Title:

Immunohistochemical expression of PAX2, PTEN and B-Catenin in hyperplastic endometria treated with LNG-IUS and correlation with response.

Applicants:

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Background:

Surgical intervention by hysterectomy is standard treatment for atypical hyperplasia (AH)/ low grade endometrioid carcinoma. In women who desire to preserve their fertility or those who have significant medical comorbidities that preclude surgical management, nonsurgical management is undertaken using progestogens which may be administered orally or via an intrauterine device such as the Mirena coil (levonorgestrel intrauterine system; LNG IUS). In the United Kingdom, AH is managed according to RCOG green top guideline[1]. Histological assessment of response to progestogen therapy is a cornerstone of nonsurgical management of atypical hyperplasia/low-grade endometrioid carcinoma by assessing response to treatment. It is well accepted that there is significant interobserver variation in diagnosis of hyperplasia[2]. This has led to investigation of various immunohistochemical markers that can separate hyperplasia from its less sinister mimics[3]. There are no established guidelines in interpretation or reporting categories of progesterone treated endometria[4]. The treating clinician is reliant on the histopathologist reports regarding maintenance or abandonment of non-surgical management. Recently, there has been some literature analysing use of immunohistochemistry in predicting treatment response in hyperplasia[5].

Hypothesis:

We would like to audit the performance of the three most validated immunohistochemical markers in the diagnosis of atypical hyperplasia (PAX2, PTEN and B-Catenin) and correlate with morphology, clinical parameters and response in a small cohort of patients in whom standard UK management guidelines have been followed. We hypothesise that there may be differences in expression of these immunohistochemical markers in responsive and non-responsive endometria.

Methods:

We aim to retrieve details of 40 patients from a prospectively collected clinical database, supplemented by those identified from histopathological records – 10 patients in each of the following categories

a. Premenopausal patients with a diagnosis of AH/ low grade carcinoma who responded to progesterone therapy
b. Premenopausal patients with a diagnosis of AH/ low grade carcinoma not responsive to progesterone therapy
c. Postmenopausal patients with a diagnosis of AH/ low grade carcinoma who responded to progesterone therapy
d. Postmenopausal patients with a diagnosis of AH/ low grade carcinoma not responsive to progesterone therapy

We will review the index and post progesterone samples and reclassify them according to the proposal of Ganesan et al[4]. We will stain the index sample and the 12-month sample with PAX2, PTEN and B-Catenin and document the staining patterns and intensity. We will record these with photomicrographs. Our clinical colleagues will examine their records for agreed clinical parameters.

Expected Results:

a. in responsive cases there may be return of normal immunoexpression preceding or synchronously with morphological changes
b. in non-responsive cases the immunomarkers may show abnormal patterns on the index sample
c. there may be a difference in marker expression in pre and postmenopausal patients
d. there may be correlation of immunohistochemical expression with clinical parameters such as body mass index, co-existence of diabetes, hypertension and/or hyperoestrogenic states

References:

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