ORIGINAL PAPER

Histopatological aspects of endometroid carcinoma in correlation to the state of tumoral progression in women patients during their premenopausal period

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Abstract

The performed study has comprised a number of 60 endometrial carcinomas, prevailed from women aged in the premenstrual period, in whose cases we have followed also the appreciation of the differentiating grading as well as the various aspects in neoplasies progression. The appreciation of the differentiating grading has allowed their placing as it follows: 39 cases of endometroid carcinoma well differentiated, seven cases of endometroid carcinoma mildly differentiated and five cases of endometroid carcinoma poorly differentiated. The correlation of the differentiating grading with the stage of tumoral progression has allowed the observation of the fact that while well invasive differentiated endometroid adenocarcinoma have been limited to the level of the uterine body, mildly and poorly differentiated invasive endometroid carcinoma besides profound myometrial invasion have associated cervical invasion and metastasis in structures situated at a real distance.

***Keywords*:** endometroid carcinoma, histopathology.

Introduction

Endometrial cancers constitute a heterogeneous group of neoplasies from biological and histological point of view, characterized through different pathogenesis mechanisms.

They develop especially in nulipar women or in those with a decreased parity, on a basis of a hormonal disorder and in the context of a prolonged estrogenic stimulation, being often tumors with a decreased degree of malignity (type I) and predominantly of an endometroid type.

Studies performed in the U.S.A. indicate this type of carcinoma as being the most frequent invasive malignant tumor of the genital feminine tract and in the same time one of the most common cancers in women, that is often associated to endometrial hyperplasy and represents about 80–85% from the majority of endometrial carcinoma [1].

The rate on incidence of endometrial carcinoma shows increased values of this one in North America and in Northern Europe, as well as their relative rarity in Asia and Africa [2, 3].

Studies concerning the age of appearance of the tumours indicate that the pick of incidence is being situated in the interval 55–65-years old, in patients found in the pre-menopausal phase [4–6].

Material and methods

The study performed has comprised a number of 60 endometrial carcinomas of an endometroid type, taken from patients hospitalized in the Clinic of Gynecology of the Emergency County Hospital of Craiova, to whom was performed a hysterectomy for uterine neoplasm.

The surgical pieces have been processed through the usual technique of introducing to paraffin and interpreted in the Anatomic Pathology Laboratory of the same hospital.

The analyzed cases have been situated also in conformity with the recommendations of WHO concerning the various lesional types and subtypes, as well as from the point of view of the progression of neoplasies appreciated according to the FIGO standards [1].

Results

The result of our study, which comprise a number of 60 endometrial carcinomas, prevailed from women aged in the premenstrual period, are shown below in the Figures 1–9.

The performed study has comprised a number of 60 cases of endometrial carcinomas, selected over a period of time of eight years (1999–2005), from patients aged between the ages 45–55.

We have been interested both in the histopathological aspect of tumors as well as in the stage of neoplasies.

The appreciation of the differentiating grading has been made as it follows: 39 cases of endometroid carcinoma well differentiated, seven cases of endometroid carcinoma mildly differentiated and five cases of endometroid carcinoma poorly differentiated.

Discussions

In what the state of tumoral progression is concerned, from the 60 cases of endometroid carcinoma, in two cases, the neoplasies have been limited to the endometer, in 76 cases the tumors have been invasive in the myometrium, but limited in the uterine body and six cases have been extended to adjacent structures of the uterine body or at a certain distance from the uterus. The histopathologic analysis of the selected cases has proved a grate variety of lesional types and subtypes.

The two cases (3.3%) of intraendometrial carcinomas (stage IA) have corresponded to some well differentiated endometroid carcinomas, made out of defined glandular structures, partly confluent, taped by epiteliums with a decreased degree of atypy. One of the criteria of diagnosis of this state is the absence of myometrial invasion (Figure 1).

The 52 cases (86.6%) of endometroid carcinomas limited to the myometrium, have corresponded in 36 cases to some invasive carcinomas up to level ½ internal of the myometrium (stage I B) and in 16 cases to some invasive carcinomas over ½ from the thickness of the myometrium, up to the level of the serous (stage I C).

