

Histopathologic aspects of the limited endometrial hyperplasias – a study concerning 149 cases

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Abstract

This study concerns 147 cases of limited endometrial hyperplasia, diagnosed at patients between IV, V, VI and VII decades of life. Histopatologically, the aspects were of basal hyperplasia – 40 cases and polypus hyperplasia – 107 cases. The polyp-like hyperplasia was present at pre and postmenopausal patients. At the premenopausal patients the polyps were hormonally active: glandular, glandular-cystic and adenomatous type polyps. In contrast, the majority of the postmenopausal patients presented hormonally inactive polyps, like cystic atrophic or fibrous polyps. Modifying the prognosis of lesions, we took in consideration the morphologic changes associated with these lesions, like epithelial metaplasia or nuclear atypia.

Keywords: limited endometrial hyperplasia, histopathology.

Introduction

Persistent estrogen stimulation of endometrium stay at the basis of the limited or diffused character proliferation of its structures (glands and stroma) and determined the apparition of lesions known as endometrial hyperplasia.

Lesions appear more frequent in menopausal period, but and in the reproductive period of life, caused by persistent estrogenism by different causes: prolonged anovulatory cycles, persistent follicles, hyperplasia of intern theca cells secondary to follicular atrophy, net insufficiency of the luteal phases, or to the presence of a ovarian estrogen secreting tumor (granulose cell tumor), hyperplasia of the hill or stroma cells, the polycystic ovarian syndrome, or may be iatrogenic, after prolonged estrogen therapy. Obesity and diabetes are considered only favoring factors of the disease [1–3].

It is appreciated that estrogens do not stimulated in the same measure the entire endometrium, for this reason sometimes it reacts only limited, in certain areas. These varieties of endometrial hyperplasia could have diverse evolution. As the time passed, they even keep the limited character of the proliferation, or regressed, or evolve to a diffuse hyperplasia, or, more to an endometrial adenocarcinoma – more frequent well-differentiated endometrioid type [4, 5].

Material and methods

This retrospective made study concern 531 cases of endometrial hyperplasia, selected in an interval of 3 years (2001–2003). 147 of these cases were limited endometrial hyperplasias, being the object of our study.

The material used was curettage products and pieces of hysterectomy, from patients hospitalized in Gynecology Clinic of the Emergency Clinic Hospital

from Craiova. The surgical pieces were processed in Pathology Lab of the same hospital by the usual technique of paraffin inclusion and Haematoxylin-Eosin staining.

Results and discussions

149 limited endometrial hyperplasias representing 28% of the all endometrial hyperplasias in the studied interval: 1999–2003. The lesions were diagnosed at patients from the IV, V, VI and VII decade of life, but the maximum incidence was in the 44–55 years interval.

Depending on the topography of lesions and the histological predominant aspect of the glandular proliferation, we classified lesions in one of the category:

- Basal endometrial hyperplasia was represented by 40 cases, respectively 21.4% of the limited glandular hyperplasia in our casuistry. Histopathologically, the changes were present only in the basal layer of the endometrium, were we noted the presence of proliferated endometrial glands, sometimes with cystic dilatations. They were lined by columnar monolayer epithelium, with elongated, hyper chromatic nuclei. Between proliferated glands, the stroma was dense, well represented, composed by elongated cells and myometrium fibres (Figure 1). The rest of the endometrium had the aspect correspondent to the proliferating phase.

- The endometrial polyps – we met in 107 cases – 71.8% of the limited endometrial hyperplasias. The patients were from the IV–VII decades of life. The lesions were localized towards the surface of endometrium, being prominent in the cavity. The rest of the endometrium was normal, with proliferating or incipient secreting aspect. Depending to the dominant aspect of proliferation, we noted aspects like:

* Glandular polyps – 39 cases – belonged to patients from the IV and V decades of life. Endometrial glands sometimes crowded together and with almost identically morphology with the normal proliferating endometrium, especially at the basis of the polypous structures composed them. Stroma was lax, but enough rich in collagen fibres and contained blood vessels, some with hyalinised walls (Figure 2).

* Glandular-cystic polyps were present in 33 cases, the patients being from the IV–VI decades of life. The histopathologic aspect was similar with the aspect from the glandular cystic hyperplasia of endometrium, but stroma between glands was rich in collagen fibers.

The endometrial glands presented cystic dilatations, with invaginations, or intra-luminal papillary proliferations and pseudo layering of the epithelium. The lining glandular epithelium had the same high like the surface epithelium, being followed by columnar cells with hyper chromatic, elongated nuclei and basophilic cytoplasm. The secretor changes – basally situated vacuoles – were rarely present (Figure 3).

