ORIGINAL PAPER

Diagnosis problems in a case of minimal deviation adenocarcinoma of the cervix

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Abstract

We present the diagnostic problems in a case of minimal deviation adenocarcinoma of the cervix. Histopathologic exam of the tumor, made on serial sections, revealed a dense and profound proliferation of the glandular structures that were lined by endocervical type epithelia with minimal cellular and nuclear atypia. The aspect suggested the diagnosis of minimal deviation adenocarcinoma endocervical type; in order to confirm the diagnosis we immunohistochemical investigate the tumor for CEA, CA125, Ki67, ER and PR. The results indicated focal positivity for CEA, CA125 lack of immunostaining for ER and PR and Ki67 positivity with a low index of proliferation. We can conclude that all these markers are useful in the diagnosis, excluding the benign endocervical lesions.

***Keywords*:** minimal deviation adenocarcinoma, histopathology, immunohistochemistry.

Introduction

Minimal deviation adenocarcinoma (MDA, malign adenoma) is a well-differentiated variety of adenocarcinoma of the cervix, characterized by the fact that the lining cells of the glands do not have malign characteristics, resembling with the normal endocervical cells. The term of minimal deviation adenocarcinoma was proposed by Silverberg and Hurst [1], subsequently being used and in other locations.

Minimal deviation adenocarcinomas are rare tumors, representing 1–3% of the adenocarcinomas with this localization and 18% from the differentiated forms of them [2]. In the literature it is mentioned the association between these tumors and mucinous or sexual-stromal ovarian tumors [3, 4].

Evolution of the tumors is difficult to appreciate, majority being diagnosticated in advanced phases. Despite the profound infiltrative growing, the cervical aspect may remain unchanged favoring the tardy detection of the tumor. In 40% of the cases in the moment of diagnosis the parameters or/and miometrium are invaded.

Some studies concerning this subject revealed a unfavorable prognosis, other studies mention a prognostic similar with well differentiated adenocarcinoma of the cervix, the five years rate of surviving being of 54% [1, 5, 6].

Material and methods

The material consists in fragments of cervix obtained by cervical biopsy, 10% formalin fixed, paraffin embedded and Haematoxylin–Eosin stained in the Pathology Laboratory of the Emergency Hospital from Craiova. Later were made serial sections immunohistochemical processed by LSAB/HRP method in the Laboratory of the Center for Microscopic Morphology and Immunology study.

Tumor was investigated for CEA (polyclonal rabbit anti-human CEA, code A0115, Ig fraction), CA 125 (monoclonal mouse anti-human CA125, clone M11, isotype Ig1, kappa, code M3520), Ki67 (monoclonal anti-human Ki67 antigen, clone MIB-1, code 724001, DAKO Cytomation), ER (monoclonal anti-human estrogen receptor, clone PPG5/10 code M7292, DAKO Cytomation) and PR (monoclonal anti-human progesteron receptor, clone 1A4, code A0098, DAKO Cytomation).

For CA125 and CEA was appreciate that the distribution of the immunostaining was focal when bellow 50% of the cells were positive, and diffuse when over 50% of the cells were positive.

For Ki67 was calculated the positivity index the number of positive cells being reported to 100 cells (positive and negative) with ×40 objective.

Results

The tumor belongs to a 32-years patient with irregular vaginal leakage and bleedings, normal cytological exam to which was performed profound cervical biopsy.

Histopathologic, on serial sections we noted glands resembling with the normal one, but much more dense with varied shapes and dimensions, distorted, irregular aspect, exceeding in depth the inferior level of the normal endocervical glands.

Together with small glands we noted the presence of large glands with polyp like proliferations frequent ramified and unregulated (Figure 1).

The glandular structures were delimited by a basal membrane and lined by a single layer of columnar, well-differentiated cells with abundant clear cytoplasm and basally situated nuclei. On limited areas were present aspects of pseudo-stratification and even epithelial stratification. Some glands presented locally slight enlarged nuclei, sometimes with eosinophilic nucleoli and reduced mitotic activity (Figure 2).

The neoplastic glands were separated each by other by fibrous stroma with low intensity desmoplastic reaction and areas of peri-glandular edema.

