RESEARCH ARTICLE

HISTOPATHOLOGICAL INTERPRETATION OF ENDOMETRIUM IN ABNORMAL UTERINE BLEEDING

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ABSTRACT

Background: Abnormal uterine bleeding is one of the most frequent problems in life of an adult female. Accurate analysis of endometrium & localization of intrauterine lesion is the goal to effective management & better outcome of problem.

Aims & Objective: To evaluate various histopathological features in D & C and/or hysterectomy in patients presenting with abnormal uterine bleeding and to find the efficacy of D & C as a better, cost effective and minimally invasive tool for screening in patients with AUB.

Materials and Methods: The present study was conducted in Department of Pathology, tertiary care hospital, Ahmedabad, Gujarat, India over a period of one and half years. A total 320 patients aged 20 years & above, presenting with AUB were included. Endometrial samples were analysed, histopathological changes identified and classified.

Results: Age of patients ranged from 21 to 70 years mean age being 42.6 ± 6.9 years, maximum patients (53.4%) belonged to 41-50 years of age group. Most common histopathological pattern was normal cyclical endometrium (47.3%) followed by endometrial hyperplasia (42.9%). Endometrial hyperplasia was most common (57.1%) in perimenopausal age group (41-50 years). The diagnostic accuracy of D &C was found to be 93.4%; amongst all histopathological patterns it was maximum for complex hyperplasia (typical and atypical) and simple atypical hyperplasia.

Conclusion: Endometrial causes of AUB are age related therefore it is specially recommended in women of perimenopausal age group to rule out preneoplastic and neoplastic etiology. D & C is an accurate, minimally invasive outdoor procedure for detecting endometrial pathology especially hyperplasia.

Key Words: Abnormal Uterine Bleeding; Dilatation & Curettage; Endometrium; Hyperplasia; Perimenopausal

Introduction

Abnormal Uterine Bleeding (AUB) is defined as any bleeding that does not correspond with the frequency, duration or amount of blood flow of a normal menstrual cycle[1], and could be a sign of simple hormonal imbalance or a serious underlying condition necessitating aggressive treatment including a major surgical procedure.[2] The causes for AUB can be categorized into: (A) Organic, such as genital tract infections, tumors (benign or malignant), adenomyosis, pregnancy and its complications, systemic disorders and iatrogenic[3] accounting for 20% of cases; (B) Dysfunctional Uterine Bleeding (DUB) caused by anovulation or oligovulation[3] is responsible for 80% of menorrhagia[4] & diagnosed after exclusion of all conditions enumerated in (A).[5] Anovulation & oligo-ovulation resulting in hyperestrinism, cause prolonged stimulation of the endometrial lining and increase the risk of both endometrial hyperplasia and carcinoma.

Many women with abnormal uterine bleeding may undergo unwarranted hysterectomy without a definite diagnosis.[6] In women ≥ 40 years and certainly in menopausal patients, it mandates evaluation to confirm benign nature of the problem, so that medical treatment or conservative surgery can be offered and unnecessary radical surgery can be avoided.[7] Dilatation and curettage is a useful and cost effective method of detecting intrauterine pathologies and very few lesions escape detection.[8] It clearly shows the hormonal response of endometrium and provides useful information regarding atrophy, specific and non-specific infections, polyps and/or malignancy.[9] The wide range of morphologic patterns resulting from both normal and abnormal changes offer a diagnostic challenge to histopathologists. Our study is aimed at determining the types and frequencies of endometrial pathologies in patients presenting with abnormal uterine bleeding at our hospital and to find the diagnostic accuracy of D&C as a screening tool.

Materials and Methods

The present study was conducted in the Department of Pathology, at a tertiary care hospital in Ahmedabad, Gujarat, India over a period of one and half years with the approval IEC. A total of 320 patients aged 20 years & above presenting with AUB were included. All patients with pregnancy related complications, cervical pathologies, systemic causes and bleeding diathesis were excluded. The clinical data was obtained from patient's medical records. Endometrial specimens were received in the form of D&C material and hysterectomy specimens.

