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Original Research Article

Endometrial pathology in abnormal uterine bleeding

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is a common presenting symptom in gynecological outpatient department. Endometrial sampling could be used as the first diagnostic step in AUB. Aim of our study was to evaluate the endometrial causes of AUB and to observe the incidence of various pathology in different age groups.
Methods: A study was conducted on 167 patients who presented with AUB, during the period from July 2015-January 2017.All endometrial curettage and hysterectomy specimens received in the Department of Pathology, Kannur Medical College during this period were included.
Results: Maximum numbers of patients were in the perimenopausal age group and normal cycling endometrium was the commonest pattern observed (41.3%).Abnormal patterns noted were hyperplasia without atypia (20.9%), disordered proliferative pattern (16.1%) and endometrial carcinoma (1.7%).
Conclusion: Histopathological examination of endometrium showed wide spectrum of lesions from normal endometrium to malignancy. Accurate analysis of endometrial sampling is important in the management of AUB.

Keywords: Abnormal uterine bleeding, Endometrium, Histopathology

INTRODUCTION

Abnormal uterine bleeding (AUB) is one of the commonest presenting symptoms in gynecology clinics. Prevalence of AUB in women between menarche and menopause is around 9-14%. The reported prevalence of AUB in India is around 17.9%.[1] AUB is defined as change in frequency of menstruation, duration of flow or amount of blood loss. The mean duration of menstruation is 4.7 days and average blood loss per cycle is 35ml.[2] It includes both organic and non-organic causes of uterine bleeding. Endometrial biopsy or curettage is a safe and effective diagnostic modality in evaluation of abnormal uterine bleeding after ruling out medical causes.[3] The underlying disease can be detected by histological patterns of endometrium considering the age, menstrual cycle phase and use of any exogenous hormones. Pregnancy-related and dysfunctional uterine bleeding is more common in younger patients, whereas atrophy and organic lesions become more frequent in older individuals.[4] A new nomenclature system known by the acronym PALM-COEIN (Polyp; Adenomyosis; Leiomyoma; Malignancy and Hyperplasia; Coagulopathy; Ovulatory Disorders; Endometrial factors; Iatrogenic; and Not classified) was introduced in 2011 by the International Federation of Gynecology and Obstetrics (FIGO) to standardize the terminologies of AUB. The PALM-COEIN system is etio-pathogenesis based, with PALM describing structural causes and COEIN denoting non- structural causes of AUB. Hence, FIGO nomenclature system will allow for standardization and uniformity while conducting future studies and can rectify the problem of inconsistency in AUB management.[5] This study was done to evaluate the endometrial causes of AUB and to determine the specific pathology in different age groups.

METHODS

This was a prospective hospital based observational study. This study included 167 patients who presented with clinical diagnosis of Abnormal Uterine Bleeding (AUB). Study population was patients visiting gynecology outpatient department with the clinical diagnosis of Abnormal Uterine Bleeding and had undergone endometrial sampling. Study period was from July 2015 to January 2017. Approval from institutional ethics committee was taken. Inclusion criteria was patients with isolated endometrial pathology who presented with clinical diagnosis of AUB. Exclusion criteria was patients with non-endometrial causes for AUB like leiomyoma, cervical pathology and hemostatic disorders. Samples were obtained by endometrial curettage, pipelle aspiration or by hysterectomy. Out of 167 cases studied, 76 samples were obtained from hysterectomy specimens and the rest were dilatation and curettage/pipelle cases. Patient age, clinical presentation, examination findings and surgical procedure undergone were recorded from requisition forms and hospital records. Specimens were sent to histopathology lab in wide mouthed containers with 10% formalin fixative. Gross morphology of small biopsy specimen was described in terms of size, colour and consistency. Small biopsies were entirely submitted after a minimum of 12 hours fixation. Gross morphological features were recorded for large specimens and were serially sliced to ensure fixation. Representative bits were taken post 24 hour fixation in formalin. Tissue was processed in automated tissue processor and paraffin blocks were prepared. 4 microns sections were cut and stained using H&E stain. Slides were seen by two pathologists separately to reduce bias. Various histopathological patterns were classified as the following: proliferative, secretory, menstrual, basal, atrophic, gestational, pill endometrium, disordered proliferative, endometrial hyperplasia and endometrial carcinoma. Endometrial hyperplasia were classified according to the new simplified system which now consist of hyperplasia without atypia and atypical hyperplasia/endometrial intraepithelial neoplasia. The data were entered in Microsoft Excel and statistically analyzed. Analysis was done in the form of percentage and represented as tables and figures wherever necessary.