The microscopic aspect of the lesion concerning the density and the deepness of the glandular proliferation, correlated with the minimum cellular and nuclear atypia suggested the diagnosis of minimal deviation adenocarcinoma endocervical type. In order to confirm this diagnostic, we immunohistochemical investigated the tumor for CEA, Ki67, ER and PR.

The immunoreactions for hormonal receptors (ER and PR) were negative. CA125 reaction was focal positive, staining being cytoplasmatic with increase apical intensity (Figures 3 and 4).

CEA staining was apical limited positive with focal distribution (Figures 5 and 6).

The CEA immunoexpression was slight intense comparative with CA125 expression. The investigation of the cellular proliferation made by calculation of the index of positivity for Ki67 indicated reduced values, 1% (Figure 7).

Discussions

Minimal deviation adenocarcinoma is a rare variety of invasive cervical adenocarcinoma considered unique by the diagnostic difficulties because the benign mystifying aspect of the neoplastic cells. This tumor occurs between 25 and 72 years with a media of 42 years [5].

The differential diagnosis of the minimal deviation adenocarcinoma covers a large spectrum of proliferative lesions of the endocervical epithelia. The entire area of the endocervical glandular proliferations, in which the minimal deviation adenocarcinoma represents only a lesional subset, is additionally complicated by the existence of a large number of benign proliferative lesions of the cervix that can be occasionally wrong, interpreted as adenocarcinoma. The diagnostic discordances suggest the absence of a consensus of the diagnostic criteria between benign hyperplasic lesions, minimal deviation adenocarcinoma and common cervical adenocarcinoma, consequence of the differences of interpretations concerning cellular atypia and invasion [6–8].

The benign histopathologic aspect of the proliferation in minimal deviation adenocarcinoma can determine diagnosis confusions with a set of reactive proliferations of the endocervical epithelia.

Between the benign glandular proliferations that can be over evaluated and wrong interpreted is micro-glandular lobular hyperplasia, diffuse laminar glandular hyperplasia of the endocervix, infiltrative-like tubal metaplasia [9, 10, 15].

These possible confusions impose the necessity of additional investigations that exclude such proliferations.

For the investigated lesion, we made immunostainings for: CA125, CEA, Ki67, ER and PR. The tumor was ER and PR negative, aspect mentioned and in other studies that followed the differentiation MDA from the normal endocervical epithelia or benign reactive glandular proliferations of the endocervix [11, 12].

CA125 was focal positive with cytoplasmic distribution, predominant apical. The tumor was focal CEA positive, with luminal localization and with a slight intensely expression comparative with CA125 expression. The focal positivity for CEA and CA125 mentioned and by other authors is considered useful in differentiation of the tumor from the normal endocervical epithelium that is CEA negative [11, 13–17].

Ki67 indicated a reduced index of proliferation, 1%, confirming the mitotic activity noted in usual staining. Similar immunohistochemical studies made comparatively for minimal deviation adenocarcinoma endometrioid type and typical endometrial adeno-carcinoma indicate similar results.

In the case of minimal deviation adenocarcinoma the authors communicate focal positivity for CEA and values of the Ki67 index between 0 and 1%, comparative to the diffuse positivity for CEA and Ki67 between 20 and 30% for the typical endometrioid adenocarcinoma [18].

Conclusions

Minimal deviation adenocarcinoma represents a diagnostic problem because of the benign aspect of the proliferation, which frequent delayed the diagnostic and aggravates the prognostic of neoplasia.

Useful in the diagnosis are immunohistochemical investigations that can decide the diagnostic.

The focal positivity for CEA and CA125, the lack of immunostaining for ER and PR, together with a reduce index of proliferation for Ki67 represents useful diagnostic markers for minimal deviation adeno-carcinoma, differentiating it for benign glandular proliferations of the cervix.