Out of total 380 specimens, 221 were hysterectomy and 159 were D&C specimens which were processed in automated tissue processor and 3-5 micron thick sections were stained with Hematoxylin and Eosin (H&E). Microscopic examination and histopathological reporting was done by two histopathologists. Various endometrial patterns were classified as follows: Proliferative, Secretory, Atrophic, Unsatisfactory, Chronic Endometritis, Polyp, Submucosal Leiomyoma, Hyperplasia and Carcinoma. Endometrial Hyperplasia was classified according to World Health Organization (WHO), originally proposed by Kurman & Norris, into simple and complex on the basis of architecture and each was further subdivided into typical and atypical, based on cytology.[10] Data was collected and analyzed.

Results

Out of the total of 380 specimens received as D & C and/or hysterectomy specimens from patients aged 21-70 years with a mean age of 42.6 +/- 6.9 years, the most common histology observed was normal cyclical endometrium (47.3%, comprising of 38.1% proliferative & 9.2% secretory) (figure 1 & 2 respectively). Endometrial hyperplasia was observed in 42.9%, of which simple hyperplasia (figure 3) was the most common (35.3%), followed by simple or complex atypical hyperplasia (4.7%) (figure 4) and complex hyperplasia without atypia (2.9%). Endometrial carcinoma was detected in 0.3% cases while rest of the specimens (7.3%) comprised of chronic endometritis, endometrial polyp & submucosal leiomyoma. Atrophic endometrium was observed in 1.1% in cases (Table 1).

The most common age group having complaint of AUB was 41-50 years (53.4%), of which 93.6% were diagnosed as DUB & 6.4% as organic lesions like chronic endometritis, polyp & submucosal leiomyoma. In DUB, the most common histopathological pattern was normal cyclical endometrium (47.2%) followed by simple or complex hyperplasia without atypia (40.9%) and atypical hyperplasia (4.9%). In women under 30 years of age, normal cyclical endometrium was found in 63.6% followed by simple hyperplasia in 36.4%. No atypical pattern or organic lesions were found. In the 31 – 40 years age group, 52.3% had normal cyclical endometrium, 34.6% had endometrial hyperplasia without atypia & 1.5% had atypical endometrial hyperplasia. Organic causes were found in 10% of cases, which is the maximum, as compared to other age groups. In the above 50 years age group, endometrial hyperplasia was more common (52.8%) than normal cyclical endometrium (36.1%). Endometrial carcinoma was found in 2.8% and 5.6% were having endometrial polyp & leiomyoma (Table 2).

Out of the 221 endometrial samples obtained by hysterectomy, 60 had undergone previous D & C. In 46 of these, histopathological findings were concordant with that of the previous D&C specimen & 14 cases were disconcordant (Table 3). Sensitivity, specificity & diagnostic accuracy of D & C for all endometrial pathologies included in this study are shown in Table 3.Sensitivity was least for proliferative pattern 64% with 94.12% specificity & 0.81 diagnostic accuracy. Amongst all the histopathological patterns observed, diagnostic accuracy of D & C was highest in typical complex hyperplasia and simple & complex atypical hyperplasia.