The histopathologic study of endometroid adenocarcinomas taken into consideration in this study has allowed besides the diagnosis of histopathological form and the appreciation of the degree of differentiation of these ones, taking into consideration the architectural pattern of neoplasies and the aspect of the nuclei of tumoral cells.

In 38 cases the endometroid adenocarcinoma was typically well differentiated, and in 16 cases we found different varieties of this one.

The typical forms present in 22 cases were microscopically characterized through an architectural type having the aspect of relatively uniform glandular proliferations. The glandular form structures have had a round and ovoid form, with intra-lighted papillary projections or excrescences and arborescences taped by neoplasic protruzive epitheliums in the surrounding stroma.

Both the glands and the papillary projections have been taped by differentiated stratified epitheliums, made up of cuboids or cylindrical cells analogous to those of an endometrial type, with a long perpendicular axe on basal membrane. The cytoplasm of neoplasic cells has been reduced, basophile, with unique nuclei, hyper chromatic, round or ovoid, a little enlarged in volume, often prominent nucleoli (Figure 2).

Stroma found between the glandular lumens has been reduced, desmoplasic, with necrotic focars or infiltrated with inflammatory infiltrates in the stroma or in the glanduliform structures.

In the 16 cases have been present varieties of the endometroid adenocarcinoma, together with the well differentiated zones of typical endometroid carcinoma have been present associated aspects of squamous, vilo-glandular, secretory differentiation and aspects of micro glandular adenocarcinoma.

In nine of the cases to moderated endometroid adenocarcinomas that have presented histopathological have presented besides the rare glandular zones, less defined than in the previous form, and compact carcinomatous masses. Both the epiteliums from glandular zones of neoplasies, as well as those from the compact zones, made up of cell similar enough to the endometrial ones have presented a greater atypical degree than in the well differentiated forms, and mitosis have been frequent, and mitosis have been frequent, some even atypical (Figure 3).

In some cases to poorly differentiated endometroid adenocarcinomas, characterized microscopically through the absence of glandular structures, the round neoplasic or polymorph cells, being disposed in compact isles and beaches, and the tumoral stroma less obvious. Their nuclei have been increased by volume, pleomorphic, with rough chromatin, disposed non-uniform, with prominent nucleoli and frequent atypical mitosis (Figure 4).

Myometrial invasion, no matter its depth, has had the aspect of diffuse compact masses, cords or nests of cells and endometrial glands, associated to desmoplastic stromal reaction (Figure 5).

Vascular invasion has been present in 11 cases, representing a percentage of 18.3% from the endometroid adenocarcinomas, associated to mildly and poorly differentiated endometroid carcinomas, especially to those that have invaded over ½ from the thickness of the myometrium (Figure 6).

The six cases (10%) in which endometroid carcinomas extended in the adjacent structures of the uterine body or at a distance from the uterus have corresponded: in four cases to the invasive carcinomas in the cervix and in two cases to invasive carcinomas in the structures situated at a certain distance from the uterus. Microscopically, they have been endometrial adenocarcinomas mildly differentiated in three cases and poorly differentiated in other three cases.

In the performed study, cervical invasion present in four cases (stage II B) has corresponded to some endometroid adenocarcinomas mildly differentiated in two cases and especially poorly differentiated in other two cases (Figure 7).

In the two cases of extended tumors in structures situated at a distance, the localization of metastases was in the lymphatic para-aortic ganglions, ovary and intestine. One of the tumors was accompanied by met static adenopathy and ovary metastases, and the other besides the metastatic adenopathy has presented metastases with intestinal localization. Microscopically, metastasant endometroid carcinomas were mildly and respectively poorly differentiated (Figures 8 and 9).

