

ORIGINAL PAPER

Histopathological and immunohistochemical aspects in both basaloid and spindle cell variant of cervical carcinoma

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Abstract

The study was performed by using a number of eight cases of cervical carcinomas suiting to basaloid carcinomas and spindle cell carcinomas under the circumstances of usual histopathological staining. Immunohistochemically we used anticytokeratin monoclonal antibody (AE1/AE3) to confirm the epithelial differentiation and also PCNA to evaluate the cell proliferation rate. Tumor positiveness for AE1/AE3 cytokeratin cocktail confirmed its epithelial nature. Immunoexpression for PCNA indicated a high index of cell proliferation for all the cases with a more increased value for the basaloid carcinomas.

Keywords: basaloid carcinoma, spindle cell carcinoma.

Introduction

Cervical frank invasive squamous carcinoma lies on the second place within the female oncological pathology [1].

It was estimated that 390 000 invasive cervical cancer cases were diagnosed throughout the world in 1990. Differences of the lesion incidences from different areas of the world result from both the differences of the female populations undergone to screening testes and the risk factor prevalence's.

Histopathologically, cervical poor differentiated squamous carcinomas may have different patterns of growth witch appear to be associated with the same somber prognosis of the lesions [2–4].

Among these cancers we mention the spindle cell carcinoma and the basaloid carcinoma, witch has often raised the problem of diagnosis especially when the fragment biopsies are discussed.

Material and methods

A set of eight cervical carcinomas was available for our study; the patients were hospitalized with the common diagnosis of cervical neoplasia and they underwent biopsy into the Gynecology Clinic of the Emergency County Hospital of Craiova.

The fragments removed were processed by the usual method of wax embedding and then were Hematoxylin–Eosin stained. For immunohistochemical study we used LSAB/HRP method in the laboratory of the Center for

Microscopic Morphology and Immunology Research Craiova.

Markers were used to reveal the epithelial differentiation the anticytokeratin monoclonal antibody (AE1/AE3 – Dako cytokeratin cocktail, AE1/AE3 clone) and again markers to evaluate the cell proliferation rate (PCNA – Dako, nuclear proliferation antigen, PCNA Clone PC10, NP047).

For AE1/AE3, immunomarking intensity was appreciated by using a four-degree system, such as: the absence of immunomarking (-), poor intensity (+), moderate intensity (++) and intense immunomarking (+++).

For PCNA immunostaining it was calculated a percentage index of immunostaining, by the ratio between the number of positive cells (nuclei) and the total number of counted cells (negative and positive) and the result was multiplied with 100; a number of minimum 500 nuclei were counted for each case.

Results

These eight cases studied in usual histopathological staining corresponded to basaloid carcinomas in five cases and to spindle cell carcinoma in three cases. The tumors were diagnosed in patients aged between 42 and 64 years.

Spindle cell carcinomas consisted in a proliferation of elongate, spindle and relatively uniform size neoplastic cells. They formed crossed fascicles with a pattern similar to sarcomas.

The tumor cells had vesicular nuclei with marked nuclear pleomorphism and intense mitotic activity with frequent atypical mitosis (Figure 1). None of these tumors presented necrosis or squamous differentiation areas.

Basaloid carcinomas consist in islets and nest of immature neoplastic cells with a relatively uniform morphology. They were small and oval, consistent with the basaloid appearance. Tumor cells had small amount of cytoplasm and hyperchromatic nuclei with granular chromatin and intense mitotic activity.

The tumor necrosis was frequent and often found in the center of the neoplastic islets, with a morphologic aspect characteristic to the "comedo" pattern of tumor growth (Figure 2).

The palisade orientation of tumor cell could be identified in the periphery of neoplastic islets.

Small foci of squamous differentiation and aspect of individual cell keratinisation were found in two of these tumors, but the keratotic pearls were absent. The presence of squamous differentiation areas within the neoplastic islets is a very important diagnostic element.

Immunoperoxidase study for AE1/AE3 cytokeratin cocktail shown positive stains in all studied cases. Spindle cell carcinomas presented poor immunostaining intensity (+), limited to small groups of cells (Figure 3).

For the basaloid carcinomas, it was also a poor immunostaining (+), predominantly for the cells at the periphery of carcinomatous islets and rarely for the cells within them (Figure 4).

The study of PCNA immunoperoxidase in examined squamous cell carcinomas has showed positive immunoreaction with high index in all the cases. For the spindle cell carcinomas, the immunostaining index has varied between 55% and 62%, compared with 58–72% index for basaloid carcinomas (Figures 5 and 6).

Discussions

Cervical squamous cell carcinoma both with spindle cells and basaloid are considered to be rare neoplasias included in the group of tumors with aggressive biological behavior, often associated with widespread metastasis in the time of diagnosis. While the spindle cell carcinomas, a histological variant of cervical squamous carcinoma, represent a well-recognized entity included in WHO classification, the basaloid variant of cervical squamous carcinoma has not been yet thought as a distinct entity [5].

