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Abnormal Uterine Bleeding Under the Lens: A Histopathological Study of Endometrium

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Abstract

Background: Abnormal uterine bleeding (AUB) is a major concern in the gynecological OPDs with a necessity of endometrial carcinomas and atypical endometrial hyperplasia to be ruled out. For this endometrial histopathological evaluation (HPE) is very essential.

Aims and objectives: To evaluate various patterns of endometrial histology in women with AUB due to endometrial causes, and age group and endometrial thickness (ET) distribution of these cases.

Subjects and Methods: The present retrospective observational study included the endometrial samples of AUB cases due to endometrial causes received in the Department of Pathology of a medical college and hospital over the period of three years. Relevant clinical history, examination and other findings including endometrial thickness were noted. They were subjected to routine histopathology processing and the hematoxylin and eosin stained slides obtained were studied.

Results: A total of 475 cases consisting of 176 (37.05%) endometrial biopsies and D&C materials, and 299 (62.95%) hysterectomies were included. The most common pattern was found to be normal cyclic pattern, followed by atrophy, pill endometrium and hyperplasia

without atypia. Endometrial carcinoma [1.47% (7cases)] presented predominantly in the age group 40-49 and 50-59 with all cases having endometrial thickness ≥10 mm. The endometrial hyperplasia with atypia / endometrial intraepithelial neoplasia (EIN) cases affected the age range above 30 years as well with the endometrial thickness predominantly ≥ 10 mm followed by 8.1 – 10 mm.

Conclusion: The endometrial biopsy is of high value for giving definitive diagnosis of the cause of AUB in all the age groups. Age wise and ET wise distribution of cases correlated well with their HPE diagnosis with malignant and premalignant lesions of endometrium seen predominantly in peri-menopausal and post-menopausal age with ET chiefly ≥ 10 mm.

Keywords: Abnormal uterine bleeding, Endometrium, Endometrial carcinoma, Endometrial hyperplasia, Histopathology.

Introduction

Abnormal uterine bleeding (AUB), one of the most common presenting complaints in women reporting to the gynecologist, is menstrual bleeding abnormal in terms of frequency of menstruation, duration of flow, amount of blood loss, cyclicity, or intermenstrual bleeding. A decade ago the International Federation of Gynecology and Obstetrics (FIGO) Working Group on Menstrual Disorders gave a classification system PALM-COIEN, categorizing the plethora of causes of AUB in non-gravid women of reproductive age into structural/ organic and non-structural lesions. The investigations done mainly are blood tests, radiological – including Ultrasonography (USG) and histopathological evaluation of endometrial tissue obtained by endometrial curettage or biopsy. For ruling out the important causes - endometrial carcinoma and endometrial hyperplasia with atypia - out of the various endometrial causes of AUB histopathological evaluation (HPE) of the endometrium is the gold standard. Again, increasing age is a risk factor of endometrial carcinoma, thus many institutions including American College of Obstetricians and Gynecologists recommend endometrial evaluation in women aged ≥ 35 years having AUB. {1-2}

The aim of this study was to evaluate various patterns of endometrial histology in women with AUB due to endometrial causes, and age group and endometrial thickness (ET) distribution of these cases.

Materials & Methods

The present retrospective observational study included the endometrial samples of AUB cases received in the Department of Pathology of a medical college and hospital over the period of three years from April 2018 to March 2021. Study subjects were patients presenting with complaints of AUB due to endometrial causes. Those with known pathologies as the cause, such as complications of pregnancy, fibroids, functional ovarian tumors and cervical lesions were excluded from the study, as were the autolysed and inadequate specimen. Relevant clinical history including age, chief complaint, last menstrual period, menstrual and obstetric history along with examination findings as endometrial thickness as stated in the USG in cases of curettage and biopsies were recorded. Endometrial biopsies, dilation and curettage materials, and/or hysterectomy done for diagnostic or therapeutic purposes were the specimens considered. They were subjected to routine histopathology processing and the hematoxylin and eosin stained slides obtained were studied. All the findings were entered into a master chart (Excel sheet Word) and correlated with clinical and other relevant information and statistically analyzed.

Results

A total of 475 cases consisting of 176 (37.05%) endometrial biopsies and D&C materials, and 299

(62.95%) hysterectomies were included. Age ranged from 21 yrs to 75 yrs with most common affected age group being 40-49 years [220 (46.32%) cases].