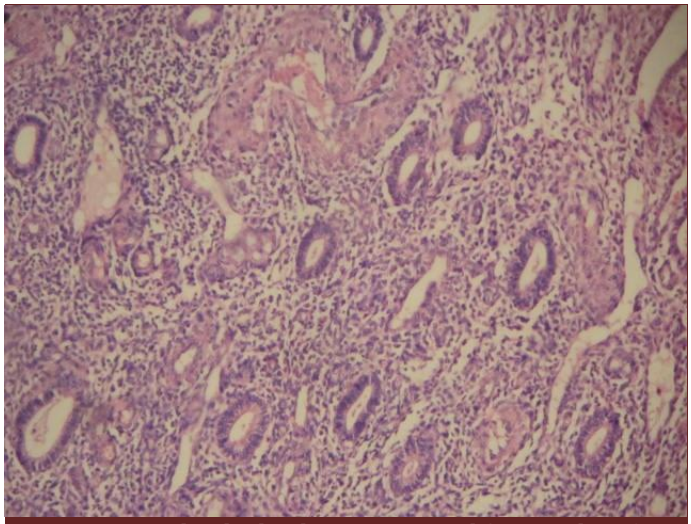

Figure-1: Normal cyclical endometrium in proliferative phase (H & E, 10X)

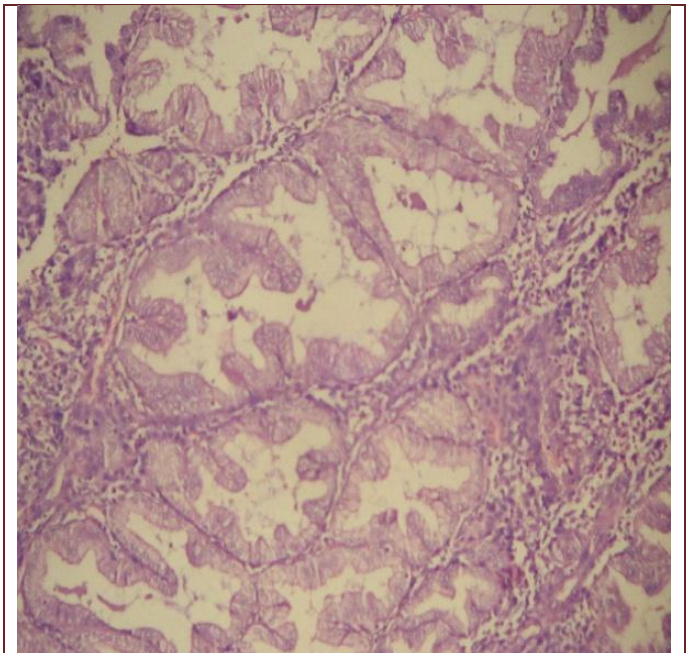

Figure-2: Normal cyclical endometrium in secretory phase (H & E, 10X)

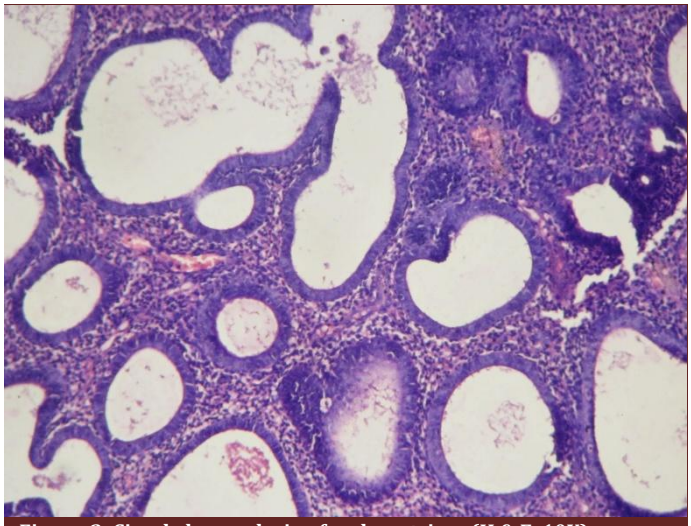

Figure-3: Simple hyperplasia of endometrium (H & E, 10X)