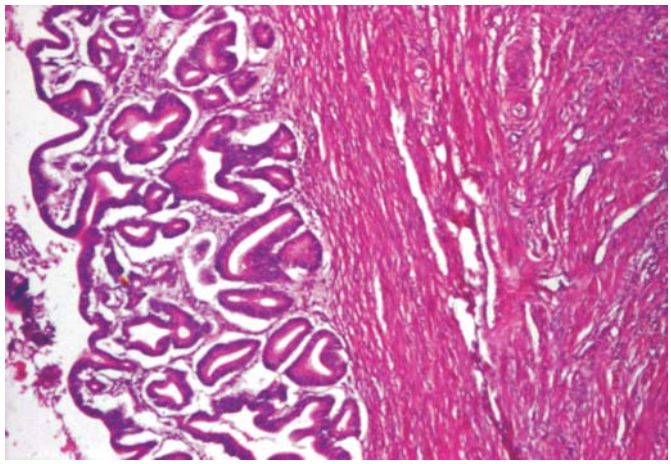

Figure 1 – ***Intra-endometrial adenocarcinoma (HE staining, ob. ×4)***

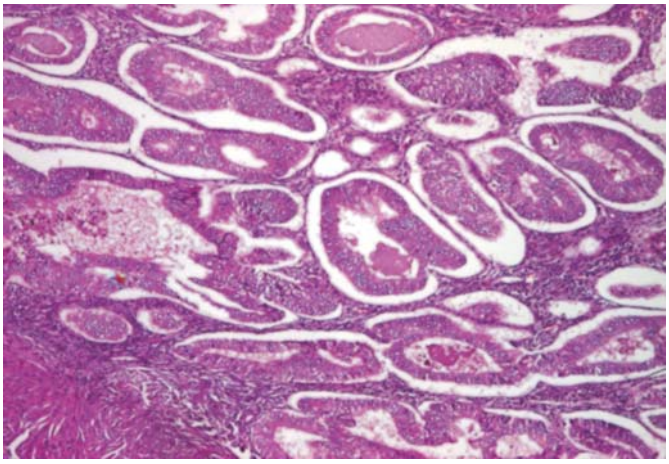

Figure 2 – ***Well-differentiated endometroid adenocarcinoma (HE staining, ob. ×4)***

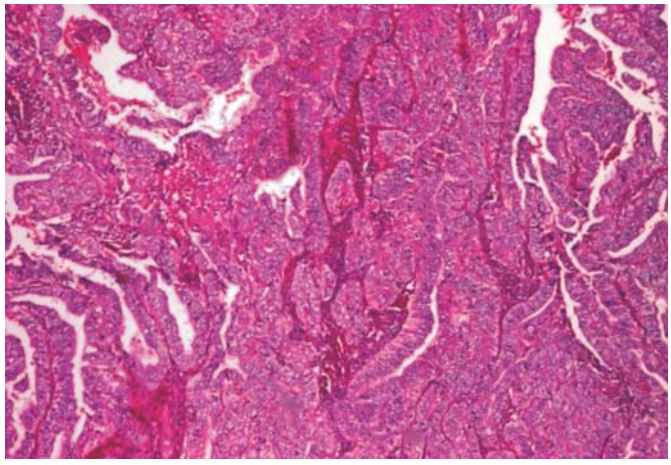

Figure 3 – ***Mildly differentiated endometroid adenocarcinoma (HE staining, ob. ×4)***

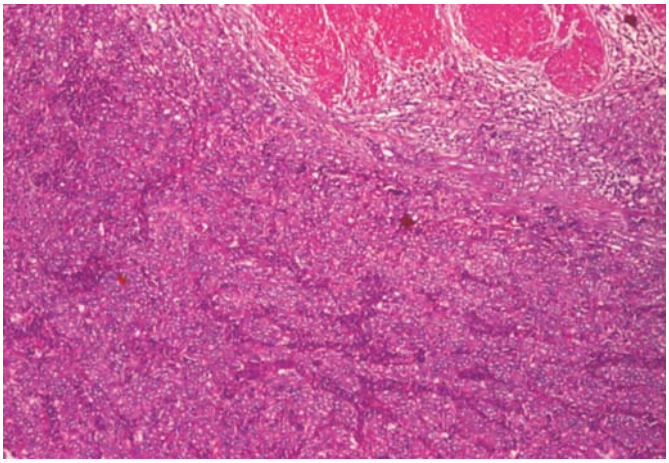

Figure 4 – ***Poorly differentiated endometroid adenocarcinoma (HE staining, ob. ×4)***

