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Concurrent endometrial intraepithelial carcinoma (EIC) and endometrial hyperplasia

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Abstract Endometrial cancer is one of the most common gynecological neoplasms in the United States. It is divided into type I and type II carcinomas based on histological features. The mixed endometrioid (type I) and serous (type II) adenocarcinomas of endometrium were reported in previous studies. The concurrence of their precursor lesions was not studied. In current study, we present five cases with concurrent precursor lesions of endometrioid (endometrial hyperplasia) and serous adenocarcinomas (endometrial intraepithelial carcinoma and p53 signature). Due to the potential progressive clinical outcome of precursor lesions of serous adenocarcinoma, caution needs to be performed to identify endometrial intraepithelial carcinoma and p53 signature in the background of endometrial hyperplasia.

1. Introduction

Statistical data from American Cancer Society's Cancer Facts & Figures showed that approximately 47,130 women were diagnosed with endometrial carcinomas in 2012, which makes them the most frequently diagnosed malignancy of the gynecologic tract, and the 4th most commonly diagnosed malignancy in women overall.

Endometrial cancers are divided into estrogen-dependent (type I) adenocarcinoma, consisting of endometrioid carcinoma and its variants, and less common but clinically aggressive estrogen-independent (type II) adenocarcinoma, consisting of prototype serous and clear cell carcinomas. Type I endometrial adenocarcinoma comprises 90% of endometrial carcinoma. It occurs in younger age group than type II endometrial carcinoma, usually with low grade clinical behaviors, with an overall 5 year survival rate of 85% [1]. On the other hand, type II adenocarcinomas occur in older patients than type I endometrial adenocarcinoma. Although less common, they account for 50% of mortality attributed to endometrial carcinoma [2–4].

The prototypes of type II endometrial adenocarcinomas include serous adenocarcinoma and clear cell adenocarcinoma, both of which are with highly aggressive clinical behaviors. Both type I and type II adenocarcinomas are preceded by precursor lesions. Endometrial hyperplasia is recognized as the precursor of endometrioid adenocarcinoma. Depending on the extent of glandular crowding and cellular atypia, endometrial hyperplasia is further divided into simple hyperplasia with and without atypia, complex hyperplasia with and without atypia. Studies showed that 1% of simple hyperplasia without

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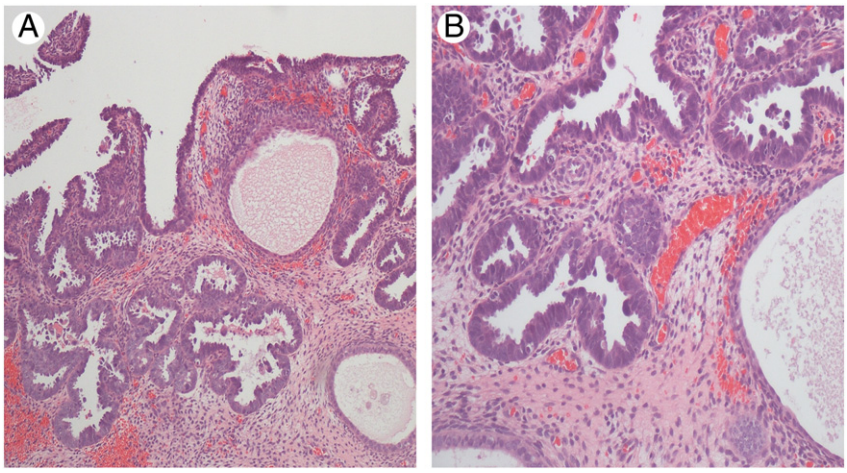

Fig. 1 A. H&E stained section (10×) showing a focus of EIC (indicated by arrow) in background of endometrial hyperplasia. B. H&E stained section (40×) showing the histological features of EIC.

atypia progresses to carcinoma; 8% of simple hyperplasia with atypia progresses to carcinoma; 3% complex hyperplasia without atypia progresses to carcinoma; 29% complex hyperplasia with atypia progresses to carcinoma [5].

Recent studies demonstrated endometrial intraepithelial carcinoma (EIC) to be the precursor of serous adenocarcinoma. Supporting evidence includes that EIC harbors the mutation of p53, which is one of the hallmarks characterizing serous adenocarcinoma [6–8]. Although confined to the epithelium, EIC has been showed to have progressive clinical course with extrauterine spread [9,10]. More recently, p53 signature was proposed to be a precursor lesion of EIC because of the presence of p53 mutation in benign appearing endometrial glands [11,12].

Although mixed endometrioid and serous adenocarcinomas were previously reported [13,14], the concurrence of their precursor lesions, endometrial hyperplasia and EIC and p53 signature has not been studied. In current study, we report 5 cases where EIC and p53 signature are associated with endometrial hyperplasia. Due to their potential aggressive clinical behaviors, identification of EIC and its precursor p53 signature in the background of endometrial hyperplasia will have significant clinical implications.

2. Materials and methods

Computerized database of surgical pathology at NYU Langone Medical Center was retrospectively searched for co-existence of diagnostic texts of endometrial hyperplasia and intra-epithelial carcinoma. Five cases were found from 2005 to 2013.

Immunostains for p53, Ki-67, estrogen receptor, and progesterone receptor were performed to highlight the presence of EIC and p53 signature in the background of endometrial hyperplasia.

3. Results

In the background of endometrial hyperplasia, EIC is characterized by focal highly atypical endometrial glands, with pseudo stratification, hobnailing, high nucleus to cytoplasm ratio, and prominent nucleoli (Fig. 1). These atypical cells are confined to endometrial glands, with no invasion through the basement membrane.

One of characteristic features of EIC is the presence of p53 mutation. We performed immunostains for p53

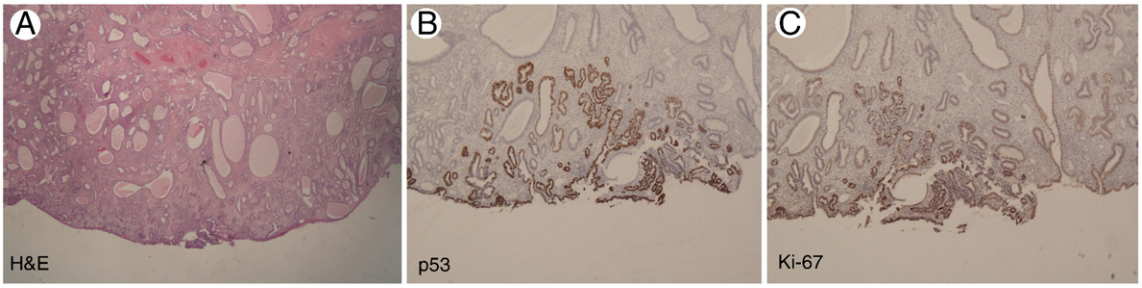

Fig. 2 H&E stained (A), p53 stained (B), Ki-67 stained (C) sections showing the EIC in the background of endometrial hyperplasia. Strong nuclear staining of p53 noted in EIC.