Review paper

Adenoid cystic carcinoma of the breast

Rak gruczołowo-torbielowaty piersi

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Słowa kluczowe: rak gruczołowo-torbielowaty piersi, rak piersi, diagnostyka, leczenie.

Abstract

Adenoid cystic carcinoma is an invasive cancer accounting for less than 0.1% of all breast cancers. It most frequently occurs as a single, clearly defined, tender tumour. Mammographic and ultrasound images are non-characteristic and may be misinterpreted as benign change. This cancer shows no expression of ER, PGR, and HER-2 receptors; however, as opposed to triple-negative breast cancers, NST has a mild course and sporadically gives rise to metastases to locoregional lymph nodes and distant metastases. There is no consensus concerning the optimum treatment. The surgeries usually performed are lumpectomy with an open sentinel lymph node biopsy and mastectomy. However, considering the low probability of the presence of metastases in the lymph nodes, doubts arise pertaining to the justification for lymph node resection. Adjuvant radiotherapy is recommended after breast-conserving surgeries, especially with positive margins. The role of chemotherapy has not been well recognised, and hormone therapy is not recommended.

Streszczenie

Rak gruczołowo-torbielowaty piersi jest nowotworem inwazyjnym stanowiącym poniżej 0,1% wszystkich raków piersi. Występuje najczęściej jako pojedynczy, dobrze odgraniczony, tkliwy guz. Obraz mammograficzny i ultrasonograficzny nie jest charakterystyczny, może być on błędnie interpretowany jako zmiana łagodna. Rak ten nie wykazuje ekspresji receptorów ER, PGR i HER-2, ale w przeciwieństwie do trójujemnych raków piersi NST ma łagodny przebieg, sporadycznie daje przerzuty do lokoregionalnych węzłów chłonnych i przerzuty odległe. Ze względu na niewielką częstość występowania tego nowotworu nie ma konsensusu dotyczącego optymalnego leczenia. Najczęściej wykonywane zabiegi to lumpektomia z otwartą biopsją węzłą wartowniczego i mastektomia. Jednak z uwagi na niewielkie prawdopodobieństwo obecności przerzutów w węzłach chłonnych pojawiają się wątpliwości dotyczące celowości resekcji węzłów chłonnych. Adiuwantową radioterapię zaleca się po wykonanych zabiegach oszczędzających, zwłaszcza przy dodatnich marginesach. Rola chemioterapii nie jest dobrze poznana, leczenie hormonalne nie jest zalecane.

Introduction

Invasive breast cancers are a heterogenous group of malignant breast carcinomas that differ in morphological, molecular, and genetic aspects. The most common type of cancer is ductal carcinoma of no special type (NST). It constitutes 75% of all types of invasive breast cancer.

Adenoid cystic carcinoma may be distinguished among rarely observed primary breast cancers. This is a malignant cancer typical of the salivary glands; however, it may also develop in other organs. There are cases that describe its occurrence in the breast, vulva, cervix, skin, lacrimal glands, upper airways, lungs, kidneys, oesophagus, and prostate gland. The progression of the disease depends on the site of origin of the cancer. Adenoid cystic carcinoma of the lacrimal glands has an aggressive course and a tendency towards local and distant metastases, whereas the same type of cancer located in the breast shows a considerably milder character, with a low tendency for the formation of metastases [1–3].

Adenoid cystic carcinoma constitutes less than 0.1% of all breast cancers. The mean age of patients

with the diagnosis of this type of cancer is 50–60 years; cases are also described in patients aged between 30 and 90 years of age. Thus, the distribution by age is similar to the age of occurrence of other types of invasive breast cancer. This cancer concerns primarily females, but single cases of the disease have been described in males [3, 4]. These are most frequently single tumours, and sporadically they are multifocal [5, 6].

Symptoms

Adenoid cystic carcinoma occurs with the same frequency in both breasts, and may be located in all quadrants; in most cases described, the changes are located in the periareolar area. The size of tumour is usually 1–3 cm (cT1–cT2), but sizes have also been diagnosed from 0.1 to 15 cm. Despite the periareolar location, pathological nipple discharge is rarely observed, while nipple retraction is more often diagnosed. These changes grow slowly and are clearly defined. The characteristic feature occurring in most patients is pain or tenderness in the area of the change. In the case of adenoid cystic carcinoma located in the salivary glands pain is caused by perineural invasion, whereas in the case of this type of cancer in the breast it has not been fully recognised. Pain complaints are probably caused by the contraction of the myoepithelium [2].

Imaging diagnostics

Similar to other types of breast cancer, the diagnostics of patients with adenoid cystic carcinoma is based on imaging and histopathological examination. It does not present a typical image of invasive cancer, neither in mammography nor in ultrasound. It is usually a tumour with clearly defined borders, local invasiveness lower than other types of breast cancer, and low infiltration of the adjacent tissues [7].

On mammographic image, the change most often presents as a density with uneven outlines; sporadically there occur microcalcifications.

On ultrasound, this cancer is described as an irregular, hypoechoic, or heterogenous change, with minimal vascularity on Doppler USG [2]. Both mammographic and ultrasound images of adenoid cystic carcinoma are non-characteristic, and may be misinterpreted as a benign change [3, 8].

The role of magnetic resonance and positron emission tomography-computed tomography (PET-CT) is unconvincing. Magnetic resonance imaging may be useful in the diagnostics of patients with dense breast glandular tissue, when it is difficult to evaluate mammographic images. On magnetic resonance imaging (MRI), the changes are described as oval or round tumours showing low contrast enhancement, but also as spiculated changes of irregular shape [8].