The most common pattern was found to be normal cyclic pattern, followed by atrophy, pill endometrium and hyperplasia without atypia. (Table 1)

The other prevalent non neoplastic lesions were hormonal effect, chronic endometritis, and endometrial polyp. Hormonal Effect (Pill Endometrium) was most prevalent in age group 30-39 and with endometrial thickness 6.1–8 mm followed by 4.1–6 mm.

Chronic Endometritis affected 40-49 age group most and the usual thickness was 6.1 – 8 mm. 40-49 was the age group in which endometrial polyp presented most commonly with most common endometrial thickness being 6.1 – 8 mm.

One case each of endometrium with osseous metaplasia (Figure 1), endometrial tuberculosis and endometrial foreign body were also found.

The endometrial hyperplasia with atypia / endometrial intraepithelial neoplasia (EIN) cases affected the age range 30-39 years, 40-49 years, 50-59 years and ≥60 years (Table 2) as well with the endometrial thickness predominantly ≥10 mm followed by 8.1 – 10 mm (Table 3).

However, endometrial carcinoma presented predominantly in the age group 40-49 and 50-59 with only one case of ≥60 years (Table 2), with all cases having endometrial thickness ≥10 mm (Table 3).

Table 1: Histopathological Diagnosis of Endometrium:

Histopathological Diagnosis	Percentage of Patients (Number of Patients)
Proliferative Endometrium	36% (171)
Secretory Endometrium	24% (114)
Atrophic Endometrium	8.63% (41)
Hormonal Effect (Pill Endometrium)	7.16% (34)
Disordered Proliferative Endometrium	2.74% (13)
Endometrial hyperplasia without Atypia	6.95% (33)
Endometrial hyperplasia with Atypia / EIN	2.11% (10)
Endometrial Carcinoma	1.47% (7)
Chronic Endometritis	5.47% (26)
Endometrial Polyp	4.84% (23)
Endometrial Tuberculosis	0.21% (1)
Endometrial Osseous Metaplasia	0.21% (1)
Endometrial Foreign Body	0.21% (1)
Total	100% (475)

Table 2: Age-wise Distribution of Histopathological Diagnosis of Endometrium.

Histopathological Diagnosis	Age Group					
	<30	30-39	40-49	50-59	≥60	
Proliferative Endometrium	5	45	79	41	1	171
Secretory Endometrium	5	35	55	18	1	114
Hormonal Effect (Pill Endometrium)	2	11	19	2	0	34
Atrophic Endometrium	0	1	12	16	12	41
Disordered Proliferative Endometrium	0	3	7	3	0	13
Endometrial hyperplasia without Atypia	3	5	15	7	3	33
Endometrial hyperplasia with Atypia / EIN*	0	3	3	2	2	10
Endometrial Carcinoma	0	0	3	3	1	7
Chronic Endometritis	2	5	15	4	0	26
Endometrial Polyp	0	6	11	6	0	23
Endometrial Tuberculosis	0	1	0	0	0	1
Endometrial Osseous Metaplasia	1	0	0	0	0	1
Endometrial Foreign Body	0	0	1	0	0	1
Total	18 (3.79%)	115 (24.21%)	220 (46.32%)	102 (21.47%)	20 (4.21%)	475 (100%)

*EIN: Endometrial Intraepithelial Neoplasia

Table 3: Endometrial Thickness-wise Distribution of Histopathological Diagnosis of Endometrium.

Histopathological Diagnosis	Endometrial Thickness					
	≤ 4 mm	4.1 – 6 mm	6.1 – 8 mm	8.1 – 10 mm	≥ 10 mm	Total
Proliferative Endometrium	92	79	-	-	-	171
Secretory Endometrium	-	47	67	-	-	114
Hormonal Effect (Pill Endometrium)	-	12	18	4	-	34
Atrophic Endometrium	41	-	-	-	-	41
Disordered Proliferative Endometrium	-	5	8	-	-	13
Endometrial hyperplasia without Atypia	-	-	9	24	-	33
Endometrial hyperplasia with Atypia / EIN	-	-	-	4	6	10
Endometrial Carcinoma	-	-	-	-	7	7