The endometrial stroma was dense, composed by elongated cells with small hyper chromatic nuclei, with areas of edema and hemorrhagic infiltrates. The spiraled arterioles were generally low developed some with lumen occupied by a hyaline thrombus.

A peculiar aspect, noted in 11 of the cases was of cystic atrophic polyps, corresponding with the regression of lesion. They were diagnosed at postmenopausal patients. Histopathologically, the cystic dilated endometrial glands were lined by cubical or flattened epithelium, and stroma was fibrous type, with areas of hyalinisation (Figure 4).

* Adenomatous polyps were present in 25 cases, at patients from the IV–VI decade of life. The histologic aspect of the glandular proliferation was similar with the one noted in diffuse adenomatous hyperplasias, but with limited character.

In 18 cases the glandular proliferation had reduced or moderated intensity, without aspects of glandular atypia, characterized by increasing of number of endometrial glands with divers shape and seize, rounded, or with occasional protrusions that determined tortuous, undulated, uniformly dilated glands. They were lined by mono or multilayered columnar epithelium, with similar size with the size of the surface epithelium, which had amphophylic or basophilic cytoplasm and hyper chromatic, elongated nuclei; with reduce mitotic activity (Figure 5).

Stroma between proliferated glands was composed by small size, elongated or rounded cells with small, hyper chromatic nuclei, with reduced mitotic activity and with a variable quantity of collagen fibers. Here and there stroma was dissociated by edema and hemorrhagic or xantomatous infiltrates.

In 7 cases the glandular architecture was complex, with dense, unregulated and crowded lumens, with frequent micro polypus intraluminal proliferations and layering. Only in one case atypia was present in the lining epithelia. Nuclear atypia were present in entire gland or with focal character, existing glands with atypical epithelia, together with gland without atypia.

In areas of atypia, the cells were big, with hypertrophic nuclei, with unregulated and thickened membrane, presenting differences in size, shape and affinity for colorants, with increase mitotic activity and absence of polarity (Figure 6).

A change associated in 14 of the cases of adenomatous polyps was the epithelial metaplasia, by the replacing the endometrial epithelium by other types of epithelium that are not normally present in this localization. The types of metaplasia met by us were:

– squamous metaplasia: two from the cases of adenomatous polyps with simple proliferation, without atypia, presented like small islands of immature squamous cells, without tendency to keratinization (Figure 7).

– cylio-tubular metaplasia: 8 cases of adenomatous polyps with simple proliferation, without atypia. In the glandular epithelia, we noted the presence of columnar ciliated cells (Figure 8).

– eosinophilic metaplasia: met in 4 of the cases of adenomatous polyps with simple and complex proliferation, without atypia. We observed the endometrial glands lined by high cells with intense eosinophilic cytoplasm and uniform, centrally situated nuclei, without mitotic activity (Figure 9).

* Fibrous polyps were present in 10 cases, belonging to patients from the VII–VIII decades of life. Histopathologically, they were composed by a low number of endometrial glands lined by cubical mono-layered epithelium, or flattened epithelium, with round, hyperchromatic nuclei and reduced cytoplasm. Endometrial stroma was composed by spindle shaped cells, with pyknotic nuclei, rich in collagen fibers, sometimes with areas of hyalinization (Figure 10).

Actually, it is considered that diffuse or localized glandular hyperplasia is determined by the persistent progesterone-unblocked estrogenism. Endometrial polyps and basal hyperplasia are considered areas of limited endometrial hyperplasia that appear as consequence of a persistent estrogenic stimulus that have different intensities in different areas of endometrium. In the areas with more intense hormonal stimulus, on the background of a diffuse hyperplasia, grow unique or multiple polyps.

In our study, limited endometrial hyperplasia represent 28.06% of the endometrial hyperplasias, pre and postmenopausal patients being from the IV–VII decades of life.

Premenopausal patients presented especially limited basal hyperplasia, more frequent polyps hyperplasias represented by hormonally active polyps (glandular, glandular-cystic or adenomatous).

Limited basal hyperplasia of the endometrium is difficult to appreciate on curettage products. In these situations, useful for diagnosis is the presence of smooth muscular fascicles unregulated disposed in stroma.

As time pass, lesions could transform in a diffuse form of hyperplasia or a polypous hyperplasia, pushing underlying endometrium.

Premenopausal endometrial polyps are hormonally active. A peculiar signification had the adenomatous polyps that can associate glandular atypia.