Microscopic diagnostics

The microscopic image of adenoid cystic carcinoma is similar to the image of this type of cancer in other organs. This is an epithelial myoepithelial carcinoma composed of two types of cells: ductal epithelial cells and basaloid myoepithelial cells. The percentage content of these cells in tumours varies. Both components do not show expression of ER, PR, and HER-2 receptors. Histologically, three types of adenoid cystic carcinoma are distinguished: tubular, cribriform, and solid. The cribriform occurs most frequently, while the solid form is the least common [3, 9].

Histological grade is an important prognostic factor. It is determined based on the percentage content of solid-type structures in the tumour. Cancers with tubular and cribriform components are classified as Grade I, cancers with solid texture £ 30% are Grade II, and those with the content of solid component above 30% are qualified as Grade III. Cancers containing the solid subtype more frequently give rise to local recurrences and distant metastases [3].

On the genetic level, adenoid cystic carcinoma of the breast is characterised by translocation t(6;9)(q22–23;p23–24), leading to the MYB-NFIB gene fusion, analogous to that occurring in adenoid cystic carcinoma of the salivary glands. This is the main oncogenic mechanism, present in more than 90% of cases of this type of breast cancer.

In contrast to triple-negative breast cancers, which are characterised by genome variability and high frequency of mutations, adenoid cystic carcinoma of the breast is a cancer with a low index of mutation and low level of genetic instability. In this cancer, no mutations were observed occurring in triple-negative breast cancers such as TP53 and PIK3CA, whereas it shows somatic mutational heterogeneity affecting the functions of, among others, chromatin remodelling and cell adhesion [10].

No relationship was confirmed between the occurrence of adenoid cystic carcinoma of the breast and the presence of BRCA1 and BRCA2 gene mutations. Also, the Ki-67 labelling index is low, even lower than in other types of breast cancer of low level of malignancy [3].

Studies are being conducted in order to determine whether the transformation is possible of adenoid cystic carcinoma to triple-negative breast cancer – a cancer with much worse prognosis – through analogy to this type of cancer occurring in salivary glands, which is capable of transforming into highly aggressive cancers of various histologic types [10, 11].

Prognosis

As opposed to other triple-negative breast cancers, and also contrary to adenoid cystic carcinoma occurring in salivary glands, the prognosis of adenoid cys-

tic carcinoma in the breast is very favourable: 10-year survival is 90–100%. Metastases to the axillary lymph nodes and distant metastases are rare. The presence of metastases to locoregional lymph nodes is observed in 0–2% of patients [12, 13]. The most frequent location of distant metastases are the lungs, more rarely the liver, kidneys, skeletal system, and the brain. Distant metastases were also diagnosed in patients who had no changes observed in the lymph nodes.

Treatment

Due to the low frequency of occurrence of this type of cancer, there is no consensus concerning optimum surgical treatment. Concerning favourable prognoses and low probability of the presence of metastases in the lymph nodes (0–2%), doubts arise pertaining to the necessity for biopsy of the sentinel lymph node or axillary lymphadenectomy in patients with clinically and ultrasound suspicious nodes [14]. According to some researchers, such management is not recommended [15, 16].

The type of surgical procedure depends on the size of the tumour and the presence of metastases in the lymph nodes. A beneficial option of surgical treatment is a breast conserving surgery lumpectomy or quadrantectomy. In the case of large tumours, when the cosmetic effect of conserving procedure would be unsatisfactory, mastectomy is recommended.

Based on the results of a retrospective study conducted by the Rare Cancer Network, when in none of the treated patients the lymph nodes are affected, it is suggested that axillary lymphadenectomy be performed only in patients with clinically and radiologically suspicious lymph nodes, with the component of other subtypes of breast cancer, as well as in the case of the solid-basaloid variant. An open biopsy of the sentinel lymph node is recommended in the case of tumours larger than 3 cm, and in the case of the occurrence of other subtypes of invasive cancer [2, 17].

The role of adjuvant radiotherapy in patients with adenoid cystic carcinoma remains unclear. A 2010 retrospective study compared total survival time and disease-related survival time in patients who had undergone radiotherapy and those who, without such a treatment, showed an improvement of both values. Also, the frequency of local recurrences was lower after the application of radiotherapy. This is recommended in patients who have undergone conserving surgery, especially with the presence of positive margins [2, 10, 18].

The role of chemotherapy has not been well recognised. It is recommended in the case of generalised disease and sometimes in patients with tumours of size exceeding 3 cm and with a high level of malignancy.

Considering the fact that adenoid cystic carcinoma of the breast is a triple-negative cancer, hormone therapy is not recommended.

Follow-up examinations

Distant metastases and local recurrences in adenoid cystic carcinoma of the breast may arise after a long time has elapsed since the treatment. For this reason, many-year follow-up examinations are indicated. In many cases, the presence of distant metastases does not correlate with the affected axillary lymph nodes. The most frequent location is the lungs; therefore, within long-term follow-up an annual performance of chest radiography is recommended.

Summary

Adenoid cystic carcinoma is a very rarely observed malignant breast cancer. Consequently, there is no consensus concerning the treatment of this disease. Genetic studies of such a heterogenous group of carcinomas as breast cancer may give a direction for the treatment and help in the development of methods of individual therapies.

Considering its characteristic pathological and clinical features and rare occurrence, attention should be paid to this subtype of breast cancer.

Conflict of interest

The authors declare no conflict of interest.

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