Chronic Endometritis	-	7	19	-	-	26
Endometrial Polyp	-	9	14	-	-	23
Endometrial Tuberculosis	-	1	-	-	-	1
Endometrial Osseous Metaplasia	-	-	-	-	1	1
Endometrial Foreign Body	-	-	1	-	-	1
Total	133 (28%)	159 (33.47%)	137 (28.84%)	32 (6.74%)	14 (2.95%)	475 (100%)

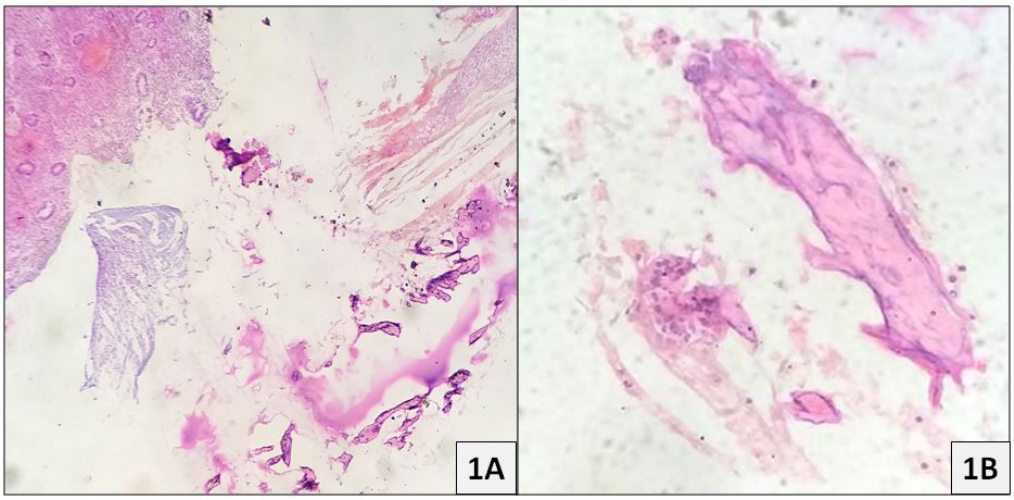

Figure 1: Osseous metaplasia in endometrium (H & E, Fig 1A – 40x, Fig 1B – 400x)

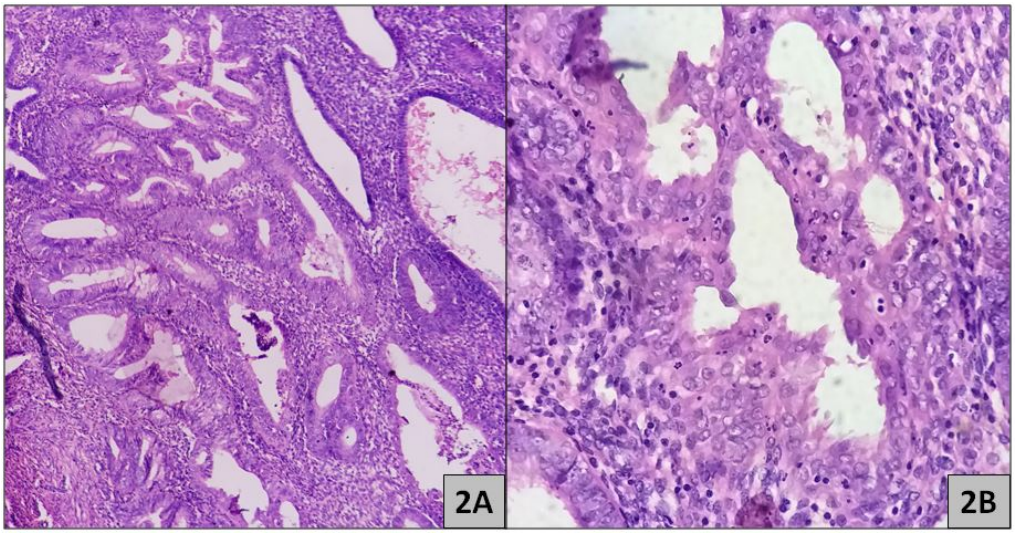

Figure 2: Endometrial hyperplasia with Atypia / endometrial intraepithelial neoplasia (EIN) (H & E, Fig 2A – 100x, Fig 2B – 400x)