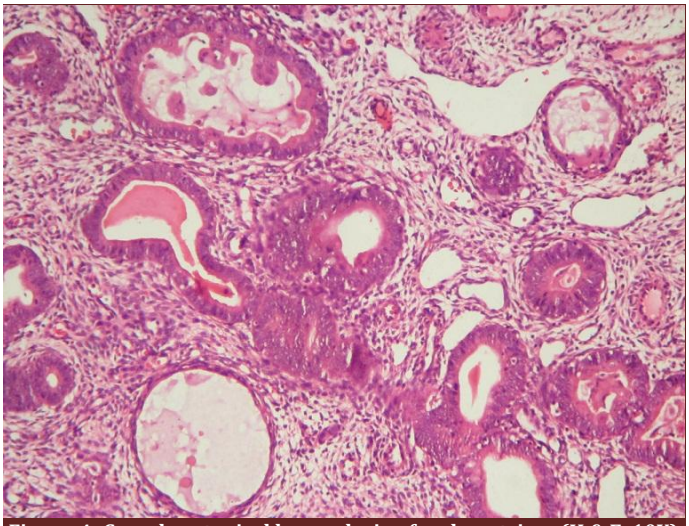

Figure-4: Complex atypical hyperplasia of endometrium (H & E, 10X)

Table-1: Frequency of Different Histopathological Patterns Of Endometrial Specimens by D&C or Hysterectomy

Histopathological Pattern	No. of Patients	%
Proliferative	145	38.1
Secretory	35	9.2
Atrophic	4	1.1
Chronic Endometritis	10	2.6
Endometrial Polyp	10	2.6
Submucosal Leiomyoma	8	2.1
Simple Hyperplasia without Atypia	134	35.3
Complex Hyperplasia without Atypia	11	2.9
Simple Hyperplasia with Atypia	6	1.6
Complex Hyperplasia with Atypia	12	3.1
Endometrial Carcinoma	1	0.3
Unsatisfactory	4	1.1
Total	380	100

Table 2: Histopathological Patterns of Endometrium according to Age Group in Years

Histopathological Pattern	21-30	31-40	41-50	51-60	> 60	Total
Proliferative	6	47	80	11	1	145
Secretory	1	20	14	0	0	35
Atrophic	0	1	2	1	0	4
Chronic Endometritis	0	5	5	0	0	10
Endometrial Polyp	0	5	4	1	0	10
Submucosal Leiomyoma	0	3	4	1	0	8
Simple Hyperplasia without Atypia	4	43	77	9	1	134
Complex Hyperplasia without Atypia	0	2	6	1	2	11
Simple Hyperplasia with Atypia	0	1	4	1	0	6
Complex Hyperplasia with Atypia	0	1	6	5	0	12
Endometrial Ca	0	0	0	1	0	1
Unsatisfactory	0	2	1	1	0	4
Total	11	130	203	32	4	380

Table 3:Diagnostic Accuracy Of Endometrial Curettage In Endometrial Pathology

Histopathological Pattern	Hysterectomy	D & C		Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
		Concordant	Disconcordant					
Proliferative	25	16	9	64	94.12	88.9	78.05	0.81
Secretory	1	0	1	0	91.38	0	98.15	0.89
Atrophic	1	1	0	100	100	100	100	1
Simple Hyperplasia without Atypia	27	23	4	85.19	83.87	82.14	86.67	0.84
Complex Hyperplasia without Atypia	1	1	0	100	100	100	100	1
Simple Hyperplasia with Atypia	1	1	0	100	100	100	100	1
Complex Hyperplasia with Atypia	4	4	0	100	100	100	100	1
Total	60	46	14					

Discussion

Endometrium is a dynamic, hormonally sensitive and responsive tissue which constantly and rhythmically undergoes changes in the active reproductive life. It is a sensitive bioassay for estrogen and progesterone, whose actions are mediated on specific receptors.[11] Dysfunctional Uterine Bleeding, very commonly seen in clinical practice, can be confirmed by the pathological changes evaluated by microscopy.[12] In normal cycles, menstrual shedding is followed by endometrial proliferation under estrogenic stimulation, when the endometrial glands grow and become tortuous.[13] Secretory activity in second half of the menstrual cycle is characterized by endothelial proliferation, thickening of the wall and coiling; forming the spiral arterioles on the ninth postovulatory day.[13,14] Excessive and irregular uterine bleeding continues to be one of the most frequently encountered complaint in Gynecology. Frequency of various causes of AUB varies with age of the patient. DUB is a diagnosis of exclusion in which no specific organic cause can be attributed for the bleeding. It is more common in early and late years of reproductive life.[15] In most instances DUB is due to the occurence of an anovulatory cycle most commonly at menarche and in perimenopausal period.[16]

