Middle East Fertility Society Journal (2015) **20**, 262–270

Middle East Fertility Society

Middle East Fertility Society Journal

www.mefsjournal.org
www.sciencedirect.com

ORIGINAL ARTICLE

Unexplained postmenopausal uterine bleeding from atrophic endometrium: Histopathological and hormonal studies

Dina Gamal Eldeen Elkholi [a,*], **Halah Mohamed Nagy** [b]

[a] *Department of Obstetrics and Gynecology, Faculty of Medicine, Tanta University, Tanta, Egypt*
[b] *Department of Clinical Pathology, Faculty of Medicine, Tanta University, Tanta, Egypt*

Received 24 September 2014; revised 28 April 2015; accepted 28 April 2015
Available online 1 June 2015

KEYWORDS

Postmenopausal bleeding;
Histological types of atrophic endometrium;
Sex steroid hormones in atrophic endometrium

Abstract *Objective:* To study the histopathology of endometrium and the serum concentration of sex steroid hormones in different types of atrophic endometrium associated with postmenopausal uterine bleeding (PMB). *Design:* Prospective observational study. *Main outcome measures:* Types of atrophic endometrium with PMB and serum concentration of sex steroid hormones in each type during and between episodes of bleeding. *Materials and methods:* One hundred and nine patients with PMB were investigated. Transvaginal ultrasonography was performed for all the cases. The endometrium was considered atrophic if its thickness was <4 mm. Endometrial sampling was done and submitted to histopathological study for 97 cases of atrophic endometrium. Serum concentration of total testosterone (T), androstenedione (A), esterone (E_1) and estradiol (E_2) and sex-hormone binding globulin were estimated for patients with atrophic endometrium during episodes of bleeding and in 47 cases were estimated also between episodes of bleeding. *Results:* Organic lesions were detected in 12 cases (11.0%) and atrophic endometrium was discovered in 97 cases (88.99%). The types of atrophic endometrium were as follow: atrophic inactive 46 cases (47.42%), atrophic/weakly proliferative 38 cases (39.19%), mixed with atrophic inactive and non-inactive 7 cases (7.21%) and cystic atrophic 6 cases (6.18%). Serum levels of all sex steroid hormones TT, A, E_1, and E_2 were significantly higher in atrophic/weakly proliferative than atrophic inactive endometria. Serum concentration of these sex steroid hormones was significantly lower during episodes of bleeding than between these episodes. *Conclusions:* There are 4 histological types

* Corresponding author at: 28 Elnaser Street, Tanta, Egypt. Tel.: +20 040 3332445, +20 040 3314036, +20 01223661218, +20 01113368930, +20 01005279419.
E-mail address: gyeldeenelkholi@yahoo.com (D.G.E. Elkholi).

Peer review under responsibility of Middle East Fertility Society.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.mefs.2015.04.005

of atrophic endometrium, atrophic inactive, atrophic/weakly proliferative (non-inactive), mixed (inactive and non-inactive) and cystic atrophic. Serum concentration of sex steroid hormones T, A, E_1, and E_2 was significantly higher and SHBG was significantly lower in cases of atrophic/weakly proliferative and mixed endometria than cases of atrophic inactive and cystic atrophic endometria. This may explain the development of endometrial adendocarcinoma on the top of atrophic endometrium. Concentration of these hormones was significantly higher between episodes of bleeding than during episodes of bleeding. This fluctuation may explain PMB from atrophic endometrium.

1. Introduction

Postmenopausal uterine bleeding (PMB) is generally regarded as an ominous and serious symptom. Organic lesions causing uterine bleeding include endometrial polyps, endometrial hyperplasia and carcinoma which should be sought by all investigations available in these cases (1). It was considered ''unexplained'' if no organic lesion that explained the bleeding was detected (2).

Often, however, an organic cause is not identifiable and curettage may show atrophic endometrium (3) proliferative endometrium (4) and rarely secretory endometrium (5).

Noteworthy is the fact that in most reports on PMB, malignancy of the uterus is not a common finding, incidence reported ranged from 3% to 14.2% (6). Instead, the more commonly encountered cause is atrophic endometrium. Miyazawa (3), for instance, reported an incidence as high as 59%. Moreover, endometrial carcinoma may develop in atrophic endometrium (7).

Focusing on these issues, the authors of this study conducted a prospective study to estimate the serum concentration of sex steroid hormones and to find the histology of ultrasonically diagnosed atrophic endometrium in PMB. The aim of the study was to find an explanation for PMB and the development of endometrial adendocarcinoma from atrophic endometrium.

2. Material and methods

During a period of about 3 years, from December 2011 to July 2014, 109 women complaining of PMB, admitted to the Department of Obstetrics and Gynecology, Tanta University Hospital were enrolled in the present study. Those with bleeding from the lower genital tract, cervix, vagina and vulva, were excluded from this series. Postmenopausal uterine bleeding was defined as bleeding after cessation of menses for at least a year (8). Kanna (2) defined PMB as bleeding occurring after 12 months of amenorrhea due to the loss of ovarian follicular activity and it was considered ''unexplained'' if no organic lesion that explained the bleeding was detected.

Patients were examined during an episode of bleeding. Through speculum examination blood should be seen coming from the external os of the cervix without cervical lesions.

The age, parity, period since menopause to PMB, body mass index (BMI) (body weight in kg/height in m^2), the pattern, duration and number of bleeding episodes were recorded.

3. Inclusion criteria

1 All cases of persistent or recurrent PMB with no organic lesion, detected on clinical examination or ultrasonography, that may explain PMB.
2 Cases of PMB with atrophic endometrium $\leqslant 3$ mm thickness
3 Endometrial tissue could be obtained for histopathological study.

4. Exclusion criteria

1 Genital tract organic lesions: genital atrophy (atrophic vaginitis and atrophic endometritis) and gross organic lesions of the uterus and ovaries.
2 Cases of PMB with endometrium $\geqslant 4$ mm thickness.
3 Women using hormone therapy during the last 3 months.
4 Patients with artificial (induced) menopause by oophorectomy or irradiation.
5 Patients suffering from liver, kidney and thyroid diseases and diabetes mellitus,
6 Endometrial tissue could not be obtained for histopathological study.

We followed the diagnostic strategies of Breijer et al. (9). The guidelines of American College of Obstetricians and Gynecologists Committee Opinion were considered (10). They suggested two possible diagnostic pathways of PMB:

(A) First pathway divided the patients into low risk and high risk cases (obesity, diabetes mellitus, chronic hypertension and >65 years old). Low risk patients were managed by expectant treatment and if PMB recurred or persisted, endometrial sampling was done. Endometrial sampling was done immediately for high risk patients. In the present study the second pathway was followed.
(B) Second pathway: transvaginal ultrasonography was performed for all cases. After exclusion of adnexal (tubes and ovaries) and cervical lesions, uterus was examined to exclude any uterine lesion and to measure the endometrial thickness (ET) in a longitudinal view of the uterus. If ET was <4 mm expectant treatment was allowed but if bleeding recurred or persisted endometrial sampling was done. If ET was $\geqslant 4$ mm endometrial sampling was done immediately without resorting to the expectant treatment. Increased ET and echogenicity, irregular margins and small amount of fluid in the