

Hystopathological aspects of the endometrial carcinomas in correlation with the tumoral grading and the invasiveness

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ABSTRACT We present a retrospective hystopathological study which comprised a number of 23 endometrial carcinomas, hospitalised and operated in the Gynecology Clinics of the Emergency Hospital of Craiova. We have analysed the following aspects of the previous mentioned cases: the average age at diagnosis, the tumoral grading, the miometrial penetration degree and the existence of the local or loco-regional invasion. The correlation of the differentiation level with that of the tumoral progression allowed us to observe the fact that while the well differentiated invasive endometroid adenocarcinomas were limited at the level of the uterine body, the moderated and the poorly differentiated ones associated, in some cases, beside cervical invasion and metastasis in structures situated at some distance, a deep myometrial invasion.

KEYWORDS endometrial carcinomas, histopathology, correlations

Introduction

Endometrial adenocarcinoma is the most common malignant tumor of the female genital tract[1,2,3], being a biologically and morphologically diverse group of tumors, with differing pathogenesis. This type of cancer develops especially in nulliparous women or in those with low parity, on the grounds of a hormonal imbalance or of a postmenopausal substitutive treatment as well as in obese, hypertensive, and diabetic perimenopausal or postmenopausal women[3]. This type of carcinoma is very rare before the age of 40, the highest incidence being around the age of 55-65, perimenopausal[2].

Material and method

The study included a total of 23 tumors from patients hospitalized in the Gynecology Clinics of Clinical Emergency County Hospital Craiova, the biological material being represented by pieces of hysterectomy for uterine neoplasm. The biological material was processed by the classical method by paraffin- embedded and Hemalaum-Eosin staining. Histopathological analysis was performed for all 23 endometrial carcinomas and included the following criteria: architectural type, tumor grade, histology type, tumor invasion and staging.

Results and discussion

The 23 endometrial carcinomas were studied, sorted and labeled according to the criteria stipulated in the OMS classification. The tumors

had the following aspects from the histopathological point of view:

– a clear predominance of the endometroid adenocarcinomas diagnosed in 20 cases which were followed by serous papillary carcinomas in 1 case, adenosquamous carcinoma, 1 case and mucinous carcinoma, 1 case. The histopathological study of the analysed adenocarcinomas allowed in addition to histopathologic diagnosis, the assessment of architectural grading by nuclear atypia and tumoral pattern.

– 12 cases of well differentiated adenocarcinomas which presented the predominance of well-formed glands while the stroma was reduced, desmoplastic, with necrotic outbreaks or inflammatory infiltrations (fig.1).

– 3 moderately differentiated cases where the glandular structures were rare and less definite, associated with compact carcinomatous masses (fig.2).

– 1 case of poorly differentiated adenocarcinoma characterized by rare pseudoglanduliform structures. The fibro-collagen type of stroma contained infiltrated inflammatory and necrotic areas, sometimes with an important character. The tumor cells had markedly enlarged and pleomorphic nuclei that contained irregularly coarse chromatin and prominent nucleoli. Mitoses were frequent (fig.3).

In 6 cases, lesional aspects such as squamous metaplasia, papillary areas, adenomatous hyperplasia or endometrial atrophy were present.