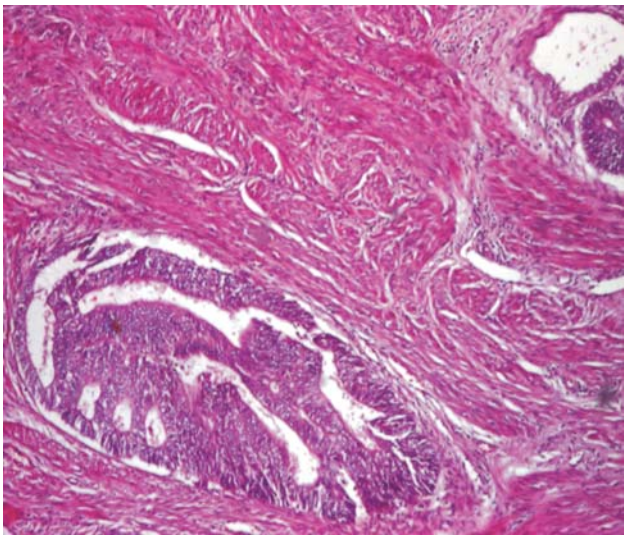

Figure 5 – ***Mildly differentiated endometroid adenocarcinoma, myometrial invasion (HE staining, ob. ×4)***

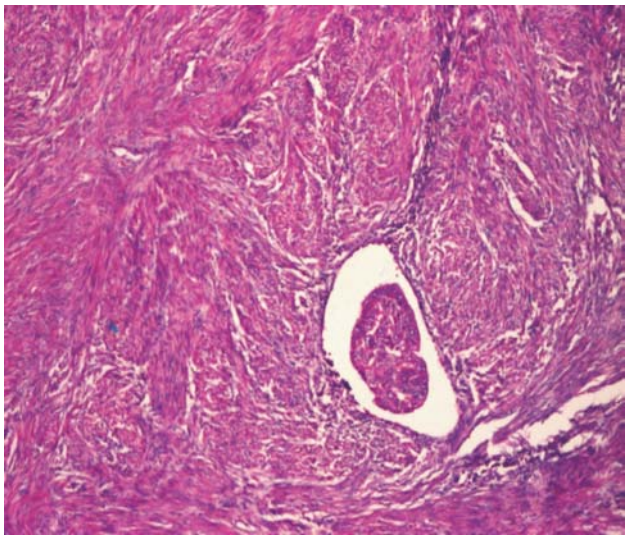

Figure 6 – ***Mildly differentiated endometroid adenocarcinoma, vascular invasion (HE staining, ob. ×4)***

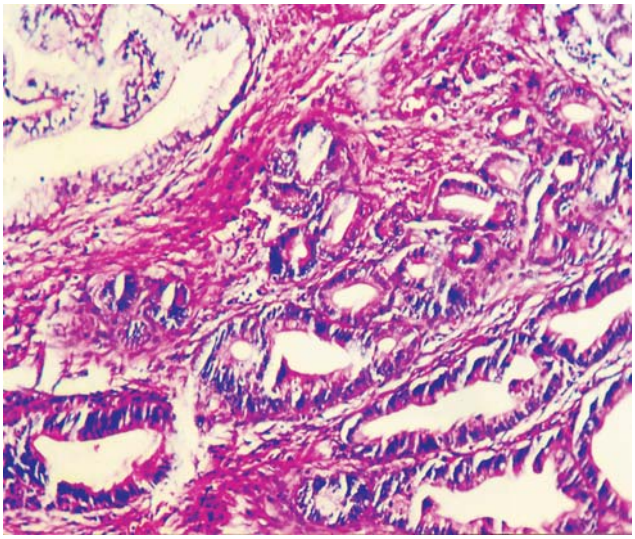

Figure 7 – ***Mildly differentiated endometroid adenocarcinoma, cervical invasion (HE staining, ob. ×4)***