Figure 1 – Basal endometrial hyperplasia (HE, ob. ×6)

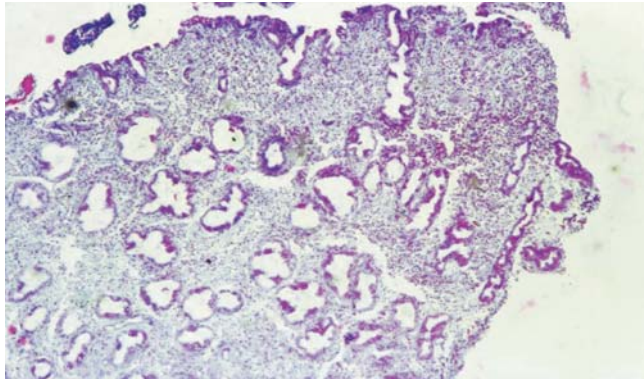
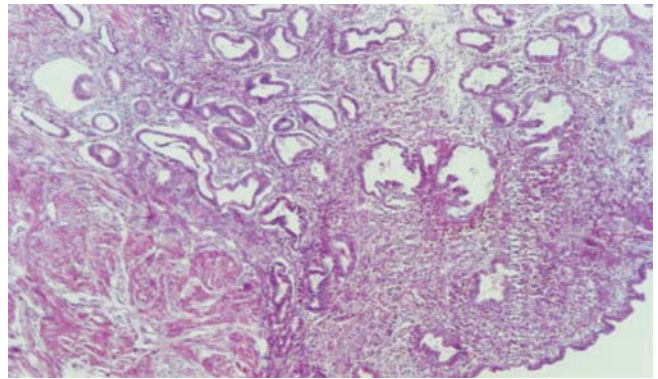


Figure 2 – Glandular polyp (HE, ob. ×6)

Figure 3 – Glandular-cystic polyp (HE, ob. ×6)

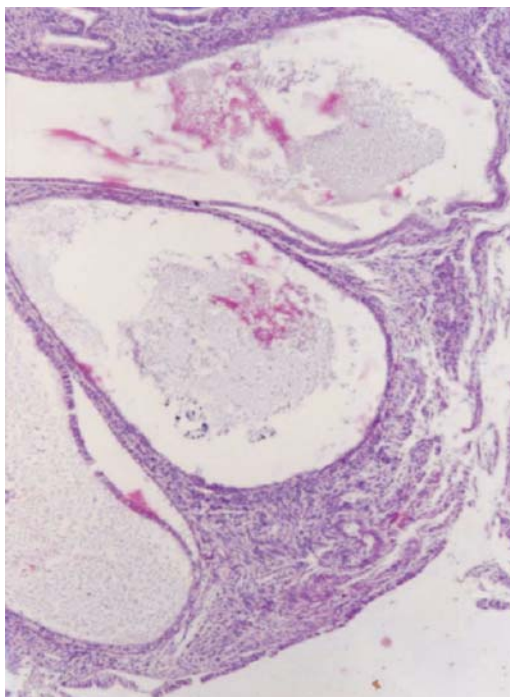
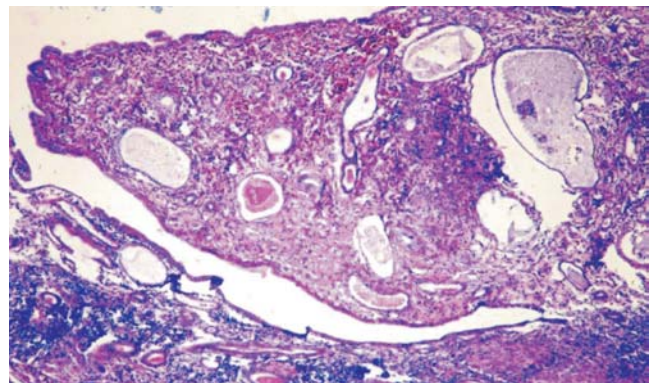


Figure 4 – Cystic atrophic polyp (HE, ob. ×6)

