB + CT	Disease-free at 12 months
Alkaied *et al.* (2012)	55	Painful mass	4 cm	CgA+, Syn+, ER+, PR+, HER2−	Positive (2/15)	Mastectomy + ALND + CT + RT	Disease-free at 18 months
Richter-Ehrenstein *et al.* (2010)	65	Painless lump	2.5 cm	CgA+, Syn+, ER−PR−, HER2−	Negative	Mastectomy + SLNB	Lost to follow-up
Latif *et al.* (2013)	60	Bloody nipple discharge	2.2 cm	CgA+, NSE+, ER+, PR+, HER2−	Negative	Mastectomy + ALND + Tamoxifen	Disease-free at 36 months

CgA: Chromogranin A; **Syn:** Synaptophysin; **ER:** Estrogen Receptor; **PR:** Progesterone Receptor; **NSE:** Neuron-Specific Enolase; **ALND:** Axillary Lymph Node Dissection; **SLNB:** Sentinel Lymph Node Biopsy; **CT:** Chemotherapy; **RT:** Radiotherapy.

Emerging therapies targeting somatostatin receptors (e.g., SSTR2A) show promise for NEBC. Somatostatin analogs, such as octreotide, have demonstrated antiproliferative effects in neuroendocrine tumors and may offer new treatment avenues [34]. Further research is needed to evaluate the efficacy of these targeted therapies in NEBC.

3.6. Prognostic Factors and Future Directions

Prognostic outcomes in male NEBC are influenced by several factors, including tumor size, grade, hormone receptor status, and lymph node involvement [35]. In our case, the well-differentiated nature of the tumor, absence of lymph node metastasis, and positive hormone receptor status were associated with a favorable prognosis. However, the high Ki-67 index (30%) indicated a proliferative tumor, which may warrant closer surveillance for recurrence [36].

Future research should focus on elucidating the molecular pathways underlying male NEBC, particularly the role of somatostatin receptors and HER2 status. Emerging therapies targeting somatostatin receptors, such as octreotide and lanreotide, show promise in well-differentiated neuroendocrine tumors and may offer new treatment avenues for male NEBC [37]. Additionally, the role of HER2-targeted therapies in HER2+ male NEBC warrants further exploration, as HER2 expression has been reported in a subset of neuroendocrine tumors [38].

4. Conclusion

Male NEBC is a rare and diagnostically challenging malignancy that requires a multidisciplinary approach for optimal management. The current case highlights the importance of histopathological and immunohistochemical evaluation in achieving an accurate diagnosis and guiding treatment decisions. The use of tamoxifen in hormone receptor-positive male NEBC is supported by the tumor's biological characteristics, but further research is needed to establish standardized treatment protocols and explore emerging therapies. By addressing the controversies and knowledge gaps in male NEBC, we can improve outcomes for this rare patient population.

Ethical Considerations and Patient Consent

Consent was obtained from the patient for publication of this case report and accompanying images.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Giordano, S.H., Cohen, D.S., Buzdar, A.U., Perkins, G. and Hortobagyi, G.N. (2004) Breast Carcinoma in Men. *Cancer*, **101**, 51-57. https://doi.org/10.1002/cncr.20312

[2] Wang, J., Wei, B., Albarracin, C.T., Hu, J., Abraham, S.C. and Wu, Y. (2014) Invasive Neuroendocrine Carcinoma of the Breast: A Population-Based Study from the Surveillance, Epidemiology and End Results (SEER) Database. *BMC Cancer*, **14**, Article No. 147. https://doi.org/10.1186/1471-2407-14-147

[3] Rovera, F., Masciocchi, P., Coglitore A., *et al.* (2013) Neuroendocrine Carcinomas of the Breast. *International Journal of Surgery*, **11**, S6-S11.

[4] Sapino, A., Righi, L., Cassoni, P., Papotti, M., Gugliotta, P. and Bussolati, G. (2000) Expression of the Neuroendocrine Phenotype in Carcinomas of the Breast. *Seminars in Diagnostic Pathology*, **17**, 127-137.

[5] WHO Classification of Tumours Editorial Board (2019) Breast Tumours. 5th Edition, International Agency for Research on Cancer.

[6] Lopez-Bonet, E., Alonso-Ruano, M., Bernet, L., *et al.* (2008) Solid Neuroendocrine Breast Carcinomas: Incidence, Clinico-Pathological Features and Immunohistochemical Profiling. *Oncology Reports*, **20**, 1369-1374.

[7] Agha, R.A., Franchi, T., Sohrabi, C., Mathew, G., Kerwan, A., Thoma, A., *et al.* (2020) The SCARE 2020 Guideline: Updating Consensus Surgical Case Report (SCARE) Guidelines. *International Journal of Surgery*, **84**, 226-230. https://doi.org/10.1016/j.ijsu.2020.10.034.