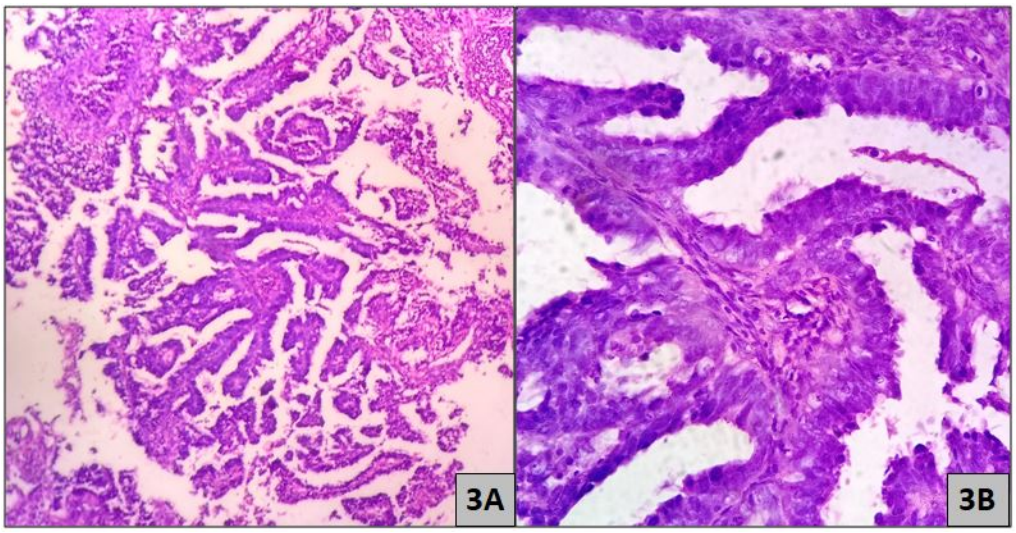

Figure 3: Endometrial Carcinoma (H & E, Fig 3A – 40x, Fig 3B – 400x)

Discussion

Abnormal uterine bleeding (AUB) is chief reason for the women visiting the gynecologist. It is considered as menstrual bleeding with an abnormality of any of the following type - frequency of menstruation, duration of flow, amount of blood loss and cyclicity, or an intermenstrual bleeding. The FIGO classification system categorized causes of AUB in non-gravid women of reproductive age into polyp, adenomyosis, leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory dysfunction, iatrogenic, endometrial, and not yet classified – with the acronym PALM-COIEN.{3} Other than the blood tests the frequent investigations done in these cases are ultrasonography (USG), and histopathological evaluation (HPE) of endometrial tissue obtained by endometrial curettage or biopsy. Of these, HPE of the endometrium forms the gold standard for the diagnosis of the endometrial pathologies mainly endometrial carcinoma and endometrial hyperplasia with atypia.

The present work analyzed the endometrial causes of AUB. The age-wise and endometrial thickness wise distributions of these cases were also studied as these causes usually relate to the age group of the patients.

In the current work most common age group sampled for AUB was 40-49 yrs (46.32%), as in other ones.{4- 8}

The most common pattern seen was normal cyclical endometrium (60%) including proliferative (36%) and secretory (24%) endometrium. The findings are concordant with the previous works,{2, 9-12} with similar proportions of cases showing normal cyclical endometrium.{9} The cases were seen in all the age groups and the endometrial thickness was corresponding well with the phase of endometrium.

The cyclical endometrium indicates presence of dysfunctional uterine bleeding (DUB), the proliferative phase suggesting anovulatory cycles and secretory due to ovulatory ones.{11} Thus, endometrial study will distinguish between these two causes of DUB. The Anovulatory DUB is seen in the polycystic ovary syndrome and at the perimenarchal and perimenopausal years due to disturbed function of the hypothalamic-pituitary-ovarian axis. In the current work maximum cases with proliferative endometrium were seen in the perimenopausal age group (40-49 years), possibly due to greater concerns of an abnormality in a previously normal menstrual flow. The ovulatory DUB has defective control of processes regulating the volume of menstrual blood loss

including decreased endometrial vasoconstriction and vascular hemostatic plug formation.{13}

This was followed by atrophy, pill endometrium and hyperplasia without atypia. There were 8.63% cases of atrophic endometrium, a little more than the incidence in various studies (1.1 – 5.6%).{2, 9, 10, 14} AUB here is hypothesized due to be due to anatomic vascular variations or local abnormal haemostatic mechanisms.