RESULTS

A total of 167 cases were included in this study. The age of patients ranged from 19 to 78 years (Table 1). Maximum numbers of patients were in the age group 40 to 49 years (48.5%). Most common bleeding pattern was menorrhagia(48%). Other patterns observed were metrorrhagia, polymennorrhea and post-menopausal bleeding. Normal cycling endometrium (41.3%) was the commonest pattern observed. Among this 69 cases of cycling endometrium, 40(23.9%) were secretory (Figure 1), 15(8.9%) were proliferative, 13(7.7%) showed basal endometrium and 1 (0.5%) in menstrual phase. Diagnoses of cycling endometrium were correlated with last menstrual period wherever possible.

Table 1: Distribution of patients in various age groups.

Age in years	No. of patients	Percentage
<20	1	0.5
20-29	10	5.9
30-39	22	13.1
40-49	81	48.5
50-59	39	23.3
60-69	11	6.5
70-79	3	1.7

Other patterns of endometrial pathology are depicted in Table 2. There were 19 (11.3%) cases of atrophic phase which showed tubular or dialated glands lined by low cuboidal to flattened epithelium without significant mitotic activity.

Table 2: Distribution of patients based on endometrial pattern observed.

Pattern	No. of cases	Percentage
Secretory phase	40	23.9
Proliferative phase	15	8.9
Basal endometrium	13	7.7
Menstrual phase	1	0.5
Atrophic phase	19	11.3
Gestational	6	3.5
Disordered proliferative	27	16.1
Pill endometrium	5	2.9
Hyperplasia without atypia	35	20.9
Hyperplasia with atypia	3	1.7
Endometrial carcinoma	3	1.7

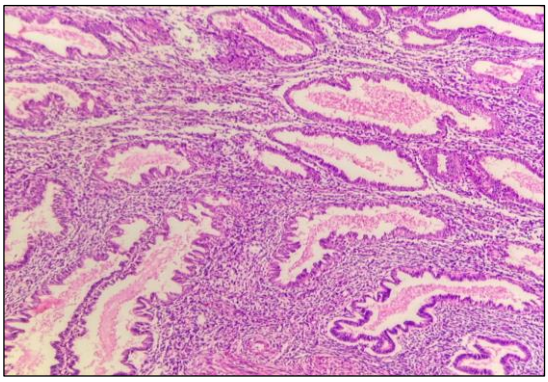

Figure 1: Tortous secretory glands with luminal secretions (H&E, 100x).

All 6 cases of gestational endometrial pattern had chorionic villi and hypersecretory glands embedded in

decidualized stroma. Five cases showed hormonal effect endometrium /pill endometrium. Inactive and exhausted endometrial glands embedded in decidualised stroma characterized this pattern.

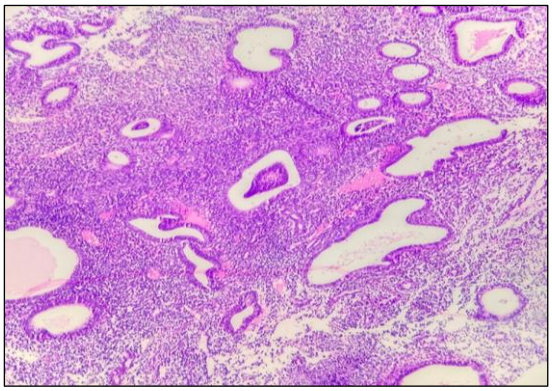

Figure 2: Dilated and branching glands set in a compact stroma. Gland to stroma ratio not increased (H&E,100x).

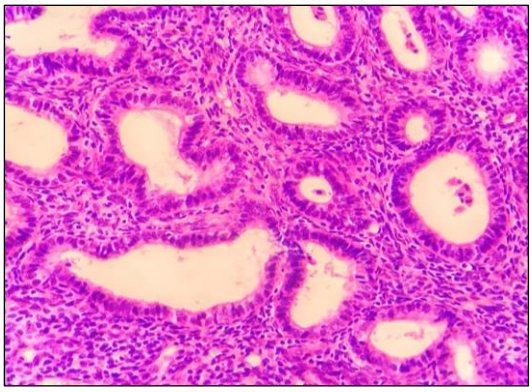

Figure 3: Closely packed endometrial glands without cytological atypia (H&E,100x).