In the present study, the most common pattern was normal cyclical endometrium: proliferative (38.1%) and secretory (9.2%), total amounting to 47.3%. This is similar

to a study by Abdullah LS et al[17] which reported normal cyclical pattern in 46.6%. The incidence of 38.1% of proliferative endometrium compares favorably with that of 33% by Riaz S et al[18] and 42% by Patil SG et al[19] but contradicts with the lower incidence of 21.74% by Saraswathi D et al[20] and 24% by Jairajpuri ZS et al[21]. This may be due to the selection criteria and timing of D & C. The incidence of 9.2% of secretory pattern in our study corresponds well with that of 10.7% by Dangal G[22], 13.8% by Taib Al-Neaimy WM et al[23] and 14% by Patil et al[19].

Simple hyperplasia was found in 35%, making it the second most common histopathological pattern in our study. Other studies have also reported simple hyperplasia as the second most common pattern though the prevalence varies, from 25% by Riaz S et al[18] to 66% by Jairajpuri ZS et al[21] & Takreem A et al[24]. Majority of patients in our study with endometrial hyperplasia (62%) are more than 40 years of age indicating the increased risk of preneoplastic conditions like hyperplasia with age. Complex hyperplasia without atypia in our study was observed in 2.9% and with atypia in 3.1%, while in the studies by Khan S et al[25] they were reported as 2.8% and 1.0% respectively and by Patil SG et al[19] as 3.0% and 1.0% respectively. Endometrial carcinoma found in 0.4% in our study, was also reported as 0.4% by Jairajpuri ZS et al[21] and Khan S et al[25] but as 1.0% by Riaz S et al[18] & 1.8% by Abdullah LS et al[17]. A higher incidence of 4.4% by Saraswathi D et al[25], 2% by Sarwat Ara et al[26] & 3.3% by Khare A et al[27] has been reported. All cases of endometrial carcinoma were found in the post-menopausal age group.

The most important etiological factor for AUB relates to the age, whether premenopausal, perimenopausal or postmenopausal[26]. The maximum frequency (53.1%) of AUB in this study was in the 41 - 50 years of age group which is in concordance with 48.1% by Muzzaffar M et al[28] & 59% by Sarwat Ara et al[26]. The high incidence in this age group could be due to the fact that as menopause approaches, decreased number of ovarian follicles & increased resistance to gonadotrophic stimulation results in a low level of oestrogen which cannot keep the normal endometrium growing.[21] Lesser number of patients seen in the above 50 age group may be due to earlier evaluation, detection as well as management of the disease.