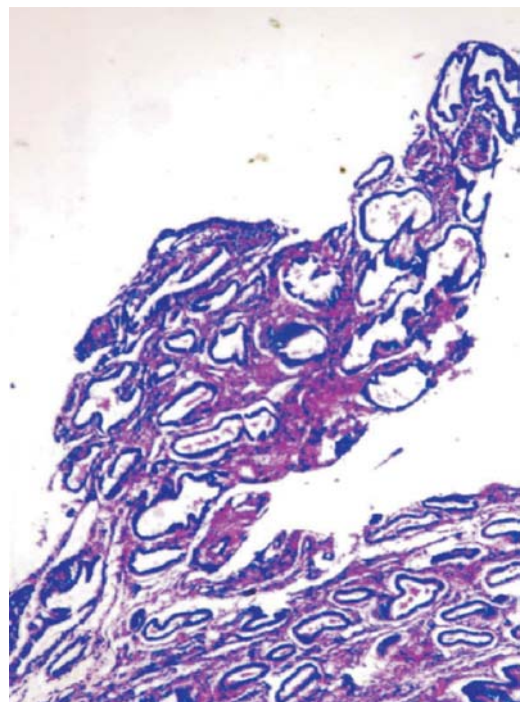


Figure 5 – Simple adenomatous polyp (HE, ob. ×6)

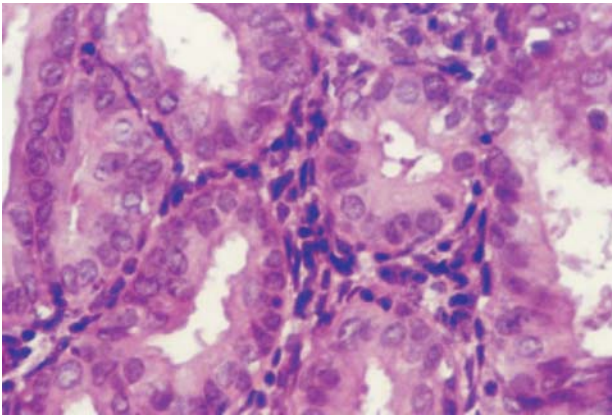


Figure 6 – Adenomatous polyp with complex glandular architecture, with areas of glandular atypia (HE, ob. $\times 20$)

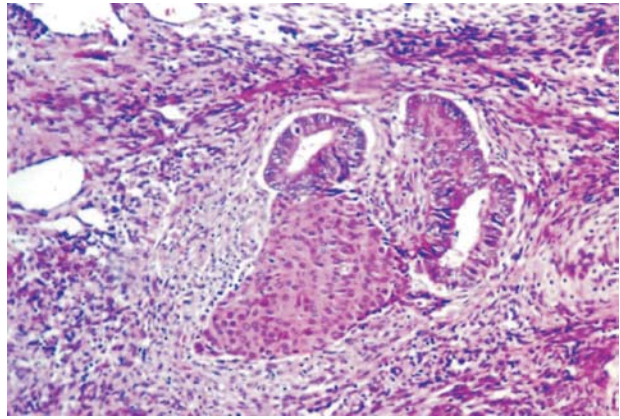


Figure 7 – Adenomatous polyp, squamous metaplasia (HE, ob. $\times 10$)

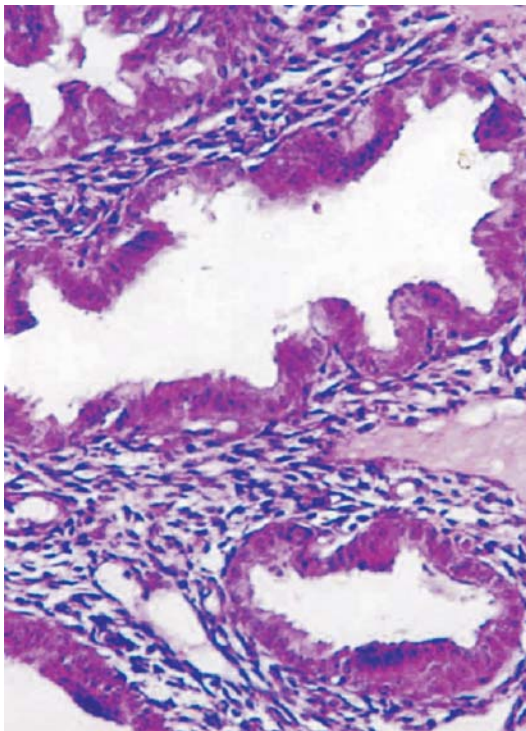


Figure 8 – Adenomatous polyp, ciliary tubular metaplasia (HE, ob. $\times 10$)