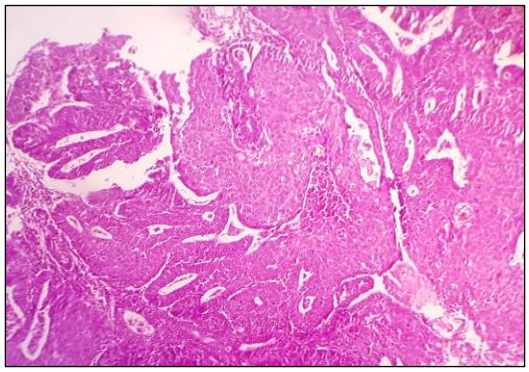

Figure 4: Endometrioid carcinoma with well differentiated glands and foci of squamous metaplasia (H&E,100x).

These were not correlated with the history of intake of exogenous hormones, as it was not available. Most common abnormal pattern observed was hyperplasia without atypia (20.9%)(Figure 3) followed by disordered proliferative endometrial pattern (16.1%) (Figure 2). Disordered proliferative endometrium was considered wherever the endometrial pattern was exuberantly proliferative and abnormal for the date of the menstrual cycle but fell short of hyperplasia in terms of glands to stroma ratio. Other findings noted in disordered proliferative endometrium were branched glands, cystically dilated glands, epithelial metaplasias and stromal fibrin.

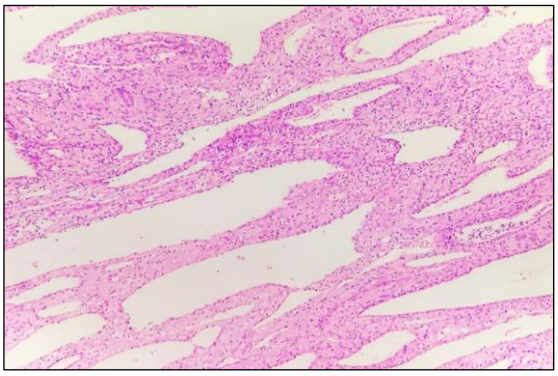

Figure 5: Atrophic endometrial glands in decidualised stroma (H&E,100x).

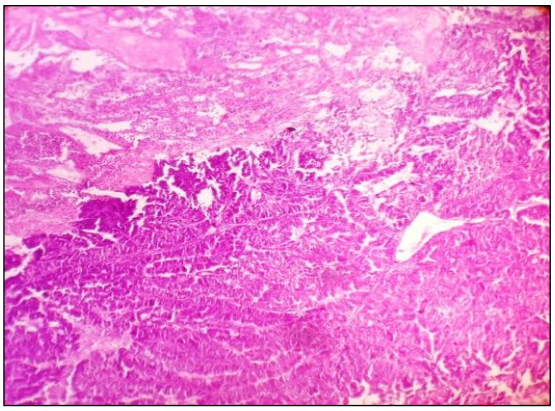

Figure 6: Serous type endometrial carcinoma with papillary pattern and extensive areas of necrosis (H&E,100x).

The key feature that distinguished disordered proliferative endometrial pattern from hyperplasia was the presence of maintained gland to stroma ratio. Cases of hyperplasia without atypia (20.9%) showed crowded glands, stratified glandular epithelium, scanty intervening stroma apart from increased gland to stroma ratio. Nuclear enlargement, rounding of nuclei, coarse chromatin and nucleoli were the grounds on which cytological atypia in hyperplastic endometrium (1.7%) was given. Glands with significant architectural complexity like solid areas, papillary configurations, maze like glands, cribriform pattern were categorized as carcinoma rather than atypical hyperplasia. All three cases (1.7%) of endometrial carcinoma presented as post-menopausal bleeding. Two cases were type 1 endometrial carcinoma (endometrioid type) and one was type 2 endometrial carcinoma (serous type). Both type 1 carcinomas (Figure 4) were well differentiated, exhibited confluent glandular pattern, focal solid areas and showed

involvement of less than half of myometrium. Lymphovascular invasion was absent in both. Serous type endometrial carcinoma (Figure 6) showed papillary architecture, numerous psammoma bodies, high mitotic activity and extensive areas of necrosis.

