MORPHOLOGICAL CHARACTERISTICS OF METASTATIC BRAIN TUMORS AND THEIR PRIMARY SOURCES

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ABSTRACT

Evaluation of morphological differences between primary tumors and their intracerebral metastases was performed in operational specimens from 41 patients with intracerebral metastases (carcinoma in 80,5±6,19 %, melanoma in 19,5±6,19 %) and primary tumors: skin melanoma (8 cases), lungs carcinoma (17 cases), breast carcinoma (16 cases). Standard basic micromorphological processing was performed. The structure of intracerebral metastatic melanoma foci had similarities with primary foci, but with higher atypicity, vascularity, surrounding by "muffs" of tumor cells, hemorrhagic, inflammatory and necrotic foci. Tumor tissue of lungs-derived metastatic focus repeated the structure of primary tumor, in patches glandular formations go with solid layers of acinar structures in the center, stroma in these places is not prominent giving an evidence of de-differentiation. In primary breast tumors and their brain metastases morphology was almost identical. It was proved that brain metastatic tumor tissue is characterized by lower differentiation comparing with primary tumor.

KEYWORDS

Skin Melanoma, Lung Carcinoma, Breast Carcinoma, Brain metastasis, Morphology

1. INTRODUCTION

Metastatic affection of brain by its prevalence, medical and social importance and economical burden represents a topical medical problem in neurosurgery and adjacent medical specialties [1, 2].

The statistical data about the frequency of metastatic brain tumors (MBT) among all cerebral neoplasms are discrepant and vary, according to different sources, from 1,2 % to 50 % [3, 4, 5]. The frequency of malignant tumors brain metastasis is about 0,5 % of all cases of oncological pathology; it was noted what in 23-39 % of oncological patients with metastases to central nervous system the affection of brain is first and sometimes only manifestation of latent course of primary malignant tumor [6, 7, 8].

The problem of MBT treatment in Ukraine and all the world is one of the most topical because the frequency of the diseases is growing from year to year due to increase of primary pathology incidence, such as lung cancer, breast cancer and other.

2. MATERIAL AND METHODS

The aim of the research was evaluation of morphological differences between primary tumors of different locations and their intracerebral metastases for optimization of diagnosis and treatment of metastatic brain tumors. In the presented in this article part of research the morphological characteristics of MBT and corresponding primary tumor foci was performed using histological microspecimens of operational material of primary tumors and their brain metastases from 41 patients obtained from archives of pathologoanatomical departments of Kharkiv Regional Clinical Hospital – Center of Emergency Medical Care and Disaster Medicine; Kharkiv Regional Clinical Oncological Center, while in the dissertational research we cover a wider range of primary tumors locations (nephrogenic cancer, vaginal cancer, thymoma, leiomyosarcoma and unknown primary sources together with their intracerebral metastases in addition to what was mentioned above). By histological structure the metastases were represented by carcinoma in 33 cases (80,5±6,19 %), by melanoma – in 8 cases (19,5±6,19 %), and by primary tumors: skin melanoma (8 cases), lungs carcinoma (17 cases) and breast carcinoma (16 cases).

The preparation of histological specimens was standard. Tissue samples has been fixed in 10 % solution of buffered (neutral) formalin, then processed though alcohols in gradually increasing concentration, Nikiforoff's fluid (96 % ethylic alcohol and diethylic ether in 1:1 ratio), chlorophorm, after what filled with paraffin. From prepared in such a manner blocks the serial sections of $4\text{-}5\times10^{-6}$ m width have been produced with microtome. The morphological processing included the routine method of hematoxylin and eosin staining. The histological methodics mentioned above is conducted by the prescriptions described in the guidelines of histological technics [9, 10]. Microscopy and photographing has been performed with Olympus BX-41 microscope. The critical value of p-level was 0.05.

The research has been conducted according to requirements of European Convention (Strasburg, 1986), ICH GCP (2008), GLP (2002) principles, local Ukrainian legislation.

The statistical analysis has been performed using non-parametric methods with critical p-level of 0.05.

3. RESULTS AND DISCUSSION

One of tumors often associated with brain metastases is melanoma. In our research we have revealed epithelioid-cellular (6 cases) and spindle-cell (2 cases) histological variants of primary melanoma foci.

Below morphological characteristics of primary tumor tissue foci and its intracerebral metastases of most often melanoma histological variant – epithelioid (carcinoid) form is represented (our own observation).