Recently, data from literature consider the cervical basaloid carcinomas as histological variant of squamous cell carcinoma included into the category of high malignant cervical tumors alongside with the adenoid cystic carcinomas and neuroendocrine tumors with large cell [4].

Microscopic criteria of diagnosis include the following: the evidence of ulcerative and infiltrative growth pattern; the presence of islets or ribbons of small basaloid cells; palisade orientation of neoplastic cells in periphery of the tumor islets; the lack of significant stromal reaction [4, 6].

Despite of these observations, the basaloid carcinomas were only recently classified as variant of cervical squamous cell carcinoma [7].

The eight cases analyzed by us were diagnosed in patients aged between 42 and 64 years. Data from literature appreciate that these tumors are usually diagnosed in patients in large group of age, between 29 and 76 years, with an average age of 48 [3].

Histopathologically, both the spindle cell and basaloid variant of cervical squamous cell carcinoma may give rise to the problems of differential diagnosis especially in cases lack of squamous differentiation or when the fragment biopsies are discussed. In these cases beside the characteristic histological patterns of both neoplasias, the immunohistochemical study becomes a very useful method of diagnosis.

In our study, the immunoreactions for AE1/AE3 cytokeratin cocktail even with a poor intensity and limited extent of staining were positive for all the investigated cases, confirming the epithelial nature of tumors. Similar studies also indicate the positiveness of these variant of cervical carcinomas for cytokeratin immunostaining. Such a study performed on 12 cases of spindle cell carcinoma has communicated the cytokeratin–vimentin coexpression in all these tumors and further more, the positiveness of neoplasias with prominent spindle cell component for smooth muscle actin [3].

The study of PCNA immunoperoxidase has indicated a high index of cell proliferation in all the cases, varying between 55% and 62% for spindle cell carcinomas and slightly elevated values between 58% and 72%, for basaloid carcinomas. Similar studies performed on cervical squamous cell carcinomas indicated increasing PCNA immunoperoxidase index with tumors progression [8, 9].

Conclusions

The poorly differentiated squamous cell carcinomas of the cervix, especially the spindle cell and basaloid variants, may give rise to diagnosis difficulties.

The immunoperoxidase of cytokeratin cocktail AE1/AE3 in these tumors correlates with the histological degree of differentiation, being mostly useful to confirm the epithelial nature of tumor.

PCNA immunoperoxidase indicated in all the cases a high index of cell proliferation, more increased in basaloid variant. The study of PCNA and AE1/AE3 immunoperoxidases indicated a reverse correlation between these two immunomarkers, namely a focal pattern of cytokeratin expression and a high value of PCNA index, both of them being factors with prognostic significance.

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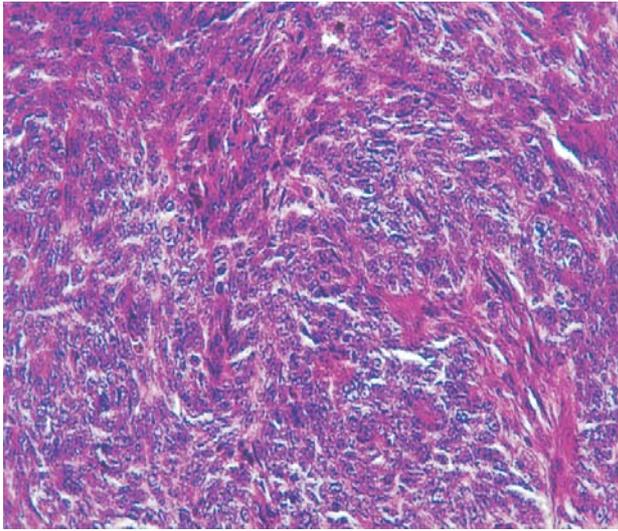


Figure 1 – Basaloid carcinoma
(HE staining, ob ×10)

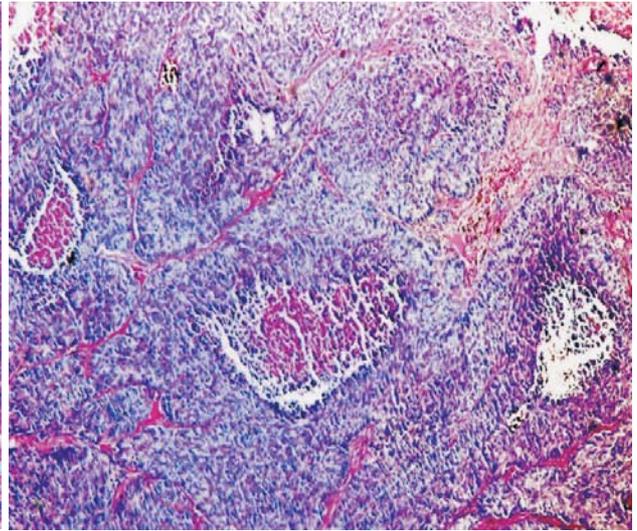


Figure 2 – Spindle cell carcinoma
(HE staining, ob ×10)