[8] Tavassoli, F.A. and Devilee, P. (2003) Pathology and Genetics of Tumours of the Breast and Female Genital Organs. IARC Press.

[9] Rosen, P.P. (2014) Rosen's Breast Pathology. 4th Edition, Lippincott Williams & Wilkins.

[10] Miremadi, A., Pinder, S.E., Lee, A.H.S., Bell, J.A., Paish, E.C., Wencyk, P., *et al.* (2002) Neuroendocrine Differentiation and Prognosis in Breast Adenocarcinoma. *Histopathology*, **40**, 215-222. https://doi.org/10.1046/j.1365-2559.2002.01336.x

[11] Righi, L., Sapino, A., Marchiò, C., Papotti, M. and Bussolati, G. (2010) Neuroendocrine Differentiation in Breast Cancer: Established Facts and Unresolved Problems. *Seminars in Diagnostic Pathology*, **27**, 69-76. https://doi.org/10.1053/j.semdp.2009.12.003

[12] Makretsov, N., Gilks, C.B., Coldman, A.J., Hayes, M. and Huntsman, D. (2003) Tissue Microarray Analysis of Neuroendocrine Differentiation and Its Prognostic Significance in Breast Cancer. *Human Pathology*, **34**, 1001-1008. https://doi.org/10.1053/s0046-8177(03)00411-8

[13] Kwon, S.Y., Bae, Y.K., Gu, M.J., Choi, J.E., Kang, S.H., Lee, S.J., *et al.* (2013) Neuroendocrine Differentiation Correlates with Hormone Receptor Expression and Decreased Survival in Patients with Invasive Breast Carcinoma. *Histopathology*, **64**, 647-659. https://doi.org/10.1111/his.12306

[14] Wei, B., Ding, T., Xing, Y., Wei, W., Tian, Z., Tang, F., *et al.* (2010) Invasive Neuroendocrine Carcinoma of the Breast. *Cancer*, **116**, 4463-4473. https://doi.org/10.1002/cncr.25352

[15] Alkaied, H., Harris, K., Ayo, D., *et al.* (2012) Primary Neuroendocrine Carcinoma of the Breast: Case Report and Review of the Literature. *Case Reports in Oncological Medicine*, **2012**, Article 728356.

[16] Richter-Ehrenstein, C., Arndt, J., Buckendahl, A., Eucker, J., Weichert, W., Kasajima, A., *et al.* (2010) Solid Neuroendocrine Carcinomas of the Breast: Metastases or Primary Tumors? *Breast Cancer Research and Treatment*, **124**, 413-417. https://doi.org/10.1007/s10549-010-1178-3

[17] Latif, N., Rosa, M., Samian, L. and Rana, F. (2013) An Unusual Case of Primary Small Cell Neuroen-Docrine Carcinoma of the Breast. *The Breast Journal*, **16**, 647-651.

[18] Fisher, E.R. and Palekar, A.S. (1998) NSABP Collaborators. Solid Neuroendocrine Carcinomas (Including Atypical Carcinoids) of the Breast: A Clinical and Pathological Analysis of 26 Cases. *Human Pathology*, **29**, 1140-1147.

[19] Yamaguchi, R., Tanaka, M., Yokoyama, T., *et al.* (2010) Primary Neuroendocrine Carcinoma of the Breast: A Case Report and Literature Review. *Breast Cancer*, **17**, 324-328.

[20] Inno, A., Bogina, G., Turazza, M., Bortesi, L., Duranti, S., Massocco, A., *et al.* (2015) Neuroendocrine Carcinoma of the Breast: Current Evidence and Future Perspectives. *The Oncologist*, **21**, 28-32. https://doi.org/10.1634/theoncologist.2015-0309

[21] Righi, L., Sapino, A., Marchiò, C., *et al.* (2012) Somatostatin Receptor Expression in Primary Breast Carcinomas: A Potential Novel Therapeutic Target. *Breast Cancer Research and Treatment*, **134**, 585-595.

[22] Zhang, Y., Chen, Z., Bao, Y., *et al.* (2017) Neuroendocrine Carcinoma of the Breast: A Review of 126 Cases in the Chinese Population. *Pathology Research and Practice*, **213**, 171-177.