The tissue of primary tumor is built from "nests" of atypical cells with big excentrically located big nucleus and clearly visualized nucleolus, present in the derma. In the cytoplasm of most cells a greyish-brown pigment (melanin) is revealed in excess quantities (figure 1).

In part of cases the multi-layer squamous epithelium does not possess a melanocyte activity; in some of samples there are signs of pseudo-carcinomatous hyperplasia of multi-layer squamous epithelium – its reactive overgrowth in form of acanthosis bundles.

The structure of MBT was similar to primary foci, while the level of differentiation of tumor tissue is lower. In the MBT preparations more intensive cellular atypism, more vessels

surrounded with “muffs” of tumor cells, foci of haemorrhage, inflammation and necrosis are present comparing with primary tissue (figure 2).

It was stated that the degree and extent of spread of melanin accumulation in a primary and metastatic tumor may be different: melanin in metastatic focus, same as in primary, is accumulated diffusely in excess amounts or melanin is metastatic tumor is present insufficiently or moderately, while in a primary focus it is present in excess quantities.

In general, in case of melanoma-derived MBT there was a low differentiation of tumor tissue: expressed cells atypism and polymorphism, multiple vessels surrounded with tumor cells which here and there form “muffs”, foci of inflammation and necrosis of tumor tissue.

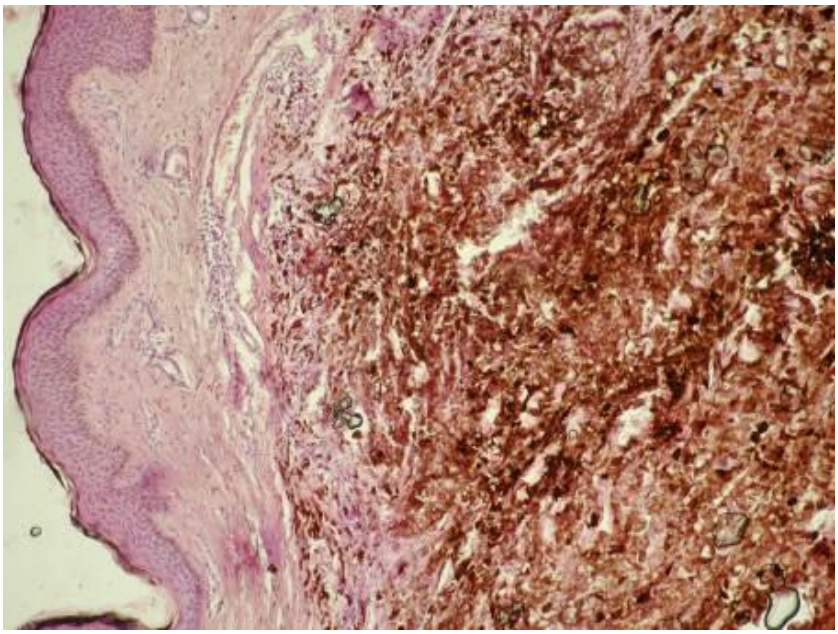

Figure 1. Skin melanoma, epithelioid cell type. Hematoxylin and eosin staining, ×100