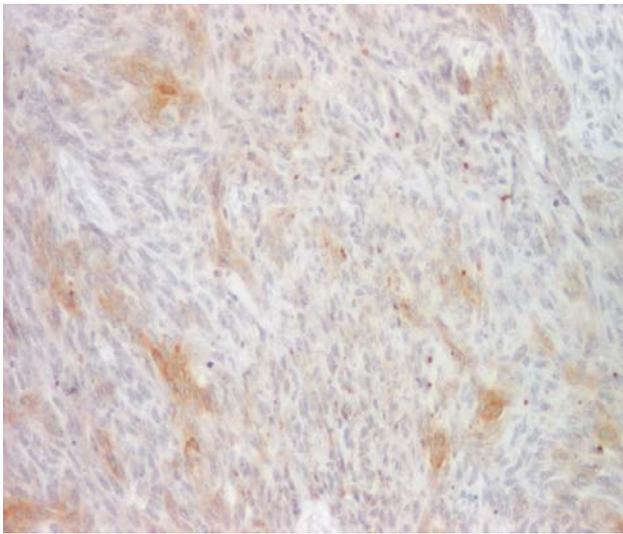


Figure 3 – Basaloid carcinoma
(AE1/AE3, ob ×10)

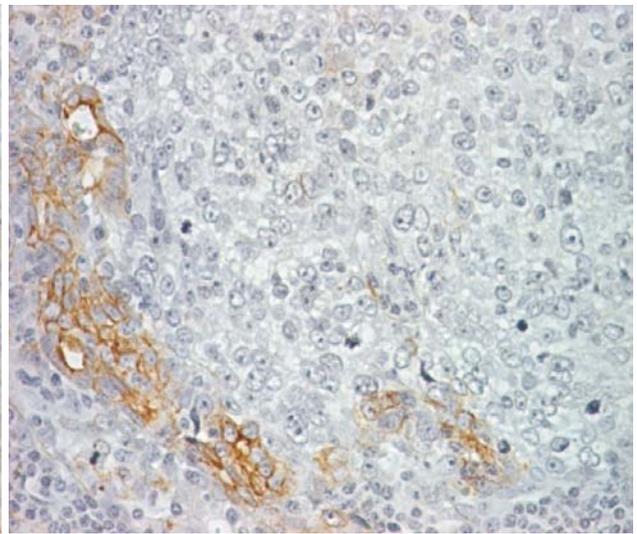


Figure 4 – Spindle cell carcinoma
(AE1/AE3, ob ×10)

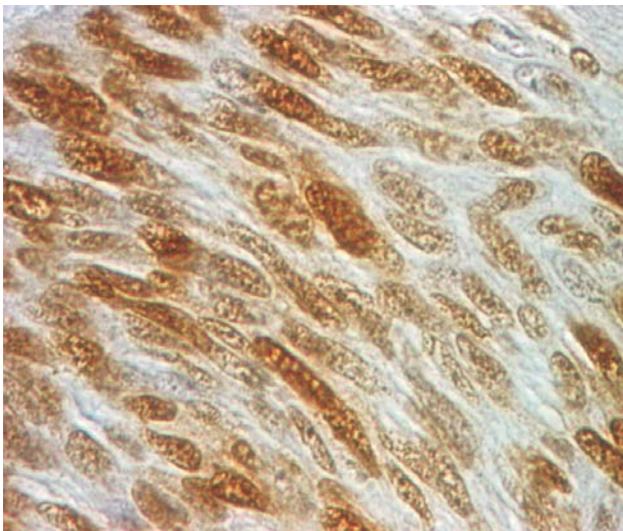


Figure 5 – Basaloid carcinoma
(PCNA, ob ×40)

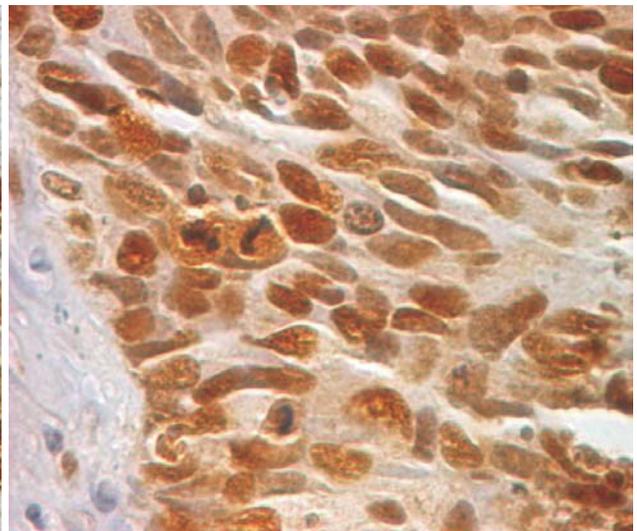


Figure 6 – Spindle cell carcinoma
(PCNA, ob ×40)

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