Neuroendocrine carcinoma of the mammary gland. A case report of synchronous occurrence of two different carcinomas in one breast

Neuroendokrynny rak gruczołu piersiowego. Opis przypadku jednoczesnego występowania dwóch różnych raków w tej samej piersi

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ABSTRACT

The paper presents a case of primary neuroendocrine breast carcinoma that coexisted with a typical infiltrating carcinoma (BC) within the same mammary gland. It was diagnosed post-operatively on histopathological examination and confirmed by immunohistochemical analysis.

KEY WORDS
breast cancer, imaging, neuroendocrine carcinoma

STRESZCZENIE

W pracy przedstawiono przypadek pierwotnego neuroendokrynynego raka piersi, który współwystępował z typowym rakiem naciekającym (BC) w tym samym gruczołę piersiowym. Został zdiagnozowany pooperacyjnie w badaniu histopatologicznym i potwierdzony w badaniach immunohistochemicznych.

SŁOWA KLUCZOWE
rak piersi, diagnostyka, rak neuroendokrynny

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INTRODUCTION

The incidence of neuroendocrine breast carcinomas (NEBC) in the whole group of breast cancers is low. From the procedural point of view, it is crucial to make a distinction between primary tumours and metastases, since this translates into significant differences in therapy [1,2,3]. Differentiation in neuroendocrine cells can be found in various histological types of breast carcinoma. Existing literature is scarce in describing cases of primary neuroendocrine breast carcinoma [4]. The prognosis for this rare carcinoma is dependent on similar factors as those in the case of typical infiltrating (invasive) carcinomas: the tumour size, clinical staging, the ER and PR expression as well as the Ki67 index are essential in making prognoses concerning the course of the disease [5,6,7,8].

The paper presents a case of primary neuroendocrine breast carcinoma that coexisted with a typical infiltrating carcinoma (BC) within the same mammary gland. It was diagnosed post-operatively on histopathological examination and confirmed by immunohistochemical analysis.

CASE REPORT

An 81-year-old female patient presented to the Outpatient Clinic of Oncological Surgery with right breast carcinoma diagnosed by fine-needle aspiration biopsy. The patient had not previously undergone mammary gland examination. She had a medical history of diabetes, arterial hypertension and atrial fibrillation. There was no family history of cancers. Clinical examination revealed a palpable tumour measuring 3 x 3 cm in diameter in the right breast, at the border of the upper-outer quadrant, movable in relation to the muscle, with unremarkable skin over the tumour. No other focal lesions were identified in either breast upon clinical examination. In the axillary fossae, there was bilateral presence of a single, movable lymph node with the diameter of 1.5 cm. The supra- and infraclavicular fossae were uninvolved. Low-energy images of spectral mammography showed two tumours in the right breast: one in the upper-outer quadrant at 10 o’clock, measuring 2.5 x 2 cm, of an irregular shape and blurred, spicular contours, and the other at the border of the lower quadrants, deep at the thoracic wall, measuring 3 x 1.5 cm, polycyclic, partially well-circumscribed (Fig. 1).

The 10 o’clock lesion was examined by core-needle biopsy (CNB) under ultrasound supervision, leading to the diagnosis of infiltrating lobular carcinoma G II. Receptor status: progesterone receptors positive Allred 4 points (1+3), oestrogen receptors positive Allred 7 points (4+3), protein Her-2 negative – negative reaction, Ki67 below 1% cancer cells. The diagnostics of the lymph nodes in the regional lymphatic drainage revealed no metastases (clinical examination, ultrasound and fine-needle aspiration biopsy) and excluded the presence of remote metastases. This was the basis for the c T2, N0, M0 diagnosis. Thorough analysis and examination included computed tomography (CT), which revealed no presence of any primary tumours. Due to the reasonable suspicion that the neoplastic process was multicentric, the patient was qualified for a total right mastectomy with sentinel node biopsy (SNB). The surgery was performed in July 2016.

Postoperative histopathological examination confirmed the presence of infiltrating lobular carcinoma in rants, deep at the thoracic wall, there was a focal lesion of an hour-glass shape and an approximate size of 3 x 1.5 cm, manifesting strong intensification upon contrast medium administration. The left breast was without significant abnormalities (Fig. 2).

Summary: The right breast containing the two focal lesions classified as BIRADS 5. The left breast BIRADS 2.
the upper-outer quadrant (at 10 o’clock in the spectral mammography, verified by core-needle biopsy) as well as in the second focus another concomitant carcinoma of an infiltrating mucinous nature (visible on the spectral mammography close to the thoracic wall, at the border of the lower quadrants) with neuroendocrine differentiation (ABpaS(+), chromogranin(+), synaptophysin(+)). The tumour diameter was 1.6 x 0.7 x 1.2 cm. Neuroendocrine differentiation was visible in more than 50% of the cancer cells (Fig. 3–7). The results of analysis for the presence of receptors in the cancer cell nuclei were the following: progesterone receptors positive Allred 4 points (1+3), oestrogen receptors positive Allred 7 points (4+3), protein Her-2 negative – negative reaction, Ki67 below 1% of cancer cells. The sentinel lymph node was free of metastasis. The surgical margins were free of neoplastic infiltration (R0 resection).