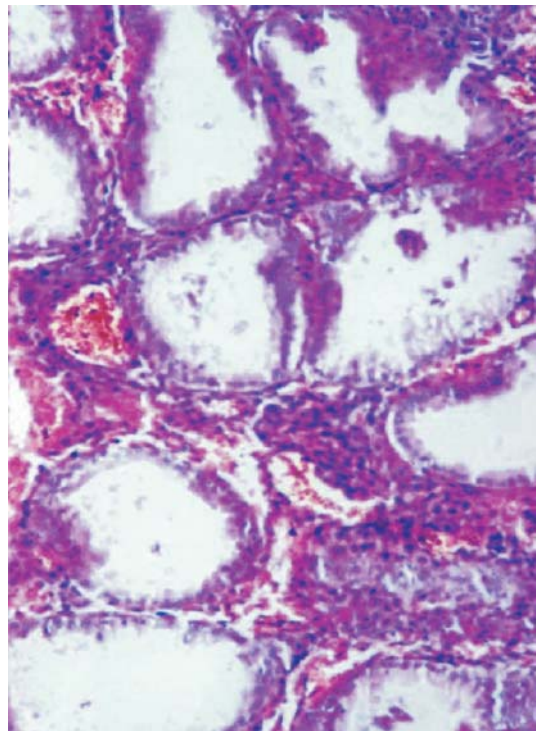


Figure 9 – Adenomatous polyp, eosinophilic metaplasia (HE, ob. $\times 10$)

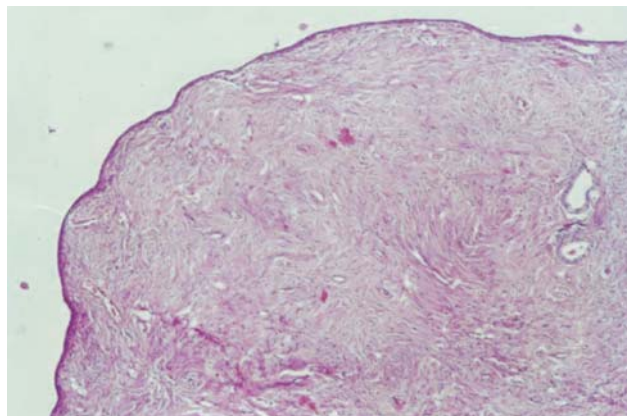


Figure 10 – Fibrous polyp (HE, ob. $\times 6$)

In our study, the glandular atypia was present only in one case of adenomatous polyp, the aspect being similar with complex hyperplasia with limited character atypia.

Having malign potential, the presence of nuclear atypia, in the context of a complex glandular architecture, changes the prognostic of the lesion. Recent studies revealed the increase of risk of malignisation in polyps with severe nuclear atypia linked by tamoxifen administration [4–6].

Other changes associated with limited endometrial hyperplasia, but without prognostic significance are the secretor aspects and the epithelial metaplasia. The occasional presence of secretor changes in glandular cystic and adenomatous polyps can be explained by the synthesis of small quantity of progesteron in the mature follicle by a mechanism similar with a transient luteinisation [1, 7].

It is considered that the association of metaplasia with limited endometrial hyperplasia is determined by the same condition of apparition: persistent estrogenism. Endometrial epithelial metaplasia occurs especially at women that followed estrogenic therapy and the young women that have prolonged anovulatory cycles or primitive sterility. In the absence of cellular and nuclear atypia, endometrial epithelial metaplasia do not aggravated the prognosis [8–10].

Postmenopausal women had more rare active endometrial polyps, adenomatous type polyps; more frequent the aspect being of cystic atrophic or fibrous polyps. The last two varieties of polyps are hormonally inactive, them significance being of regressive, inactive hyperplasia. This subclassification of the postmenopausal polyps is very useful for physician in establishing the adequate therapy.

✉ Conclusions

Our study concerned 149 cases of localized endometrial hyperplasias, diagnosed at patients from the IV, V, VI and VII decades of life, with maximum incidence between 45–55 years.

Histopathologically and topographically, the lesions were basal hyperplasia in 32 cases and polipous hyperplasia in 107 cases. Most premenopausal patients had basal hyperplasias and active endometrial polyps.

At the postmenopausal patients, hormonal active polyps were rare, with aspect of adenomatous polyps. In this group, inactive polyps, cystic atrophic type or

fibrous type represented the majority of limited hyperplasias.

Adenomatous polyps could be associated with nuclear atypia. Such cases are premalign lesions, presence of atypia changing the prognostic. In the absence of nuclear atypia, the presence of epithelial metaplasia do not changes the disease prognosis, but, increasing the complexity of the morphologic aspect, can determine the apparition of diagnostic problems by overvaluation.

The importance of problem consists in the possibility for this type of lesions to become malignant, grossly, endometrial cancer being vegetant – polyp-like in the majority of cases. This fact imposes a correct diagnosis and accurate treatment for each lesion.

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