DISCUSSION

Abnormal uterine bleeding is a broad term that describes irregularities in the menstrual cycle involving frequency, regularity, duration and volume of flow outside of pregnancy. A normal menstrual cycle has a frequency of 24-38 days, last 7-9 days with 5-80 ml of blood loss. Variations in any of these 4 parameters constitute AUB.[6]

PALM-COEIN is a useful acronym provided by International Federation of Obstetrics and Gynecology to classify the etiologies of AUB. Causes of AUB are structural like polyps, adenomyosis, leiomyoma, malignancy and hyperplasia. Non-structural causes of AUB are coagulopathy, ovulatory dysfunction, endometrial disorders, iatrogenic and not otherwise classified.[4]

Routine non-invasive investigations for AUB were carried out which included CBC, platelet count, LFT, PT, APTT to rule out bleeding and coagulation disorder. In a woman of reproductive age group, serum and urine HCG was evaluated to rule out pregnancy. As thyroid is the commonest endocrinological cause encountered, TFT was done.

On ruling out these, D and C was done as a diagnostic as well as therapeutic procedure. The sensitivity of endometrial biopsy for detection of endometrial abnormalities has been reported to be as high as 96%.[7,8]

Women with AUB who have completed their family and those not responding to hormonal treatment were subjected to hysterectomy.

Etiology of AUB relates to the patients age as to whether the patient is premenopausal, perimenopausal or postmenopausal.[9]

Youngest patient in our study was a 19 year old girl who presented with gestational endometrium and oldest was a 78 year old lady with atrophic endometrium.

Majority of cases in the present study showed normal cycling patterns of endometrium comprising of proliferative, secretory and atrophic endometrium.

In the 21-30 year age group majority of cases presented with complications of pregnancy. This may be attributed to the fact, that majority of women conceive in this age group.

Maximum number of patients in our study (48.5%) belonged to the age group 40-49 years. Apart from normal cycling endometrium, the pathological lesions at this age group was hyperplasia in 18% and disordered proliferation in 11%. The reason for AUB at this perimenopausal age group may be due to anovulatory cycles consequent to decrease in ovarian follicles and estradiol levels.

In this study a significant proportion of cases showed disordered proliferative pattern (27%). Disordered proliferative endometrium was commonly seen in perimenopausal age group. It denotes an endometrial appearance that is hyperplastic but without an increase in endometrial volume. It resembles simple hyperplasia, but the process is focal rather than diffuse.[10]

This study showed higher incidence of disordered proliferation compared to Doraiswami et al (20.53%), Bashir H et al, (12.17%) and Vaidya et al, (13.4%).[2,11,12] This may be due to earlier stage of presentation as a consequence of increased health awareness. Early detection and treatment help to prevent the progression of disease to hyperplasias and carcinomas.

Another pathological pattern seen in our patients was endometrial hyperplasia of which majority was without atypia(20.96%) and 1.8% cases showed atypia. Our incidence was comparable to the study of Muzhafar et al, who reported 24.7% cases of endometrial hyperplasia and Shilpa et al, who reported 24% cases of hyperplasia without atypia and 1.5% cases of hyperplasia with atypia whereas Dorai swami et al reported a lower incidence of hyperplasia (6.1%).[13,14] Similar lower incidence was reported by Parmer et al, endometrial hyperplasia without atypia ,0.05% and with atypia 0.04%.[15]

Higher incidence of endometrial hyperplasia in our study group may be due to sedentary lifestyle, and presence of risk factors like obesity, diabetes, and increased intake of animal fat, as majority belongs to higher socioeconomic status.

Hyperplasias were more common in the 41-49yr age group similar to the studies done by Kurman et al.[16]

Identification of endometrial hyperplasia is important as they are thought to be the precursors of endometrial carcinoma. This is supported by the studies done by Lacey et al, and Chambian and Taylor, who found that the risk of progression into carcinoma was more in case of atypical hyperplasia.[17,18]

In this study endometrial carcinoma constituted only 1.8% of cases. A similar incidence was reported by Anuradha et al, (1.84%).[19] In our study endometrial carcinoma was seen in the 60-69yr age group. Similar lower incidence of endometrial carcinoma was reported by Dangal et al, in Nepalese woman, which according to him was due to the practice of early childbearing and multiparity.[20] Same factors might have contributed to the lower incidence of endometrial carcinoma in our population.

CONCLUSION

Endometrial causes of AUB are age related pathology. Histopathological examination of endometrium is the gold standard to evaluate AUB. Accurate analysis of endometrial sampling is the key to effective therapy.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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