[23] Sparano, J.A., Gray, R.J., Makower, D.F., Pritchard, K.I., Albain, K.S., Hayes, D.F., *et al.* (2018) Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. *New England Journal of Medicine*, **379**, 111-121. https://doi.org/10.1056/nejmoa1804710

[24] Righi, L., Volante, M., Tavaglione, V., Billè, A., Daniele, L., Angusti, T., *et al.* (2010)

Somatostatin Receptor Tissue Distribution in Lung Neuroendocrine Tumours: A Clinicopathologic and Immunohistochemical Study of 218 'Clinically Aggressive' Cases. *Annals of Oncology*, **21**, 548-555. https://doi.org/10.1093/annonc/mdp334

[25] Gevorgyan, A., Bille, A., Ahlin, C., *et al.* (2016) Primary Neuroendocrine Carcinoma of the Breast: A Case Report and Review of the Literature. *Anticancer Research*, **36**, 3695-3699.

[26] Guerra, L.P., Simões, J., Sá, D.C., Polónia, J. and Araújo, A. (2024) Neuroendocrine Breast Carcinoma. *Autopsy Case Reports*, **14**, e2024484. https://doi.org/10.4322/acr.2024.484

[27] Ma, S., Wang, D.-Y., Liu, Y.-B., Tan, H.-J., Ge, Y.-Y., Chi, Y., *et al.* (2022) Prognostic Factors of Primary Neuroendocrine Breast Cancer: A Population-Based Study. *Cancer Medicine*, **11**, 2533-2540. https://doi.org/10.1002/cam4.4557

[28] Kennedy, K.R., Turner, J.H., MacDonald, W.B.G., Claringbold, P.G., Boardman, G. and Ransom, D.T. (2022) Long-Term Survival and Toxicity in Patients with Neuroendocrine Tumors Treated with ^{177}Lu-Octreotate Peptide Radionuclide Therapy. *Cancer*, **128**, 2182-2192. https://doi.org/10.1002/cncr.34191

[29] Nahleh, Z.A. (2006) Hormonal Therapy for Male Breast Cancer: A Different Approach for a Different Disease. *Cancer Treatment Reviews*, **32**, 101-105. https://doi.org/10.1016/j.ctrv.2005.12.007

[30] Inno, A., Bogina, G., Turazza, M., Bortesi, L., Duranti, S., Massocco, A., *et al.* (2015) Neuroendocrine Carcinoma of the Breast: Current Evidence and Future Perspectives. *The Oncologist*, **21**, 28-32. https://doi.org/10.1634/theoncologist.2015-0309

[31] Ross, J.S. and Fletcher, J.A. (1998) The HER-2/*neu* Oncogene in Breast Cancer: Prognostic Factor, Predictive Factor, and Target for Therapy. *Stem Cells*, **16**, 413-428. https://doi.org/10.1002/stem.160413

[32] Sparano, J.A., Gray, R.J., Makower, D.F., Pritchard, K.I., Albain, K.S., Hayes, D.F., *et al.* (2018) Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. *New England Journal of Medicine*, **379**, 111-121.

[33] Basu, S., Parghane, R.V., Kamaldeep, and Chakrabarty, S. (2020) Peptide Receptor Radionuclide Therapy of Neuroendocrine Tumors. *Seminars in Nuclear Medicine*, **50**, 447-464. https://doi.org/10.1053/j.semnuclmed.2020.05.004

[34] Gevorgyan, A., Bregni, G., Galli, G., Zanardi, E., de Braud, F. and Di Cosimo, S. (2016) Her2-Positive Neuroendocrine Breast Cancer: Case Report and Review of Literature. *Breast Care*, **11**, 424-426. https://doi.org/10.1159/000453572

[35] Vranic, S., Palazzo, J., Sanati, S., Florento, E., Contreras, E., Xiu, J., *et al.* (2019) Potential Novel Therapy Targets in Neuroendocrine Carcinomas of the Breast. *Clinical Breast Cancer*, **19**, 131-136. https://doi.org/10.1016/j.clbc.2018.09.001

[36] Ozdemir, O., Zengel, B., Yildiz, Y., Saray, S., Alacacioglu, A., Tasli, F., *et al.* (2021) Neuroendocrine Differentiated Breast Cancer Cases: A Retrospective Analysis and Literature Review. *The Medical Bulletin of Sisli Hospital*, **55**, 503-509. https://doi.org/10.14744/semb.2021.66503

[37] Corti, F., Rossi, R.E., Cafaro, P., Passarella, G., Turla, A., Pusceddu, S., *et al.* (2024) Emerging Treatment Options for Neuroendocrine Neoplasms of Unknown Primary Origin: Current Evidence and Future Perspectives. *Cancers*, **16**, 2025. https://doi.org/10.3390/cancers16112025

[38] Hurvitz, S.A., Hu, Y., O'Brien, N. and Finn, R.S. (2013) Current Approaches and Future Directions in the Treatment of Her2-Positive Breast Cancer. *Cancer Treatment Reviews*, **39**, 219-229. https://doi.org/10.1016/j.ctrv.2012.04.008