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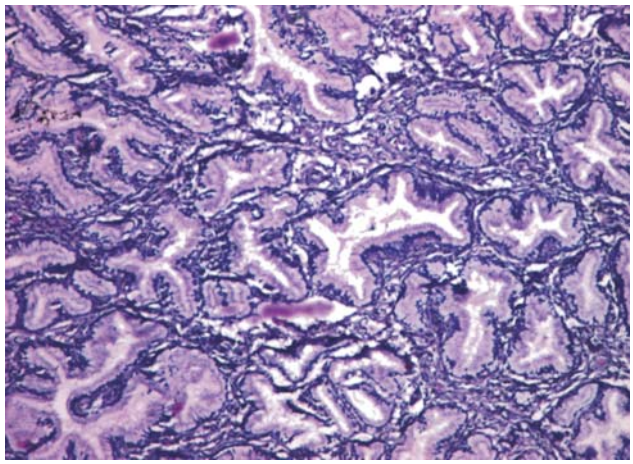

Figure 1 – ***Minimal deviation adenocarcinoma (HE stain, ob. ×10)***

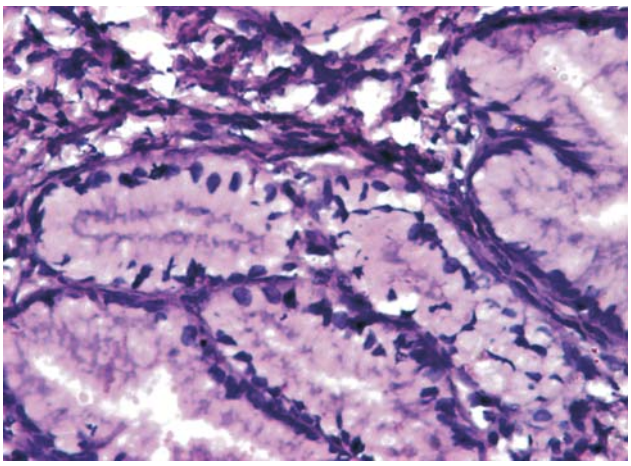

Figure 2 – ***Minimal deviation adenocarcinoma (HE stain, ob. ×20)***

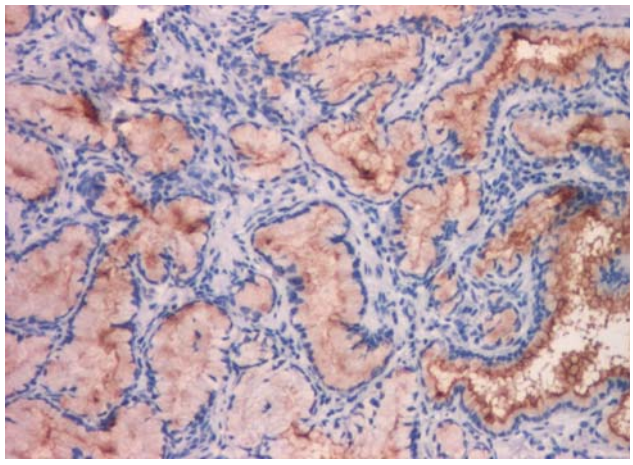

Figure 3 – ***Minimal deviation adenocarcinoma (Ca125, ob. ×10)***

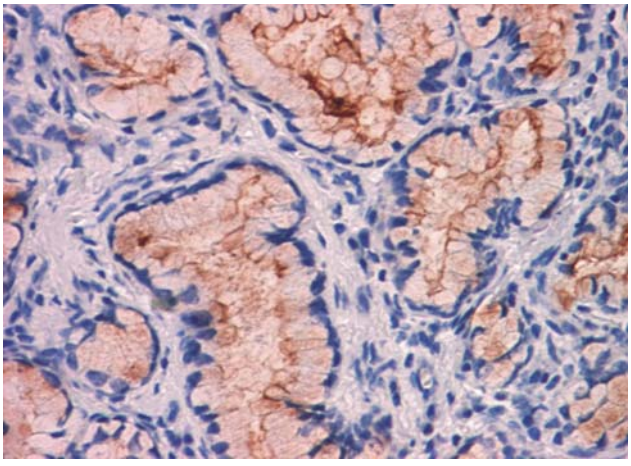

Figure 4 – ***Minimal deviation adenocarcinoma (Ca125, ob. ×20)***