Chronic endometritis made up 5.47% of cases, also one case of tubercular endometritis was seen. In the later case the patient was nulliparous, with clinical history of infertility and AUB. Grossly there was absence of endometrial cavity and histology showed caseating granulomas in the endomyometrium.

The hormonal endometrium and endometrial polyp were more prevalent in present study than others.{9} The polyps show distinctly prominent thick walled blood vessels. Maximum cases were seen in the age group 40-49 years. None of the postmenopausal endometrial polyp cases were found to be associated with malignancy, a feature to be cautiously evaluated.

In the continuum of the lesion due to the prolonged estrogen stimulation, disordered proliferative endometrium and the endometrial carcinoma form the two extremes. Disordered proliferative endometrium was found to be 2.74% with majority of cases belonging to perimenopausal (40-49 years) age group, findings concordant with previous works.{9}

A lower incidence of the endometrial hyperplasia without atypia (6.95%) as compared to other authors (10-25%) was found.{2, 9-10} However, the prominent age group involved was 40-49 years, similar to others. The chief distinguishing feature between disordered proliferative endometrium and endometrial hyperplasia without atypia is the increased gland is to stroma ratio (>3:1) in the later.

Endometrial hyperplasia with atypia, the premalignant condition, was found to be 2.11%, majority in 30 – 49 years of age. These findings are comparable to few studies.{9} Distinction of endometrial hyperplasia with atypia from without atypia depends on presence of nuclear atypia in the former (Figure 2). The importance of indentifying atypia lies in the fact that 28% of these cases may progress to carcinoma without hysterectomy and presence of adjacent endometrial carcinoma in 43% of cases. Adjacent endometrial carcinoma was not identified in none of our cases.

Endometrial carcinoma is the most dreaded finding in endometrial biopsies, endometrioid subtype being the commonest. Only one serous endometrial carcinoma was seen in the present research, rest being endometrioid [overall 1.47% (7cases)] (Figure 3). The proportion of cases found was comparable with the other studies.{9, 11, 14}

Age wise HPE patterns showed benign conditions to be present in most patients of AUB <40 years; proliferative conditions including proliferative lesions such as disordered proliferative pattern, endometrial hyperplasia without atypia and benign endometrial polyp, and chronic endometritis being common in 40-49 years patients. The majority of malignant lesions were seen in women more than 50 years of age. These findings are concordant with the other works.{4, 5} However, there was occurrence of considerable proportion of premalignant and malignant lesions in the perimenopausal age in the present research.

The endometrial thickness (ET) in the premalignant and malignant lesions in this study was found to be in the range ≥ 8mm and ≥ 10 mm respectively. In contrast, the disordered proliferative endometrium and endometrial hyperplasia without atypia cases had ET ranging in 4.1 – 8 mm and 6.1 to 10 mm respectively (Table 3). Only few cases of hormonal effect belonged to ET 8.1 – 10 mm. In

these cases grossly there was an appearance of endometrial hyperplasia but microscopically extreme decidualization was evident. In postmenopausal patients, the ET was >4mm in majority of those with hyperplasia and >10.1 in majority of malignancies in the previous work.{15}

A case of osseous metaplasia of endometrium was found, a rare occurrence, showing bony spicules and trabeculea adjacent to the endometrial tissue (Figure 1). There was no associated history of loss of pregnancy in the recent past. Thus, chronic endometritis causing the plueripotent endometrial stem cells to undergo metaplastic change to osteoblastic cells laying down bone in this case can be the acceptable pathogenesis.

Also, a single case of foreign body in endometrium was found, a vegetable matter. It is known that as a part of quack practise for abortions and treatment of menstrual irregularities a large variety of foreign bodies including household things like knitting needle, crochet hook, hair pin or other objects as uterine sound, curette, catheter douche, canula and bamboo stick are inserted into uterine cavity.{16} However the cause in this case could not be ascertained.

Conclusion

Yet again the endometrial biopsy has been proved to be of high value for giving definitive diagnosis of the cause of AUB in all age groups in this study. Also, age wise and ET wise distribution of cases correlated well with their HPE diagnosis.

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