

ARGIROPHYL, „CARCINOID-LIKE“ BREAST CANCER

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ARGIROFILNI „KARCINOID-LIKE“ KARCINOMI DOJKE

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SAŽETAK

Mnogobrojna istraživanja poslednjih decenija su pokazala prisustvo neuroendokrinih tumora i njihovih ćelija u mnogim organima.

U našem radu je proučavano prisustvo i distribucija neuroendokrinih markera u različitim tipovima karcinoma dojke.

Korišćeno je 30 uzoraka karcinoma dojke ukalupljenih u parafinske blokove. Na preseccima debljine 5–6 mikrometara su primenjene klasična HE metoda za verifikaciju patohistoloških lezija, argirofilna metoda po Grimeliusu i imunocitoheimijska ABC tehnika sa anti-hromograninom, anti-NSE i anti-kalcitoninom.

Grimeliusova reakcija je bila pozitivna u 65% karcinoma. hromogranini su se javili sa istom učestalošću i rasporedom kao i argirofilija. NSE je prisutna u većine neoplastičnih ćelija. Kalcitonin je nađen samo u hromogranin-pozitivnim ćelijama.

Naši rezultati sugerišu endokrinu prirodu nekih argirofilnih karcinoma dojke. U radu se diskutuje o ulozi polipeptidnih hormona u regulaciji rasta tumora.

Ključne reči dojka, karcinomi, neuroendokrine ćelije

ABSTRACT

A great number of studies in the last decades confirmed neuroendocrine tumours and their cells in many organs.

In our work we were studying the presence and distribution of neuroendocrine markers of different types of breast cancers.

Thirty (30) samples of breast cancers were used which have been gathered in paraffine blocks on 5–6 micrometre cross sections. The classic method was used in order to verify pathohistological lesions, argirophil method by Grimelius and ABC immunocitochemical technique with an anti-chromogranine, anti-NSE anti-calcitonine.

Grimelius reaction was positive in 65% of cancers. Chromogranines showed as same frequency and arrangement as argirophyll. NSE persist in majority of neoplastic cells. Calcitonine is found in chromogranin-positive cells only.

Our results suggests on an endocrine nature of some argirophil breast cancers.

It is discussed about polipeptide hormone function in regulation of tumour growth.

Key words: breast cancer, neuroendocrine cells.

INTRODUCTION

The growing frequency of breast cancer, all around the world, as well as in our country, is continuously attracting attention of scientists of all profiles. The traditional attitude that hypophysis-gonad axis hormones play the capital role in the genesis of breast cancer was largely changed and corrected with the discovery of Pears's APUD (Amine Precursor Uptake and Decarboxylation), mainly in the our understanding of paracrine and autocrine characteristics of the regulary peptides (1, 2).

The study of APUD or neuroendocrine sells in the breast has started with Feyrter's acknowledgement of the presence of „bright cells“ in the normal breast tissue, between the mioepithelial and excretory epithelial cells. Argyrophyl type of the neuroendocrine cells has been first described by Feyrter and Hartmann(1963) with the mucine breast cancer and they have classifies it in the „diffuse endocrine system“ (3). Regardless to the decades which have passed, there is a lack of information about the presence of neuroendocrine cells in breast diseases, so consequently the aim of our work was the study of distribution and morphological characteristics of argirophyll neuroendocrine cells in the lobular and scirrhous breast adenocarcinoma.