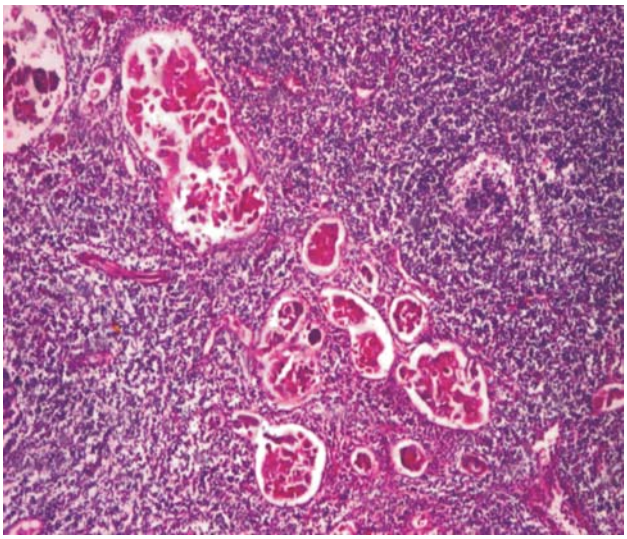

Figure 8 – ***Ganglionar metastases of a mildly differentiated endometroid adenocarcinoma (HE staining, ob. ×4)***

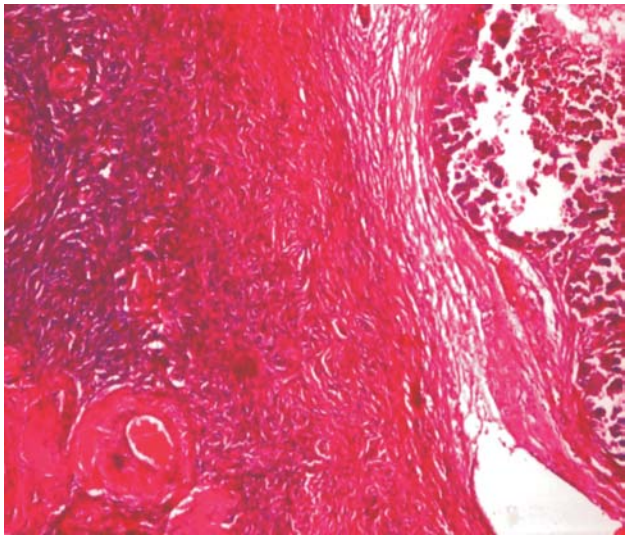

Figure 9 – ***Ovarian metastases of a mildly differentiated endometroid adenocarcinoma (HE staining, ob. ×4)***

The study performed has followed the various histopathological aspects of the endometroid adenocarcinomas selected within a period of time of ten years from the patients aged between the premenopausal period (45–55 years). Besides their histopathological forms we have been interested in the various aspects tied to the progression of tumors, directly correlated to the prognosis.

The histological stadialisation of the endometrial carcinoma has constituted over the years a complex and controversial problem. Despite the meticulous criteria of placement, this stadialisation still presents some exceptions as a result of the non-concordance between the architectural pattern and the nuclear degree.

Taking into consideration the recommendations of WHO for this group of neoplasies, the 60 cases of analyzed endometroid carcinomas have corresponded: in 39 cases to well differentiated endometroid adenocarcinomas, in seven cases to mildly differentiated endometroid adenocarcinomas and in five cases to poorly differentiated endometroid adenocarcinomas.

The 39 cases of well-differentiated endometroid adenocarcinomas, according to the FIGO standardization, have corresponded: in two cases to intraendometrial carcinomas, respectively to stage I A, and in 37 cases to the carcinomas limited at the level of the uterine body, invasive in the myometrium. From these in 37 cases the invasion has been up to the ½ internal level of the myometrium, corresponding to stage I B and only in two cases the carcinomas have invaded ½ from the thickness of the myometrium, corresponding to stage I C. In none of the cases were present aspects of vascular invasion.