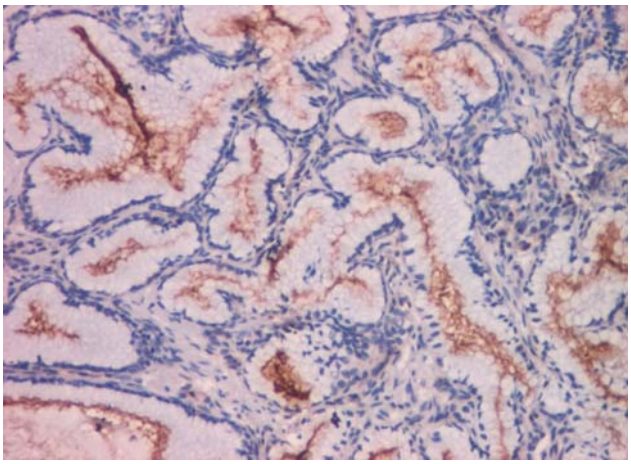

Figure 5 – ***Minimal deviation adenocarcinoma (CEA, ob. ×10)***

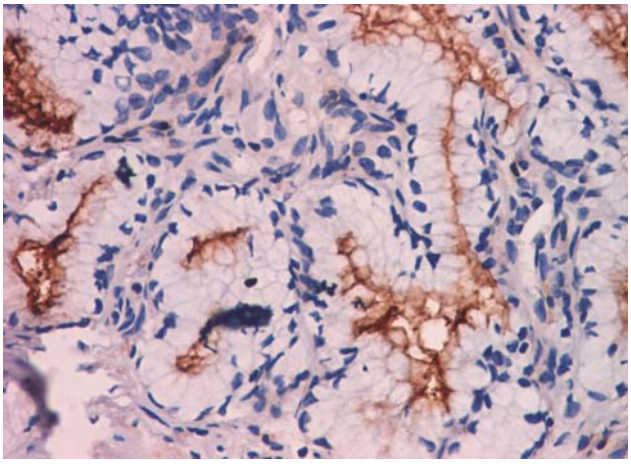

Figure 6 – ***Minimal deviation adenocarcinoma (CEA, ob. ×20)***

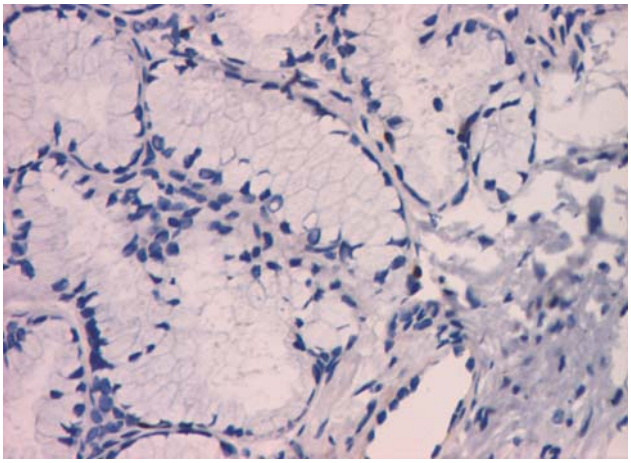

Figure 7 – ***Minimal deviation adenocarcinoma (Ki67, ob. ×20)***

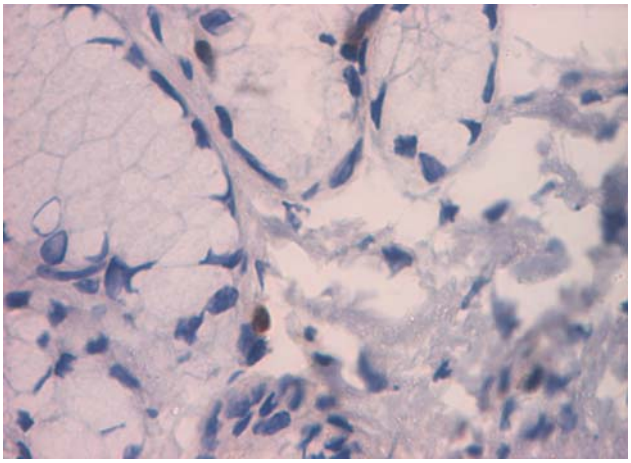

Figure 8 – ***Minimal deviation adenocarcinoma (Ki67, ob. ×40)***

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