MATERIAL AND METHODS

Retrospectively, 30 samples of breast cancer have been used (15 scirrhous adenocarcinomas and 15 lobular) which were embedded in paraffin. Namely, it is about the practical material which was fixed in the Bowen's solution for 24 hours, and afterwards processed and embed-

ded in paraffin. The cross sections of 5 micrometers were done from the paraffin blocks and the following histological techniques were used:

1. Standard HE method, verifying pathohistological lesion
2. Gomori's histochemical methods, colouring reticular fibres
3. Van-Gieson histochemical methods, presenting collagen fibres.
4. Grimelius's cytochemical argirophyll reaction (1968)
5. Immunocytochemical ABC method (1981) with anti-chromogranin and anti NSE (1:1600, DAKO)

RESULTS

Numerous argirophyll cells in both histological types of breast cancer have been acknowledged by Grimelius's cytochemical reaction. In the scirrhous adenocarcinoma the neuroendocrine cells are mainly individual, arranged multifocally, fairly extended and largely argirophyll (Figure 1), while in the lobular carcinoma these cells are notably smaller in size, have cytoplasmic extentions, are frequently in groups and largely argirophil, too. Argyrophil cells have been present in 65% of examined tumours (in 19 cases).

In both variations of tumour, neuroendocrine cells which have chromogranine are verified, and it is a general specific marker of these cells. In the scirrhous adenocarcinoma, neuroendocrine cells which have chromogranine express notable immunoenzymatic polymorphism. Thus, in some tumours, the cells are of larger size, circular or po-

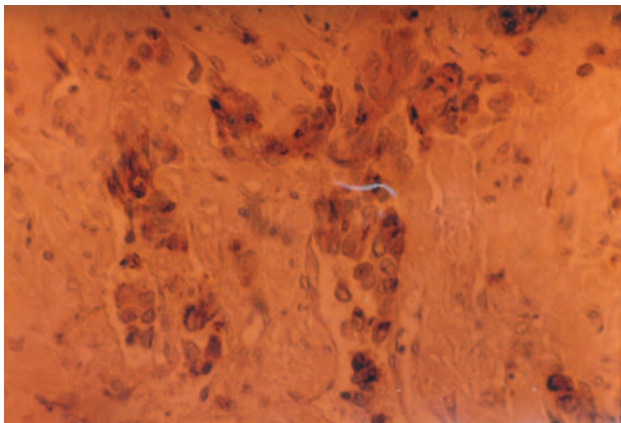


Figure 1. Large argyrophyl neuroendocrine cells in the scirrhous carcinoma

ligonal and form platelets divided into collagen stroma (Figure 2), in other tumours they are tiny, circular and multifocally arranged, and sometimes they are individual, extended with cytoplasmic extensions which are passing by between the neighbouring epithelial cells.

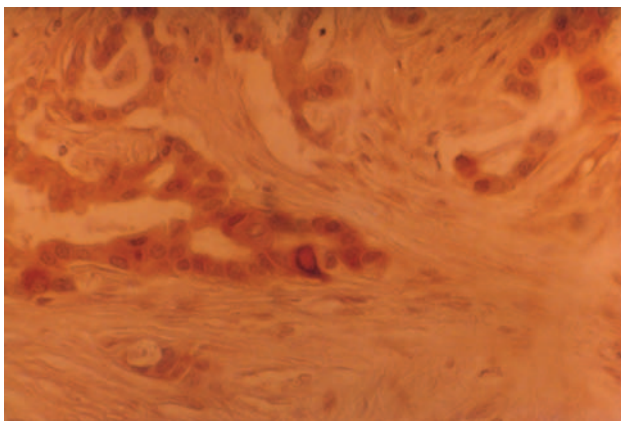


Figure 2. Large polygonal cells into collagen stroma

In the lobular carcinoma chromogranines are found in circumferential position, in parabasal cells (Figure 3), as well as in squamous epithelium of the cystic duct.

