ORIGINAL ARTICLE

Histomorphological Spectrum of Lesions in Endometrial Biopsy in Patients Presenting with Abnormal Uterine Bleeding - A Study of 202 Cases

Sarika More[1], Pritam S Khairkar[1], Gopalkrishna Sawake[2] ,Nileema Sawake[2], MeghaPandey[3], Aashish Pandey[3]

1. Associate Professor, Pathology, Chirayu Medical College and Hospital, Bhopal, Madhya Pradesh
2. Professor, Pathology, Chirayu Medical College and Hospital, Bhopal, Madhya Pradesh
3. Assistant Professor, Pathology, Chirayu Medical College and Hospital, Bhopal, Madhya Pradesh

Abstract

Background: *Abnormal uterine bleeding is the most common presentation amongst the women of all age groups attending the gynecology Out Patient Department. Abnormal uterine bleeding (AUB) refers to a symptom of excessive, scanty, prolonged, cyclic, unexpected or acyclic bleeding regardless of diagnosis or cause.* ***Material & Method:*** *The study was carried out in the Department of pathology, Chirayu Medical College & Hospital Bhopal, India, over a period of 1 year from May 2015 to May 2016. Detailed clinical history like age, menstrual status including dysmenorrhoea, menorrhagia, period & regularity of cycle were obtained from the case records. Endometrial samples were obtained from dilatation and curettage or endometrial biopsy. Specimens were received in 10% formalin. These were studied grossly and were processed in automated tissue processor. Four to five micron thick paraffin embedded serial sections were taken and stained by Haematoxylin and Eosin. Special stains like ZN stain were done as per the case requirement.* ***Results:*** *The most common age group presenting with AUB was 41-50 years (40.09%). The commonest pattern in these patients was proliferative endometrium (41.58%), and secretory endometrium (17.32%). The commonest pathology was endometrial hyperplasia (15.34%). Hormonal changes were seen in 6.43% cases and endometrial carcinoma in 1.98%.* ***Conclusion:*** *Patients with AUB show variable pathology on endometrial biopsy ranging from inflammatory cause to malignancy. Hence, we recommend the pathologist should be vigilant while reporting endometrial biopsy which can have impact on patient's life.*

Keywords*: Abnormal uterine bleeding, Endometrial lesions, Dysmenorrhoea, Menorrhagia*

Address for correspondence: Dr. Sarika More. Associate Professor, Department of Pathology, Chirayu Medical College and Hospital, Bhopal. Mob No.9977097943. Email: dr.sarikamore@rediffmail.com

Received on :15/07/2016 Revised :24/07/2016 Accepted : 28/07/2016

Introduction

Endometrium is continuously under the effect of hormones throughout the life span of women.[1] Abnormal uterine bleeding is the most common presentation amongst the women of all age groups attending the gynecology Out Patient Department. Abnormal uterine bleeding (AUB) refers to a symptom of excessive, scanty, prolonged, cyclic, unexpected or acyclic bleeding regardless of diagnosis or cause.[2] Recently the International Federation of Gynecology and Obstetricsworking group on menstrual disorders has developed a classification system (PALM‑COEIN) for causes of the AUB in non‑gravid women of reproductive age.[3] There are nine main categories, which are arrangedaccording to the acronym PALM‑COEIN: Polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial;iatrogenic; and not yet classified. According to the proposed classification system, non-specific term like dysfunctional uterine bleeding should be abandoned tofavor a more specific etiology like ovulatory dysfunction[3]. Endometrial atrophy manifests as abnormal

bleeding and endometritis causes irregular shedding and thus evaluation is mandatory. Endometrial pathology can better be evaluated on endometrial biopsies or curettage. This study was done to find out the various endometrial pathologies causing AUB in different age groups.