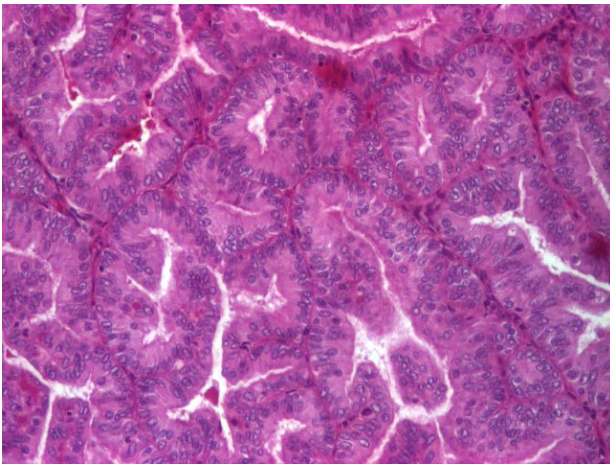


Figure 1 : Well-differentiated endometrial adenocarcinoma, HE stain, Obx4

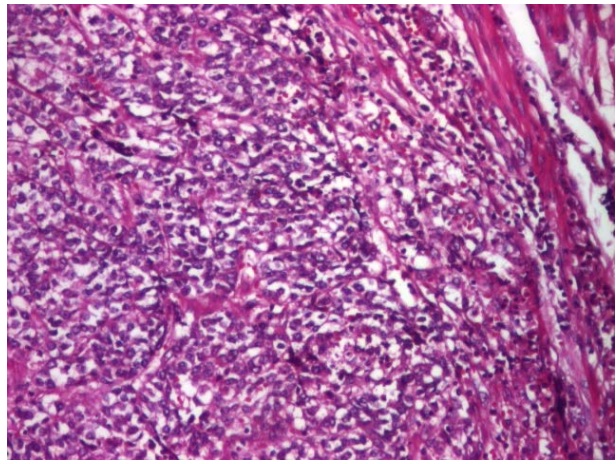


Figure 3 : Poorly differentiated endometrial adenocarcinoma, HE stain, Obx4;

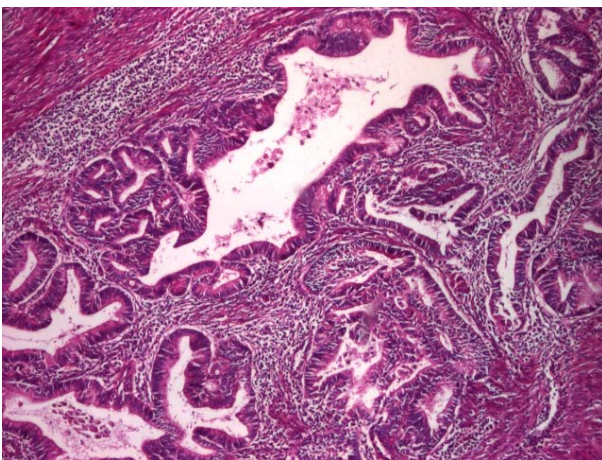


Figure 2: Moderately differentiated endometrial adenocarcinoma, HE stain, Obx4

In terms of tumor progression, of the 20 cases of endometrial carcinomas, 9 cases were strictly intraendometrial, 4 of them presented an invasion in the internal half of the myometrium while the rest of 7 cases had a deep myometrial invasion and in 4 of these cases there was local expansion and metastasis.

From the grading point of view, the 9 intraendometrial adenocarcinomas were well differentiated, presenting a definite glandular pattern with low atypia .

The 11 cases of adenocarcinomas extended to the myometrium, according to the depth of the invasion, corresponded in 4 cases to invasive carcinomas up to the internal half of the myometrium, without being associated with closer or further extension, while the carcinomas which invaded more than 2/3 of the myometrium proved to be loco regional expansive.

The myometrial invasion, regardless of its depth, presented the aspect of some compact diffuse masses, nests of cells and endometrial glands associated with desmoplastic stromal reaction (fig. 4).

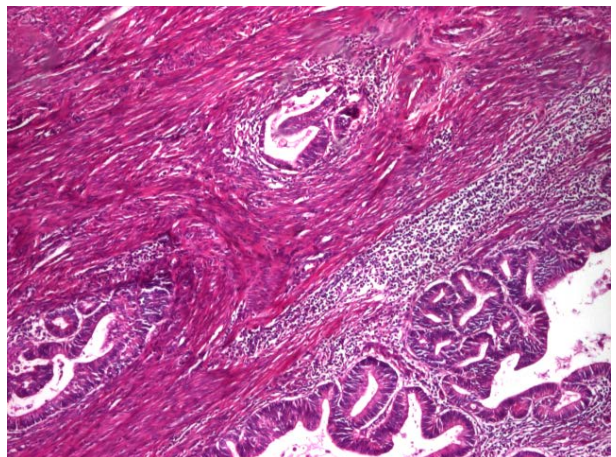


Figure 4 : Well-differentiated endometrial adenocarcinoma with myometrial invasion, HE stain, Obx4

The 4 cases of local expansion and metastasis are reflected such as follows:

- 1 case of invasive carcinoma in the ovary, fallopian tubes, paracolic nodes and sigmoid (fig.5).
- 1 case of cervical invasion, iliac nodes
- 1 case of tumor and periaortic lymphadenopathy
- 1 case of unilateral adnexal invasion, liver metastasis (fig. 6).