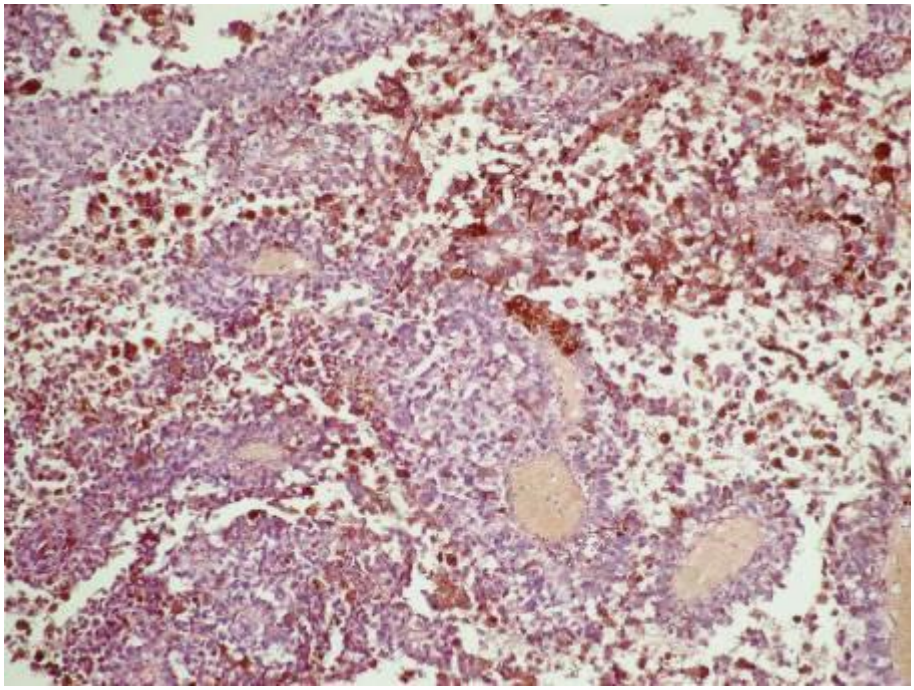

Figure 2. Brain metastases of epithelioid cell skin melanoma. Hematoxylin and eosin staining, ×100

It is known that most often origin of MBT are tumors of lungs and breast. This has got a confirmation in the results of our research.

Metastatic brain tumors derived from malignant tumors of lungs were represented mostly by glandular tumor tissue – metastases of adenocarcinoma, in part of cases – by metastases of squamous-cellular and non-differentiated cancer. Cases of primary tumors observed by us on histological specimens represented most often highly-differentiated adenocarcinoma of lungs – in 10 cases (the morphological characteristics of primary tumor and MBT tissue from our own observations is represented below), moderately-differentiated – in 2 cases, low-differentiated – in 1 case, large-cell (clear-cell variant) – in 3 cases, squamous-cell – in 1 case.

The primary tumor tissue of lung – highly-differentiated adenocarcinoma – consisted of atypical glandular structures of different sizes and shape covered with large prismatic cells with round-shaped or oval basally-located nuclei, the cytoplasm is well-expressed; the polymorphism of cells and nuclei was observed; papillary structures were met here and there in the tumor; the stroma was intensive enough, with loci of infiltration with lymphoid-plasmocytic cellular elements (figure 3).

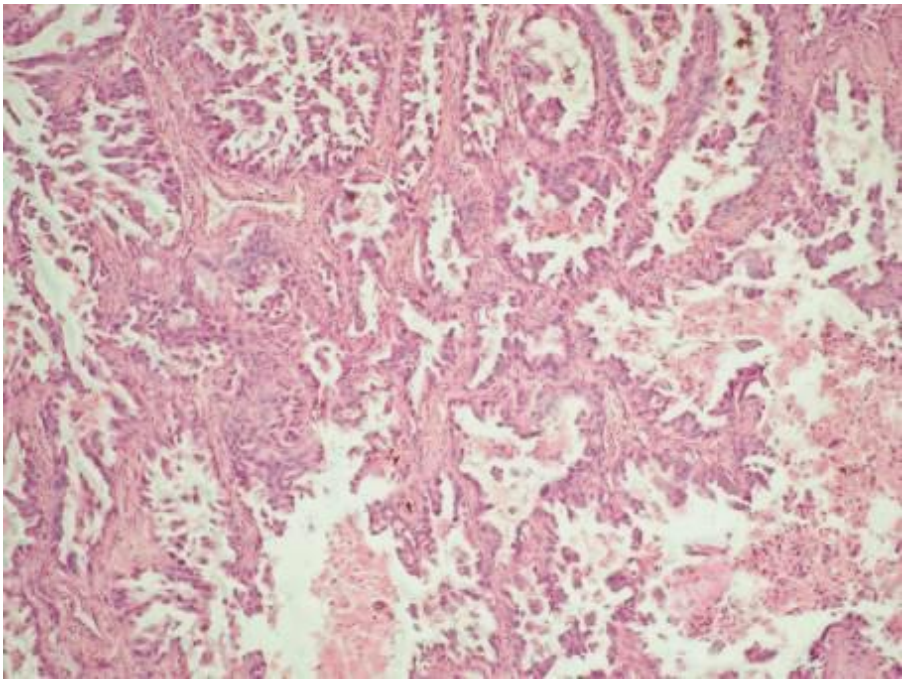

Figure 3. Highly differentiated lung adenocarcinoma. Hematoxylin and eosin staining, ×100

The tumor tissue of metastatic focus, in places, repeated the structure of primary tumor with high degree of differentiation; in places, glandular structures combine with solid layers with acinar structures in the centre, the stroma in these locations is weak (figure 4), which testify the decrease of differentiation degree of tumor tissue.