Out of total 163 cases with hyperplasia more than half (57.1%) were in 41-50 years of age (perimenopausal). Similar high prevalence of endometrial hyperplasia in perimenopausal age group was also reported as 64.8% by Jairajpuri ZS et al[21], 67.1% by Muzaffar M et al[28], 68% by Saraswathi D et al[20]. Taib Al-Neaimy WM et al[23] also found hyperplasia to be significantly associated with perimenopausal age group (P=0.002). Thus endometrial hyperplasia is a common diagnosis in perinemopausal women causing symptoms of irregular or prolonged bleeding due to anovulatory cycles. Heavy bleeding is secondary to sustained level of oestrogen causing overgrowth not only affecting glands and stroma but also abnormal vascularization.[24] The diagnosis, evaluation and follow up of patients with this condition is important because of the malignant potential, which is variable according to the type of hyperplasia.[28] Besides hyperplasia, prolonged oestrogen stimulation also results in formation of endometrial polyps. In the present study 2.63% cases of benign polyps were observed comparable to 5% by Patil SG et al[19], 2.46% by Bhatta S et al[29], 4.2% by Sarwat Ara et al[26], 1.7% by Jairajpuri ZS et al[21] & 1.2% by Muzaffar M et al[28]. 40% of these were seen in the 41-50years age group. This was in concordance with 39.1% by Saraswathi D et al[20] & 54.5% by Jairajpuri ZS et al[21]. There is a significant difference between the endometrial polyp & normal endometrium in receptor expression, cell proliferation and apoptosis regulation. These differences combined with non-random chromosomal aberrations & monoclonality suggests that polyp may provide a suitable microenvironment for the development of malignancy[20], thus endometrial polyps in perimenopausal age group require proper evaluation & follow up. Lower incidence of polyp in younger age group (21-30 years) may be attributed to a possible spontaneous regression mechanism, which is characteristic of the cyclic endometrium in reproductive age group.[20]

Chronic endometritis, diagnosed in 2.6% of cases, majority of them belonging to the 41-50 years of age group (50%), concurs with the reported incidence of 2% by Saadia A et al[30] & 1.2% by Patil SG et al[19]. Chronic endometritis, characterized by irregular fibrotic stroma & infiltrate of lymphoplasmacytic cells has been known to follow pregnancy or abortion & may be the result of IUCD or accompanied by mucopurulent cervicitis & PID.[18]

Incidence of atrophic endometrium observed in 1.1% of cases is comparable to 1% by Khan S et al[25] & 1.1% by Jairajpuri ZS et al[21]. Post-menopausal bleeding is frequently associated with an atrophic endometrium. The exact cause is not known. It is postulated that as a consequence of prolonged absence of any exogenous or endogenous estrogenic stimulation resulting in thin atrophic endometrium susceptible to minor injury and may be responsible for post-menopausal bleeding even in the absence of identifiable lesion.[29] 1.1% specimens inadequate for reporting showed scanty glands & stroma, fragmented tissue with large areas of haemorrhage.

Of the total 221 hysterectomy specimens, 60 had a previous diagnostic curettage. In 46 of these 60 cases, endometrial lesions were confirmed at hysterectomy making the diagnostic accuracy of D&C as 93.4%, which is similar to that reported by Taib Al-Neaimy WM et al[23]. In the remaining 14 there were some differences between the histopathology of curettage & hysterectomy specimens. In simple hyperplasia pattern of endometrium, 4/27 cases were discordant. The possible explanations for this include inadequate sampling, fragmentation of the specimen at curettage leading to fewer endometrial glands which cause difficulty in interpretation as well as interobserver variations in histopathological assessment. In proliferative endometrial pattern 9/25 cases were found to be discordant. This may be because cases which were reported as simple hyperplasia on D&C were completely removed during curettage leaving behind the basal endometrium only, which was then reported as proliferative endometrium due to short time gap between the two procedures. In complex hyperplasia with & without atypia there was a higher concordance rate than those of other endometrial patterns because complex hyperplasia has a higher degree of glandular proliferation which is not totally scrapped out at curettage & persists in the hysterectomy specimen, thus giving a high degree of concordance.[31]

Conclusion

All patients having AUB during & after the reproductive age should be screened for endometrial pathology. Accurate analysis of endometrial samplings is the key to proper diagnosis, effective therapy and optimal outcome. The commonest pathology is endometrial hyperplasia & it is commonly seen in perimenopausal age group (41-50 yrs). Endometrial causes of AUB are age related therefore it is specially recommended in women of perimenopausal age group to rule out preneoplastic & neoplastic etiology. D&C is an accurate procedure for detecting endometrial pathologies specially hyperplasia, but focal lesions such as endometrial polyp and myometrial lesions like leiomyoma & adenomyosis can be missed. Therefore persistent uterine bleeding after curettage indicates the presence of these lesions & warrants hysterectomy.

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