Histopathologically, besides the aspect of well-differentiated typical endometroid adenocarcinoma, the tumors have associated various architectural and cytological patterns, with aspects of scuamous, vilo-glandular, secretory and of microglandular adenocarcinoma differentiation, without any correlation to the profoundness of the myometrial invasion.

Mildly and poorly differentiated endometroid adenocarcinomas, met in 14 of the cases, have constantly presented a myometrial invasion of over 1/2-internal of the myometrium and in six cases they have associated invasion in the structures adjacent to the uterine body or at a certain distance from the uterus. An observed aspect in eight of the infiltrating cases in the myometrium was the existence of vascular invasion [6].

In literature, vascular invasion is present in a percentage of 18% from the endometroid adenocarcinomas. Vascular invasion is generally appreciated in the peripheric myometrium of the tumoral mass. The lymphocytary perivascular infiltrate from the myometrium, but without lymphocytic infiltrate at the level of the junction between tumor and myometrium, represents a useful marker of vascular invasion [7].

Even though it is relatively rarely observed in the uterine endometroid adenocarcinoma, his frequency increases with the depth of the invasion, with the increase of cellular aggressively and the decrease of histological differentiation [8].

Some studies have shown the existence of a significant correlation between vascular invasion and tumoral recurrence free from the differentiation and thickness of the myometrial invasion. In an investigation of the first stage FIGO of endometroid adenocarcinoma, nine from 15 patients with lymphatic invasion have died because of the tumor, while only nine out of 78 patients without invasion have died [9].

Another similar study of the cases from stage I, consider vascular invasion a powerful predictive factor of tumoral recurrence and of extra pelvic metastases, free from the thickness of the invasion or the histological differentiation [10].

The existence of the invasion in the cervical stoma for to cases of endometroid adenocarcinomas mildly and in other two cases poorly differentiated, has determined the placing of the tumor in state II B. The mentioning of cervical implication is important because it is associated with a certain increase of the risk of recurrence and with a re falling rate of 16%, in the absence of extra uterine disease. Generally, cervical affection is associated with the increase of the tumoral degree, with the profound invasion and the increase of the tumoral volume, so the increased recurrence of these neoplasm is surprising. [11].

The association of metastases at a distance from the uterus in two cases of endometroid adenocarcinomas has placed tumors in state III A and III C (the invasion of ovaries and of para-aortic ganglions), respectively in state IV A (the invasion of the intestine). A study performed post-therapeutically has shown that the incidence of women patients who at five years did not present a decelable tumoral formation was of 36% from the patients with metastatic adenopathy.

Other modifications, which are being correlated to positive aortic ganglions, are: vascular invasion (19%), the thickness of myometrial invasion (17%), positive peritoneal cytology (16%), cervical implication (12%) and the third tumoral degree (8%) [11, 12].

Conclusions

The present study performed on a number of 60 endometroid adenocarcinomas of an endometroid type, has followed the establishment of the differentiating grading of the tumors and its correlation to the stage of progression of neoplasies.

The appreciation of the differentiating grading of the tumors has shown: in 39 cases well differentiated endometroid adenocarcinomas, in seven cases mildly differentiated endometroid adenocarcinomas and in five cases, poorly differentiated endometroid adenocarcinomas.

The evaluation of the state of tumoral progression has shown in two cases tumors limited to the endometer, in 64 cases tumors limited to myometrium, in four cases invasive tumors in the cervix and in six cases tumors associated to metastases at a certain distance from the uterus.

The correlation of the degree of differentiation of the tumors with the state of tumoral progression has shown for the well-differentiated forms of endometroid

adenocarcinomas limited invasion to the uterine body, frequently in the internal half of the myometrium (state I B and I C).

As a contrast the mildly and poorly differentiated forms of endometroid adenocarcinomas have associated more frequently profound myometrial invasion, cervical invasion and metastases at a certain distance respectively in the lymphatic ganglions, ovary and intestine (stage I C, II B, III and IV).

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