Cases of breast intracerebral metastases observed by us, in primary tumors were presented by mostly invasive ductal carcinoma – 10 cases, invasive lobular carcinoma – 3 cases, non-invasive ductal carcinoma – 1 case and mixed variants – 2 cases.

Below we present our own observations, represented by following microscopy variants of breast cancer with metastases to brain: invasive lobular, partly ductal adenocarcinoma of solid-scirrhous structure and invasive ductal cancer with cribrous structures (figure 5).

First variant of breast adenocarcinoma may be classified as moderately differentiated, because solid loci are more characteristic for high level of differentiation, scirrhous – as low-differentiated, that's why this mixed variant occupies a intermediate position. Second, cribrous, variant concerns highly-differentiated type. While, metastatic foci in brain have been observed in both cases, in spite of the fact that highly-differentiated tumors, particularly cribrous cancer, are not inclined to distribution of metastasis or do not produce them for prolonged time.

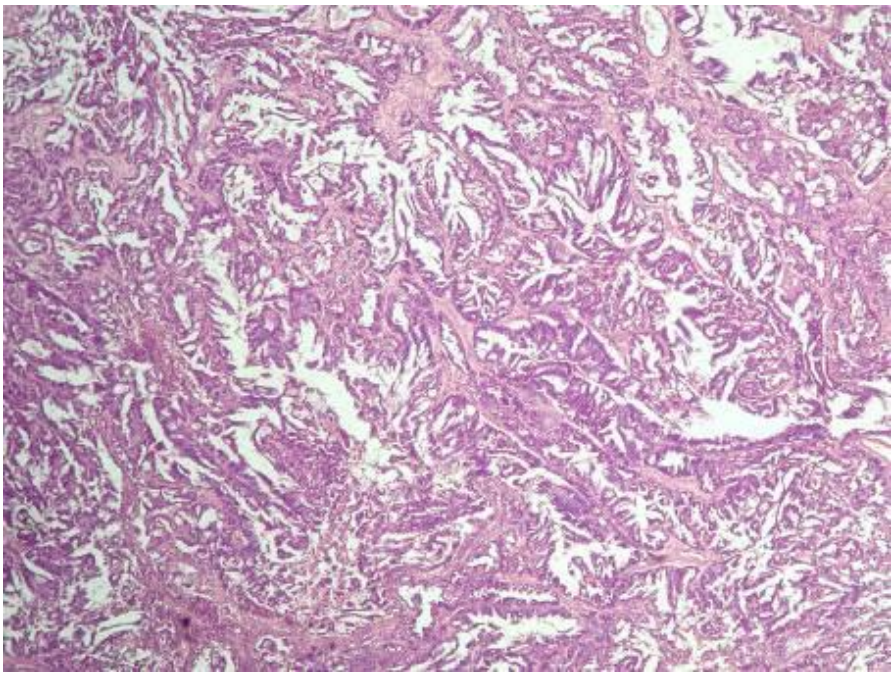

Figure 4. Lung adenocarcinoma brain metastasis. Hematoxylin and eosin staining, ×40