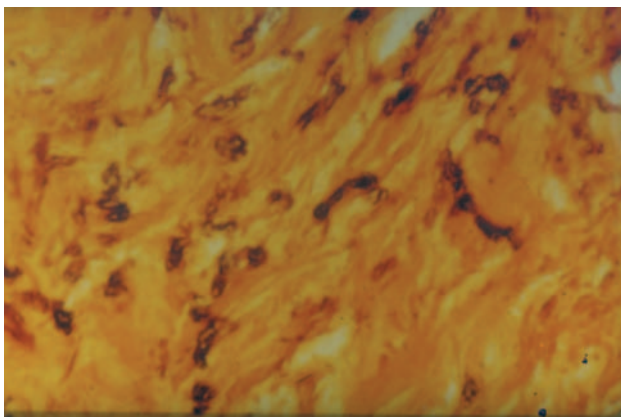


Figure 3. Chromogranines in lobular carcinoma

Whereas NSE is present only in rare individual cells in lobular carcinoma, the large NSE-immunoreactive cells form glandula formations in squamous adenocarcinoma, where NSE is found also in mioepithelial cells (Figure 4)

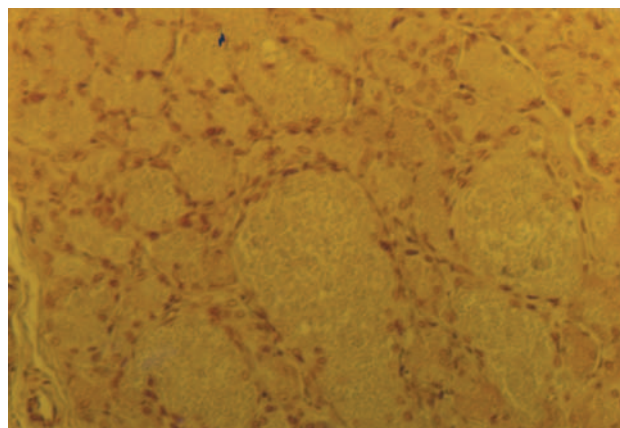


Figure 4. NSE in mioepithelial cells

We emphasise the importance that neuroendocrine cells are always more numerous in tumours of weaker differentiation.

DISCUSSION AND CONCLUSION

Apart from widely known argyrophyl characteristics of neuroendocrine peptide, the chromogranin and neuron specific enolase (NSE) are considered to be specific markers for verification. Chromogranins are extracted from the module of adrenal, divided into A, B and C types and are able to stabilize intraglanular matrix. In relation to this characteristic it is emphasized that the expression of Chromogranin A is in coorelation with the positive Grimelius's reaction. NSE is a cytosol protein so its presence is not connected with the content of the granula, so it is considered as an excellent indicator of neuroendocrine cells and their neoplasms since the reaction is positive also in case of degranulated cells (4).

The presence of neuroendocrine components in breast cancer is for a long time explained as „a reactive hyperplasia" of normally present endocrine cells. However, the announcement of Nesland and associates (1988) about the presence of these cells also in metastatic foci are in favor of neoplastic overview of this component (5). The attitude of histogenesis of neuroendocrine cells is consolidated by Damian and his associates (6) pointing out that neuroendocrine cells as well as the carcinoma originated by the multidirectional differentiation of „progenitor," cells.

In contrast to some literary announcements (7), our observation that the thickness of the neuroendocrine cells is always larger with tumours of weaker differentiation, is of great importance. On our matrial it is also noticeable the heterogenic histological image of neuroendocrine cells, from tumour to tumour as well as inside the same carcinoma. This heteromorphism is, most probably, influenced by the heterogenetic chemical content of the cell products (8).

There is a great discrepancy about the frequency of the neuroendocrine cells in breast cancer, but it also seems that everything depends on diagnostical possibilities, which are quite wide in some laboratories and they seem to be of greater frequency (9). Detecting hormones as well as/or the presence of endocrine syndromes is rarely described in literature (10).

The discovery of neuroendocrine cells in epithelial tumours has influenced the introduction of mixed-endocrine-epithelial neoplasms into oncogenic pathology. (11).

CONCLUSION

According to our results the following conclusions are drawn:

1. Carcinoid-like breast cancer is characterised by the notable hyperplasia of polymorphic neuroendocrine cells.
2. The number of neuroendocrine cells is proportionate to the degree of tumour malignant potential.

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