Materials and Methods

A retrospective study was undertaken which included 202 endometrial samples with a clinical diagnosis of AUB. The study was carried out in the Department of pathology, Chirayu Medical College & Hospital Bhopal, India, over a period of 1 year from May 2015 to May 2016. Patients with isolated endometrial causes of abnormal uterine bleeding were included for study and those with cervical, vaginal pathology and haemostatic disorders were excluded from the study. Detailed clinical history like age, menstrual status including dysmenorrhoea, menorrhagia, period & regularity of cycle were obtained from the case records. Relevant findings of general and systemic examination were recorded. Endometrial samples were obtained from dilatation and curettage or endometrial biopsy. Specimens were received in 10% formalin. These were studied grossly and were processed in automated tissue processor. Four to five micron thick paraffin embedded serial sections were taken and stained by Haematoxylin and Eosin. Special stains like ZN stain were done as per the case requirement. Detailed microscopic examination was done in each case. The data was collected in excel sheet and analyzed**.**

Results

During the study period of 1 year from May 2015 to May 2016, a total of 202 endometrial samples were received. The cases studied were categorized into eleven groups depending upon the histomorphological diagnosis(Table 1). Amongst these, endometrial samples showing proliferative phase on microscopic examination comprised the maximum number of cases i.e.84 (41.48%), followed by 35 cases (17.32%), disordered proliferation of endometrium was observed in 15 cases (7.42%) (Table 1).

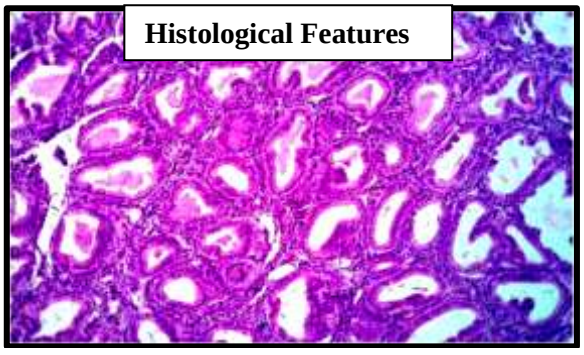
Table 1-Distribution of cases

Diseases	**Cases**	**%**
Proliferative phase	84	41.58
Secretory phase	35	17.32
Hyperplasia	31	15.34
Inadequate	06	2.97
Disordered proliferation	15	7.42
Hormonal change	13	6.43
Endometritis	6	2.97
Endometrial carcinoma	4	1.98
Endometrial polyp	3	1.48
Atrophy	4	1.98
Pregnancy changes	1	0.49
Total	**202**	

Hyperplasia was seen in 31 cases out of which 22 cases showed simple hyperplasia without atypia and whereas 7 cases showed complex hyperplasia without atypia and 2 cases showed complex hyperplasia with atypia (Figure 1).

Endometritis was seen in 6 cases, out of which 2 cases showed hallmark of tuberculosis i.e. Caseating granulomas and Langhans type of giant cells. Endometrial polyps were seen in 3 cases (1.48%). Total 4 cases (1.98%) revealed atrophic endometrium. Hormonal changes were observed in 13 cases (6.43%) whereas pregnancy related change was observed only in one case (0.49%). Endometrial carcinoma was encountered in 4 cases (1.98%). Endometrial carcinoma as widely known to be common in post menopausal women was observed in our study in 5^{th}, 6^{th}& 7^{th} decades of life (Table 2). Atrophy of endometrium, a common physiological feature after menopause was encountered during 4^{th}, 5^{th}& 6^{th} decades of life. Finally, in 6 cases (2.97%), the sample was scanty and inadequate for opinion (Table 1).

According to age, maximum number of patients were in the age group of 41 to 50 years (40.99%), followed by age group of 31 to 40 years (34.65%) (Table 2).



