УДК 618.14-002-007.61-091.8-08

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HISTOPATHOLOGICAL FEATURES AND MANAGEMENT OF ENDOMETRIAL HYPERPLASIA: A COMPREHENSIVE REVIEW

Introduction

Endometrial hyperplasia (EH) is a proliferative disorder of the endometrial glands characterized by an increased gland-to-stroma ratio. It is widely recognized as a precursor to endometrial cancer, the most common gynecologic malignancy in developed countries. EH arises primarily due to prolonged exposure to unopposed estrogen, either from endogenous sources (e.g., obesity, polycystic ovary syndrome [PCOS], chronic anovulation) or exogenous sources (e.g., hormone replacement therapy, tamoxifen). Genetic predispositions, such as Lynch syndrome, also contribute to an increased risk of developing EH and subsequent malignancy.

The diagnosis of EH relies on histopathological evaluation, with the 2014 WHO classification distinguishing between EH without atypia (benign form) and atypical EH (also known as endometrial intraepithelial neoplasia), which carries a significant risk of progression to endometrial cancer. Management strategies depend on the presence of nuclear atypia, patient symptoms, fertility status, and risk factors for malignant transformation. This review aims to analyze the pathophysiology, diagnosis, and treatment approaches for EH, emphasizing recent advancements in medical and surgical management.

Goal

To identify the etiological factors contributing to endometrial hyperplasia and its progression to endometrial cancer, evaluate the efficacy of different treatment modalities including hormonal therapy and surgical interventions and assess the role of histopathological and molecular markers in improving diagnostic accuracy and risk stratification.

Material and methods of research

A retrospective cohort study was conducted on 443 patients diagnosed with EH between 2021 and 2024 in Gomel Region. Data were collected from electronic medical records, including patient demographics, clinical presentations, histopathological findings, and treatment outcomes. The inclusion criteria were women aged 28–75 years with a histologically confirmed diagnosis of EH. Exclusion criteria included patients with a prior diagnosis of endometrial cancer, incomplete medical records, or those who had undergone hysterectomy for reasons other than EH.

Histopathological analysis was performed on endometrial biopsies obtained via dilation and curettage or endometrial sampling. Immunohistochemical staining for PTEN, p53, and Ki-67 was conducted to evaluate molecular markers associated with malignant transformation. Treatment outcomes were assessed based on response to progestin therapy, recurrence rates, and progression to endometrial carcinoma over a five-year follow-up period.

The results of the research and their discussion

Out of 443 patients, 391 (88%) were diagnosed with EH without atypia, while 52 (12%) had atypical EH.

Obesity (BMI >30) was present in 67% of patients, and 42% had a history of PCOS. Diabetes mellitus was noted in 38% of cases, reinforcing the association between metabolic disorders and EH development.

Endometrial biopsies of EH without atypia showed regular glandular proliferation without significant nuclear pleomorphism. Atypical EH cases exhibited nuclear enlargement, loss of polarity, and increased mitotic figures, raising concerns for malignant transformation.

PTEN loss was detected in 48% of atypical EH cases, while p53 overexpression was observed in 15% of cases, suggesting a higher risk of progression to endometrial carcinoma. Ki-67 proliferation index was significantly elevated ($p<0.05$) in atypical EH compared to non-atypical cases.

Among patients with EH without atypia, 82% responded to cyclic or continuous progestin therapy (medroxyprogesterone acetate 10 mg/day or levonorgestrel intrauterine system). Recurrence was observed in 12% of cases over five years. In contrast, atypical EH required closer monitoring, with 55% opting for hysterectomy due to persistent atypia or worsening histopathological features. Among those managed conservatively with progestin, 23% showed progression to endometrial carcinoma within three years, highlighting the need for vigilant follow-up.

Conclusions

EH is primarily driven by chronic estrogen imbalance due to factors such as obesity, PCOS, and exogenous hormone exposure, underscoring the need for targeted prevention strategies. Management approaches depend on histological classification, as EH without atypia responds well to progestin therapy, whereas atypical EH carries a significant malignancy risk, often warranting hysterectomy. Molecular markers, including PTEN loss, p53 overexpression, and a high Ki–67 index, have emerged as critical tools for risk stratification and prognostication. Given the potential for recurrence or progression to malignancy, long-term surveillance with periodic biopsies remains essential in high-risk individuals.

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