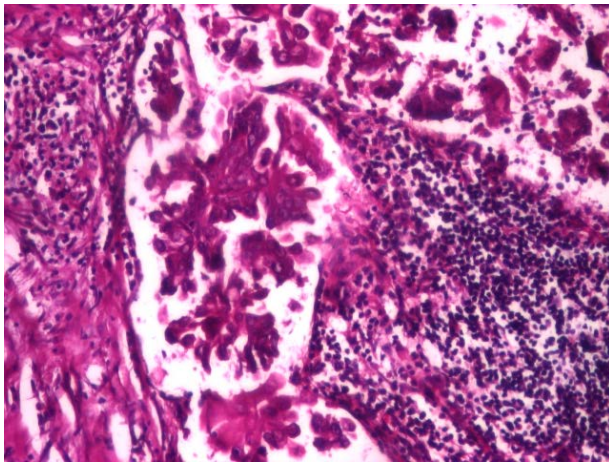


Figure 5 : Lymph node metastasis, moderately differentiated endometrial adenocarcinoma with squamous metaplasia, HE stain, Obx10

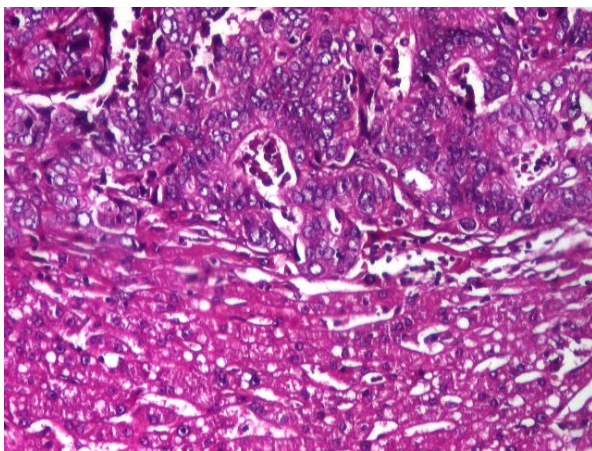


Figure 6 : Liver metastasis, moderately differentiated endometrial adenocarcinoma, HE stain, Obx10

These cases corresponded microscopically to the differentiated endometroid forms in 2 cases and to the moderately differentiated in the rest of cases, being associated with areas of squamous metaplasia and papillary areas in ½ of the cases.

As far as the appearance of the neoplasia, there were 2 patients with ages between 42 and 47, while for the rest, the average age was over 60.

The repartition of the cases analyzed on groups of age indicated a maximum incidence of the tumors in the VIth decade of life, the minimum age of the appearance being the age of 42. In the case of the youngest diagnosed patients, the neoplasia was correlated with a low degree of differentiation, high invasion and secondary dissemination, announcing a bad prognosis and a risk of recurrence. These aspects are in accordance with the literature data which indicate a high incidence of the endometroid malignant tumors in the perimenopausal period, the age for the diagnosis of the disease being somewhere between

55 and 65. In women under 40 years old the disease is appreciated to appear with a frequency under 2% or around 2% [5].

In the present study, the most frequent type of endometrial carcinoma was the endometroid adenocarcinoma. The data from the specific literature regarding the incidence of the different histopathological forms of endometrial carcinomas, appreciate the fact that it represents 80% of the cases of endometrial carcinomas.

The endometrial varieties were rarely diagnosed being present in just 3 cases. In literature, their frequency is variable, somewhere between 2-20% of the endometroid carcinomas. It is supposed that the squamous areas would come from the direct metaplasia of the glandular epithelium and thus the name of adenocarcinoma with squamous metaplasia[6].

The determination of the histopathological type of the adenocarcinomas is of great importance, being a very used criteria in the evaluation of the vital prognosis of the patients. It is appreciated that the typical endometrial adenocarcinomas have a survival rate between 72-86%, as compared to the non-differentiated ones where the survival is only of 28-58%.