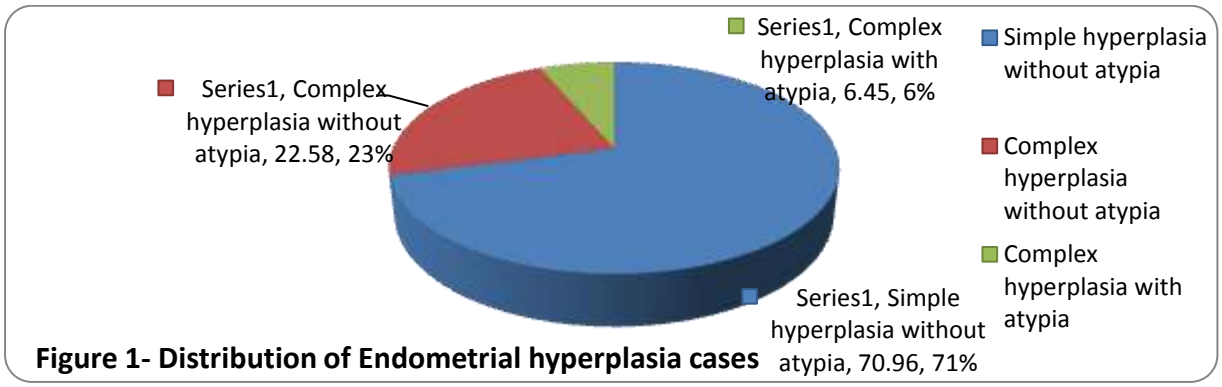


Figure 1- Distribution of Endometrial hyperplasia cases

Table 2- Distribution of cases according to age

	Age in years						
Diseases	20-30	31-40	41-50	51-60	61-70	71-80	81-90
Proliferative phase	18	21	45		-	-	-
Secretory phase	10	21	4	-	-	-	-
Hyperplasia	-	14	16	1	-	-	-
Inadequate	1	2	-	-	1	1	1
Disordered proliferation	3	7	5	-	-	-	-
Hormonal change	-	6	5	1	-	1	-
Endometritis	2	-	3	-	1	-	-
Endometrial carcinoma	-	-	1	1	2	-	-
Endometrial polyp	1	1	-	-	1	-	-
Atrophy	-	-	2	2	-	-	-
Pregnancy changes	1	-	-	-	-	-	-
Total	**36**	**72**	**81**	**5**	**5**	**2**	**1**

Discussion

Endometrial biopsy has been a continuous source of frustration for the pathologist because of minimal clinical information and biopsy taken at an inappropriate moment of menstrual cycle; one is unable to recognize the abnormality.[2] The endometrium undergoes regular cyclical changes under recurrent hormonal changes of the ovulatory cycles [1].

AUB with organic cause can be due to reproductive disease, iatrogenic causes and systemic diseases. When no specific organic cause of AUB is found, then by exclusion, a diagnosis of dysfunctional uterine bleeding (DUB) is assumed. However, well defined organic abnormality is seen only in 25 % cases of abnormal uterine bleeding.[4]

The etiology of AUB relates to the patient's age as to whether the patient is premenopausal, perimenopausal or post menopausal.[5]In present study it was found that the incidence of menstrual disorders increases with advancing age. The commonest age group of 41-50 years presented with excessive bleeding. Similar finding was reported by Doraiswami S *et al*, Yusuf *et al* and Muzaffar*et al* in their study of endometium.[6,7,8]

Normal physiological phases of endometrium, such as proliferative and secretory pattern were encountered in maximum number of cases. Proliferative endometrium comprised of total 84 cases (41.58%) in our study, this finding is in very much alliance with the studies done by Rajshri P Damle*et al*,[9] Khare*et al* [10]&Doraiswami S *et al*.[6] The bleeding in the proliferative phase may be due to anovulatory cycles and because of ovulatory dysfunctional uterine bleeding in the secretory phase.Our study showed secretory endometrium in 35 cases (17.32 %), similar to the study done by Spencer CP [12] which showed incidence of 16.1%. However the other two studies showed an increased incidence of 32.4% and 23 % respectively.[11,13]

The third commonest lesion was hyperplasia with maximum number of patients in the age group of 41 to 50 years (19.75 %), which is little less as compared to Slobada L[14] (22.6%),

Dangal G[15] (23%), Khare*et al*[10] (36.2%) and DoraiswamiS et al[6] (68%) who observed a high incidence of endometrial hyperplasia in the same age group. The incidence of simple hyperplasia was more common in the perimenopausal age group; this can be explained by the fact that there is failure of ovulation during this period which leads to persistent exposure of endometrium to the estrogenic action.