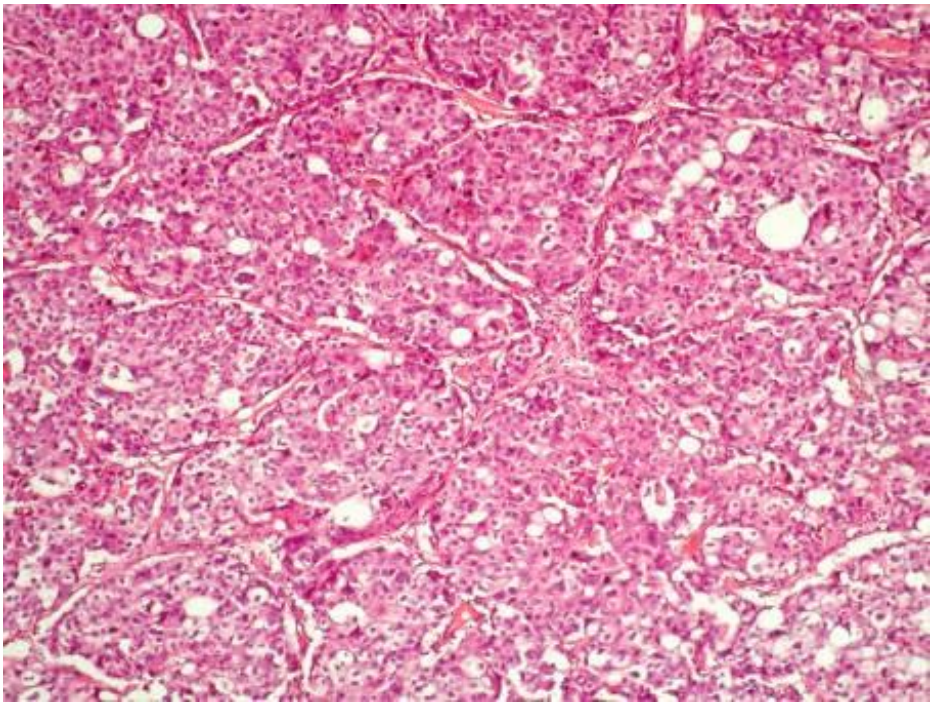

Figure 5. Invasive ductal breast adenocarcinoma. Hematoxylin and eosin staining, ×100

Metastatic tumor tissue in first variant was represented by partly solid foci with more or less expressed stromal component (figure 6), in second variant – in metastatic foci the tumor tissue was represented mostly with cribrous structures; apart of this, multiple full-blooded vessels, inflammatory infiltration and small necrotic foci were observed.

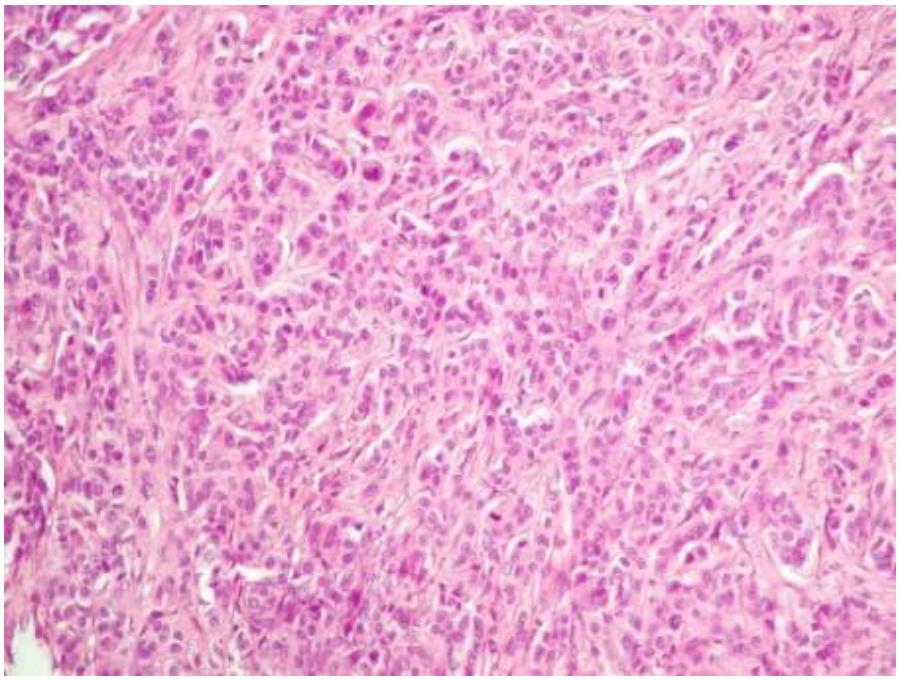

Figure 6. Brain metastasis of invasive lobular, partly ductal breast adenocarcinoma. Hematoxylin and eosin staining, ×200

4. CONCLUSIONS

Thus, the carried-out research of microscopic structure of MBT and primary tumor foci let us to prove the fact that metastatic tumor tissue in brain is mostly characterized by lower differentiation comparing with primary tissue.

In turn, the lower is a differentiation of tumor tissue, the more aggressive is a so-called clinical behaviour of the neoplasm, and this plays a significant role in the choice of treatment tactics and prognosis for working capacity and life of a patient.

Perspective of further researches might be connected with revealing of morphometric, histochemical, immunohistochemical peculiarities and development of derivative index parameter considering the nature of brain metastasis and integrative for neoplasms of different origin and histological structure.

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