As far as the differentiation degree, the well differentiated endometroid carcinomas correlated with a low aggressiveness and invasiveness degree, the prognosis being relatively favorable as compared to the low differentiated one whose prognosis was bad.

Another prognosis element which we have tried to appreciate on the examined histopathological items was represented by the tumoral invasion. The myometrial invasion can be correctly appreciated only on the pieces of surgical ablation and without pre surgical radiotherapy. The myometrial invasion as well as the endocervical extension mark the aggressiveness of the tumors and are usually associated with a low differentiation, having a reserved prognosis. We have noticed that the differentiated endometrial tumors have the tendency to expand in surface. Our observations are in compliance with the data from the literature. We have also observed the presence of the myometrial invasion in the medium and low differentiated forms.

The existence of the invasion in the cervical stroma in the endometroid adenocarcinomas is associated with some rise in the recurrence risk and with a relapse rate of 16%, in the absence of extra uterine disease. In general, the cervical affection is associated with the rise of the tumoral degree, with the profound invasion and the rise of

the tumoral volume as well as with the high recurrence of these neoplasms[7].

The association of metastasis at some distance of the uterus found in 3 cases of endometroid adenocarcinomas placed the tumors in the IIIA and IIIC stages (ovary and periaortic nodes invasion), and IV A stage (intestinal invasion). A post therapeutical study indicated that the incidence of patients who in 5 years' time did not present any detectable tumoral formation was of 36% from the patients with metastatic adenopathy comparatively with 85% in the case of those without metastatic adenopathy. Other changes correlated with the positive aortic nodes are: vascular invasion (19%), the depth of the miometrial invasion (17%), the positive peritoneal cytology (16%), cervical implication (12%) and tumoral grade 3 (8%) [8, 9].

Conclusions

The present study performed on 23 endometrial carcinomas underlines the differentiation grading of tumors and its correlation with the occurrence average age, the tumoral grading, the myometrial penetration level and the existence of the local and loco regional invasion. The evaluation of the tumoral progression stage marked in 4 cases the superficial invasion of the myometrium, in 7 cases there was a deep invasion, in one case the invasive tumor in the cervix and in 3 other cases tumors associated with metastasis situated as some distance from the uterus. The correlation of the differentiation degree of the tumor with the stage of the tumoral progression indicated for the well differentiated forms of the endometroid adenocarcinomas limited invasion to the uterine body, frequent in the internal half of the myometrium(stages IB and IC). The average and low differentiated forms of the endometroid carcinomas associated more

frequently deep myometrial invasion, cervical invasion and distance metastasis in lymphatic nodes, ovary and intestine.

Thus the most important negative prognosis factors proved to be the young age of the occurrence of the neoplasia, the low degree of differentiation, adenocarcinomas associated with various forms of metaplasia, varieties of uterine adenocarcinoma as well as the deep invasion in the myometrium locally and loco regionally. The association between these factors proved to have a bad diagnosis with a high degree of recurrence and fatality.

References

1. Rosai J.- Ackerman's Surgical pathology, CV Mosby Company, Ed. 8., 1996
2. Fletcher Christofer DM - Diagnostic Histopathology of tumors, vol I, II, 2007.
3. Florescu M, Cernea N, Simionescu C - (1998) Endometrul, Editura medicala, București.
4. Silverberg SG et al.- Silverberg's principles and practice of surgical pathology and cytopathology, vol.II, 2006, 1950-1968
5. Kempson RL, PokornyY GE - Adenocarcinoma of the endometrium women age forty and younger, 1968, Cancer, 21, 650.,
6. Abeler VH, Kjørstad KE - Endometrial adenocarcinoma with squamos cell differentiation,1993, Cancer, 69, 488-495.
7. Mutter GL, Nogalles F - Endometrial cancer, In: Tavassoli FA, Stratton MR: WHO classification of tumors. Pathology and genetics. Tumor of the breast and female genitale organs. Lion France, 2003, 233-245.
8. Morrow CP, Bundy BN, Kurman RJ et al.- Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. Gynecol Oncol; 1991, 40: 55-65.
9. Mutter GL, Crum CP - Tumors of the endometrium. In: Fletcher CDM. Diagnostic histopathology of tumors; 2000, 1: 648-668.

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