In our study there was only one case of complex hyperplasia with atypia in the postmenopausal age group, this is in contrast to the findings of Rajshri P Damle*et al*,[9] Khare*et al*[10] who observed a high incidence of 19.35 % & 33.3% respectively.

Fifteen cases (7.42%) showed disordered proliferative pattern in our study, which is in accordance with Jetley S *et al*.[11] The term "disordered proliferative endometrium" is difficult to understand. It denotes an endometrium that is hyperplastic but without an increase in endometrial volume.[16]It refers to proliferative endometrium not matching to the time of menstrual cycle but is not abnormal enough to be called hyperplastic. Disordered proliferative pattern resembles a simple hyperplasia, but the process is focal rather than diffuse.

Diagnosing the patients at the earliest stage of this spectrum will be of definitive help to the practicing gynaecologists to prevent the disease progression, because on the other end of the spectrum is the endometrial carcinoma.[16]

Hormonal change on endometrium was seen in 13 cases (6.43%) in our study whereas Khare*et al*[10] showed effects of hormones in 9 cases only whereas Abid et al. [17] showed a higher incidence of 27 %.

Patients with chronic endometritis can present with AUB, pelvic pain and infertility. It needs to be diagnosed because with specific treatment endometrium starts functioning normally. In our study this condition was diagnosed in few patients (6 cases), whereas other studies found a higher incidence.[6,9]

Tuberculous endometritis, which is characterized by granulomatous inflammatory response, is rare in the United States but still, it is a relatively common cause of infertility in developing countries like India.[18] It is highly recommended to examine multiple levels of curettings as the tubercles may be missed and that the biopsy be taken during late secretory phase since the granulomas tend to concentrate in the superficial layers of endometrium.[2] In both our cases classical granulomas were observed and were positive for AFB staining.

Atrophic endometrium was seen between 41 - 60 years age group. The incidence in present study (1.98%) is lower as compared with results shown by Adullah LS *et al*.[19] It is well known that atrophic endometrium leads to bleeding, however the exact cause is unknown. It is postulated to be due to anatomic vascular variations or local abnormal haemostatic mechanisms. Thin walled veins, superficial to the expanding cystic glands make the vessel vulnerable to injury.

The incidence of endometrial polyp was 1.48% in our study, all were hyperplastic polyps characterized by simple hyperplasia without atypia. JetleyS *et al*[11] found endometrial polyp in 2.7% cases and Doraiswami S *et al*[6] in 11.2% cases. Polyps are difficult to be recognized on curettage specimen. They can be identified as polypoidal fragments lined with epithelium on three sides, fibrous stroma and thick walled blood vessels.

Total 4 cases of endometrial carcinoma were found in this study out of which 3 cases were in post menopausal age group. Similar observation is done by Khare*et al*.[10] The risk factors for endometrial carcinoma are generally known, the most common denominator being endogenous or exogenous hyperestrogenism and the most common precursor lesion is the endometrial hyperplasia.[20]

Changes of pregnancy were seen in only one case (0.49%) in 20 -30 years age group. Patient's presenting in this age group with abnormal uterine bleeding should be investigated and evaluated for pregnancy by doing urine gravindex test.[21]

Finally in six cases (2.97%) the endometrial biopsies were scanty and were inadequate for opinion. A study was done in Philadelphia to evaluate the negative predictive value of endometrial samples in 2004, were it was observed that an inadequate endometrial sample may be sufficient to rule out endometrial neoplasia because of its high negative predictive value.[22]

Conclusion

Present study confronted a wide spectrum of histomorphological changes in endometrial biopsies of patients presenting with AUB ranging from normal endometrium to malignancy. Most of these are age related pathologies. Hence, vigilant histopathological screening of endometrial samples obtained from patients with AUB should be done, since it plays a cornerstone role in making the specific diagnosis which can help the clinicians for successful management of AUB which is otherwise practically difficult.

