Endometrial carcinoma and hormonal disturbances in middle-aged women – an overview

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Summary

Endometrial hyperplasias and endometrial adenocarcinomas present a morphological continuity. In 1,150 cases of patients admitted to two hospitals over the past two years with diagnosed irregular bleeding, suspected ultrasonography findings and positive family history, we performed, not only hormonal examinations, but also fractioned explorative curettage after receiving patient consent.

Key words: Endometrioid carcinoma; Hyperplasia; Adenocarcinoma.

Introduction

Distinguishing hyperplasia from well-defined adenocarcinoma presents a major problem. Physiological hyperplasia of the endometrium is very common. Hypersecretory endometrium is a functional alteration associated with the simultaneous presence of two corpus luteum or estrogen-progesterone usage [3, 5]. Endometrial hyperplasia is divided into two phases: proliferative and remodulating. The proliferative phase is characterized by an increased number of cells and increased endometrial volume with mild architectural changes. The condition is generated by the action of estrogen which is not inhibited by cyclic progesterone [1, 2]. It is possible that certain cells do not react to progesterone, thus there is increased growth and adenomatous hyperplasia with architectural and cytological abnormalities [4, 6, 7]:

Table 1. — *Causes of endometrial hyperplasia.*

Endogenous	Exogenous (iatrogenic)
Normal estrogen/decreased progesterone	1. Birth control pills 2. Intrauterine contraceptive 3. Wide spectrum antibiotics
1. Steroid tumors of the ovary (granulosa cell tumor, thecoma)	4. Other drugs
2. Hyperthecosis	5. Estrogen therapy
3. Stein-Leventhal syndrome	– dysgenetic gonads
4. Obesity	– hypopituitarism
5. Androgen-estrogen conversion	– menopause – breast carcinoma

Table 2. — *Classification of endometrial precancerous lesions.*

1. Cystic hyperplasia (mild precancerous changes)
2. Atypic (proliferative) hyperplasia – cellular and architectural
3. Atypic secretory hyperplasia
4. Carcinoma *in situ*
5. Polyps, presenting with the above-mentioned changes
6. Mixed changes [1-5]

Table 3. — *Simplified and practical division of hyperplasia.*

Simplex endometrial hyperplasia (focal, diffused)
Cystic endometrial hyperplasia (focal, diffused)
Glandular endometrial hyperplasia (adenocarcinoma) in situ
Endometrial adenocarcinoma

Table 4. — *Clinical stages according to FIGO* [2].

Stage I:
- Ia: Tumor limited to endometrium
- Ib: Myometrial invasion less than one-half of the width
- Ic: Myometrial invasion more than one-half of the width

Stage II:
- IIa: Inclusion of endocervical glands
- IIb: Invasion of the cervical stroma

Stage III:
- IIIa: Tumor invades serosa and/or adnexa with positive peritoneal cytology
- IIIb: Vaginal metastases
- IIIc: Metastases into pelvic and/or paraaortal lymph nodes

Stage IV:
- IVa: Tumor invades urinary bladder and/or bowel mucosa
- IVb: Distant metastases including intraabdominal and/or inguinal lymph nodes.

Material and Methods

Examination of the endometrium and its possible malignant alterations relies to a great extent on general risk groups (age, obesity, positive family history, smoking, etc.) and non-invasive Doppler flow of the arcuate and uterine arteries [3]. By ultra-

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sonographic examination revealing uneven endometrial spots and decreased resistance, malignant alterations can be found, but obviously this is not sufficient.

In 1,150 cases of patients admitted to two hospitals over the past two years with diagnosed irregular bleeding, suspected ultrasonography findings and positive family history, we performed, with the patients' consent, not only hormonal examinations but also fractioned explorative curettage. Although the mean age of the patients was 40 ± 2, we obtained remarkable data. In 27% of the cases (310 patients), positive findings of malignancy were found. Of this number, 54% of the cases were endometrial adenocarcinoma Stage Ib, 34% of the cases were Stage IIb and 12% were Stage IIIa.

Consequently, we removed the uterus and adnexae bilaterally by surgery. Together with oncologic surgeons, cleaning of the ischiorectal fossa and iliac cavities and paraaortal glands was performed. Omentectomy was performed in all patients. There were no significant pathological changes in other parts of the abdominal cavity.

At the Institute of Oncology further treatmant was performed on patients in Stage IIIa of the disease and 85% of the patients in Stage IIa.

Discussion and Conclusion

Endometrioid carcinoma is discovered in Stage I in about 75% of patients, while the distribution in other stages is usually even [2]. Before the introduction of therapy routine laboratory tests, lung X-rays, intravenous pyelogram and abdominal ultrasound examination, etc. need to be carried out to completely evaluate the patient. In the case of a palpable mass outside the uterus, it is necessary to perform rectosigmoidoscopy. In advanced stages, bipedal lymphography is recommended.

Prognostic factors for endometrioid carcinoma include age, tumor stage, histological type, subtype and nuclear grade, myometrial penetration, metastases in the regional lymph nodes and positive peritoneal cytology.

– Any irregular bleeding in patients over 40 years of age, regardless of hormonal disturbances, necessitates minor surgery – fractional explorative curettage. By cytological examination it is possible to discover changes in a timely manner.

– The increased incidence of malignancies in our country demands a strick following of medical protocols and urgent surgeries.

References

[1] American College of Obstetricians and Gynecologists. Carcinoma of the endometrium. Technical Bulletin 162. Washington, DC: ACOG, 1991.

[2] Peterson F.: "Annual report on the results of treatment in gynecological", ed. Cancer, vol 19. FIGO, Stockholm, 1985.

[3] Burke T.W. *et al.*: "Endometrial hyperplasias and endometrial cancer". *Obstet. Gynecol. Clin. North. Am.*, 1996, *23,* 411.

[4] Skov B.G. *et al.*: "Comparison of the reproducibility of the WHO classifications of 1975 and 1994 of endometrial hyperplasia". *Int. J. Gynecol. Pathol.*, 1997, *16*, 33.

[5] McDonald T.W., Malkasian G.D., Gaffey T.A.: "Endometrial cancer associated with feminizing ovarian tumor and polycystic ovarian disease". *Obstet. Gynecol.*, 1977, *49,* 654.

[6] Terakawa N. *et al.*: "The behavior of endometrial hyperplasia: a prospective study. Endometrial Hyperplasia Study Group". *J. Obstet. Gynaecol. Res.*, 1997, *23,* 223.

[7] Kaku T. *et al.*: "Endometrial carcinoma associated with hyperplasia". *Gynecol. Oncol.*, 1996, *60,* 22.

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