**DISCUSSION**

Primary neuroendocrine breast carcinomas (NEBC) are rare neoplasms that constitute less than 0.1% of all breast cancer cases [1,9]. They derive from neuroendocrine cells that are present in the entire human body, primarily in the bronchial system, the gastrointestinal tract wall and the pancreas [10]. Neuroendocrine breast carcinomas produces differentiated images upon microscopic examination: these cancer cells may be arranged in nests separated by fibrous streaks, create rosette-like systems or palisade-like formations located in the outer edges of the tumour [11]. Specific and commonly measured markers include synaptophysin and chromogranin [5,6]. Neuron-specific enolase (NSE) is less specific [12]. In 2003, primary neuroendocrine carcinoma was identified as a separate entity by the World Health Organisation (WHO) in the classification of tumours. The WHO classification defined primary neuroendocrine carcinoma as a tumour that manifests the expression of several neuroendocrine carcinoma markers. The diagnosis of NEBC is based on immunohistochemical analysis when at least 50% of the cancer cells manifest the expression of neuroendocrine markers [2,11]. The 2012 revision of WHO classification grouped neuroendocrine carcinoma amongst a subtype of rare epithelial carcinomas including: carcinoma with neuroendocrine features, a well-differentiated neuroendocrine tumour, poorly differentiated neuroendocrine carcinoma and carcinoma with neuroendocrine differentiation [13]. Differential diagnostics encompasses Merkel cell carcinoma, lymphoma, carcinoid and melanoma [14].

The described case met the criteria for NEBC diagnosis. Immunohistochemical analysis demonstrated positive staining for the oestrogen receptor (ER) and progesterone receptor (PR), positive chromogranin staining in over 50% of the cells, positive synaptophysin
staining and mucus (Fig. 3–7). The case was defined as mucinous carcinoma with neuroendocrine differentiation.

According to data obtained through the analysis of case reports, the diagnostic incidence of NEBC increases in women over 50 years of age and primarily affects patients in their sixth or seventh decade of life [2]. Physical examination usually reveals the presence of a breast tumour. The literature provides no data concerning the incidence rate of NEBC in particular locations of the mammary gland. Some reports suggest that NEBC are less common than the typical infiltrating breast cancer (BC) to metastasise to axillary lymph nodes [11].

Metastases to supra- and infraclavicular lymph nodes were not described. The literature describes no cases of the coexistence of NEBC and typical BC within one breast.

In the case described by us, the NEBC focus was located deep in the breast, very close to the thoracic wall and was not palpable upon physical examination. The regional lymph nodes raised no suspicions. No particular differences can be observed in the clinical features of neuroendocrine tumours and the tumours of other breast malignancies, either on clinical examination or imaging [11,15,16].

On a mammogram, it may appear as a well-circumscribed focal lesion without accompanying microcalcifications, similar to a benign lesion [1].

In the case described by us, the morphology of the NEBC focus, located at the border of the lower quadrants, manifested a difference in relation to the typical BC in the upper-outer quadrant. The difference between the two tumours was visible on spectral mammography in low-energy images and concerned their shape and contours. However, spectral mammography revealed differences in imaging as regards features that are typical of tumours suspicious of neoplastic proliferation (Fig. 1–2).

Attention is drawn to the fact that the spectral mammography image of the NEBC tumour, both in low-energy images and after contrast medium administration, was almost twice as large as in the post-operative histopathological examination 3 x 1.5 cm versus 1.6 x 1.2 cm. Is such an effect likely to be caused by the desmoplastic reaction in the surroundings of the tumour?

Upon identification of a suspicious breast lesion (BIRADS – 4.5), it is necessary to verify it under a microscope by performing core-needle biopsy (CNB). In the described case, it was difficult to perform CNB of the lesion at the border of the lower quadrants due to its depth and closeness to the thoracic wall as well as to diagnose invasive BC in the second focus. As a consequence, further microscopic diagnosis in the pre-operative procedure was abandoned. After excluding the presence of secondary lesions, surgical treatment was carried out. Due to the fact that the neoplastic process was suspected to be multicentric and taking into account the patient’s will, a total right mastectomy was performed along with the sentinel node diagnostic procedure. Upon receipt of the histopathological report, supplementary hormonal therapy was indicated.

The treatment of primary neuroendocrine carcinoma is a multidisciplinary issue. Nonetheless, it seems that primary surgical treatment should be treated as priority. Due to its rare incidence, the data concerning the prognostic factors of NEBS and, consequently, the indications for systemic treatment and radiotherapy are only obtained from case reports and, more often than not, are the same as those for the treatment of typical BC. In the present case, both the NEBC focus and the lesion with typical BC tissues demonstrated high expression of steroid receptors, which – in the absence of other risk factors – constitutes an indication for hormonal therapy as the only form of supplementary treatment.

In conclusion, a primary NEBC is a very rare neoplasm and its coexistence with other breast carcinomas has not been described so far. The recommendations with regard to the diagnostics and treatment are extrapolated from the indications concerning the management of “ordinary” infiltrating breast cancer.

Author’s contribution

Study design – A. Lorek
Data collection – A. Lorek
Data interpretation – A. Lorek, A. Boratyn-Nowicka
Statistical analysis – A. Lorek
Manuscript preparation – A. Lorek, A. Boratyn-Nowicka
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