Conflict of Interest: *None declared*
Source of Support: *Nil*
Ethical Permission: *Obtained*

References

1. Deligdisch L: Hormonal Pathology of the Endometrium. Modern Pathology, 2000;13(3):285–294.
2. Rosai J: Female reproductive system-uterus-corpus. In: Rosai and Ackerman's Surgical Pathology. 9th Edn.; Mosby: An Imprint of Elsevier, Missouri, 2005;pp.1579-1615.
3. Munro MG, Critchley HO, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM‐COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J GynaecolObstet 2011;113:3‐13.
4. Brenner PF. Differential diagnosis of AUB. Am J Obstet Gynecol. 1996;175:766–9.
5. Dahlenbach-Hellweg G. Histopathology of endometrium. 4th ed. New York: Springer-Verlag; 1993.
6. Doraiswami S, et al. Study of endometrial pathology in abnormal uterine bleeding. The Journal of Obstretics& Gynecology of India. 2011;61(4):426-430.
7. Yusuf NW, Nadeem R, Yusuf AW, et al. Dysfunctional uterine bleeding. A retrospective clinicopathological study over 2 years. Pak J ObstetGynaecol. 1996;9:27–30.
8. Muzaffar M, Akhtar KAK, Yasmin S, et al. Menstrual irregularities with excessive blood loss: a clinico-pathologic correlation. J Pak Med Assoc. 2005;55:486–9.
9. Rajshri P. Damale et al. Clinicopathological Spectrum of Endometrial Changes in Peri-menopausal and Post-menopausal Abnormal Uterine Bleeding: A 2 Years Study. Journal of Clinical and Diagnostic Research. 2013 Dec, Vol-7(12): 2774-2776
10. Khare A, et al. Morphological spectrum of endometrium in patients presenting with dysfunctional uterine bleeding. Peoples's Journal of scientific research. 2012; 5(2):13-16.
11. Jetley S et al.Morphological spectrum of endometrial pathology in middle‐aged women with atypical uterine bleeding: A study of 219 cases. Journal of Mid-life HealthOct-Dec 2013 **;** Vol 4 **:** Issue 4
12. Spencer CP, Whitehead MI. Endometrial assessment revisited. Br J ObstetGynaecol 1999;106:623‐32.
13. Scommenga A, Dmowski WP. Dysfunctional uterine bleeding. ClinObstetGynecol 1973;16:221.
14. Sloboda L, Molnar E, Popovic Z, Zivkovic S. Analysis of pathohistological results from the uterine mucosa 1965-98 at the gynecology department in Senta. Med Pregl 1999; 52(6-¬8):263-65.
15. Dangal G. A study of endometrium in patients with abnormal uterine bleeding at Chitwan valley. Kathmandu University Medical Journal. 2003; 1(2):110-12.
16. Steven SG. Problems in the differential diagnosis of endometrial hyperplasia and carcinoma. Mod Pathol. 2000;13:309–27.
17. Abid et al. Clinical pattern and spectrum of endometrial pathologies in patients with abnormal uterine bleeding in Pakistan: need to adopt a more conservative approach to treatment. BMC Women's Health 2014, 14:132
18. Margolis K,WranzPA,Kruger TF, et al.Genital tuberculosis at TygerbergHospiatl: prevalence, clinical presentation and diagnosis, S Afr Med J 1992;81:12-15
19. Abdullah LS, Bondagji NS: Histopathological Pattern of Endometrial Sampling Performed for Abnormal Uterine Bleeding. Bahrain Medical Bulletin, 2011;33(4):1-6.
20. Bohiltea RE et al. Clinical and pathological correlations in endometrial pathology. Journal of Medicine and Life Vol.8,Issue4, October-December 2015,pp552-562
21. Kilbourn CL, Richards CS. Abnormal uterine bleeding, diagnostic considerations, management options. Postgrad Med. 2001; 109:137–50
22. Harmanli OH, Shunmugham S, Shen T, Houck KL, Chatwani AJ. The negative predictive value of inadequate" endometrial biopsy in diagnosing endometrial neoplasia. J Gynecol Surg 2004;20:13-6.