

Morphological Spectrum of Endometrial Lesions

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Abstract:

Introduction: Abnormal uterine bleeding is one of the commonest presentations in the gynecological clinic in patients of all ages. Most of the cases are managed medically; endometrial biopsy is an important investigation to diagnose the underlying cause after excluding the organic causes of abnormal uterine bleeding.

Objective: To determine the frequencies of various endometrial pathologies that are the cause of abnormal uterine bleeding.

Methodology: A total of 485 cases of abnormal uterine bleeding were included in this cross-sectional study. Patients with pregnancy related bleeding were excluded. The diagnosis was made on H&E sections and frequencies were calculated by SPSS version 20.

Results: Most of the patients with abnormal uterine bleeding undergoing endometrial biopsy were in the age range of 30-40 followed by 40-50 years age. The pathologies related to progesterone excess including estrogen dominance, anovulatory cycles and disordered proliferative endometrium were the most common (39%) underlying cause of abnormal uterine bleeding. 41% of patients had normal proliferative or secretory endometrium. Inadequate samples were only 1%.

Conclusion: Endometrial biopsy is important diagnostic investigation to determine treatable causes of endometrial pathologies.

Key Words: Endometrial Biopsy, Histopathology, Abnormal Uterine Bleeding, Pipelle Sampling

Introduction

The pathological spectrum of endometrial pathologies is diverse and ranges from subtle abnormalities to life threatening malignancies. The lesions of endometrium also influence the fertility capacity of the female, even if the pathology itself is a minor one. Early diagnosis of endometrial pathologies and their treatment is important for the patient health and also the well being of the social environment of the patient.¹

Endometrial pathologies range from simple endometritis to various malignancies. There is a direct relation of hormonal status with various pathologies. Abnormal uterine bleeding (AUB) categorized as heavy menstrual bleeding, frequent menstrual cycles, irregular bleeding, and post-coital bleeding, is the most common clinical presentation in patients with endometrial pathologies. It accounts for 12% of all gynaecology referrals.²

A variety of methods for endometrial assessment among women with AUB are available. Endometrial sampling is the standard method to diagnose these pathologies.³ It is simple, safe, and effective method.⁴ Indications for endometrial biopsy include abnormal uterine bleeding above 35 years of age, long-term anovulation, endometrial thickness ranging from 5 to 12mm with abnormal uterine bleeding, presence of endometrial thickness more than 12 mm, and also evaluation for endometrial cancer or hyperplasia⁵. This study was conducted to assess the frequency of various endometrial pathologies diagnosed on pipelle biopsy specimens in patients with AUB.

Material & Methods

This cross-sectional study was carried out in Al Nafees Medical College and Hospital. The study duration was one year from January 2016 to January 2017. Convenient sampling was done. All patients presenting with AUB and had undergone endometrial sampling were included in the study. Patients of all ages were included. Patients having pregnancy related bleeding or abortion were excluded. Also the

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samples with artifacts which included poorly processed samples were excluded from the study. All specimens were collected in formalin and routinely processed in automated tissue processor. The paraffin embedded blocks were then used for section cutting and then stained with H&E. The slides were examined under the microscope, the morphological features of each case were recorded and diagnosis was made. Frequencies of different endometrial lesions and the age groups were obtained by using SPSS version 20.

Results

485 cases were collected during the study period from January 2017 to December 2017. All patients presented with abnormal uterine bleeding. Age range of the patients was 25 to 65 years with the mean age of 36±2 years. The most of the specimens 38% (n= 182) were taken from patients in the age group of 31-40 years followed by 34% (n= 167) from 41- 50 years age group. The different diagnosis made and their number with percentages is shown in the Table1. Normal proliferative and secretory phase was seen in majority of the cases. These cases, where no pathology was detected in the endometrium were further investigated and it was found that 24% cases had organic cause of AUB including leiomyoma, adenomyosis or endometrial, cervical polyps detected on hysterectomy later on. In 17% cases there was no pathology detected and remained undiagnosed. Inadequate specimens in which no diagnosis was possible mostly comprised of blood mixed with endocervical tissue, necrotic debris and mucin, or had only a few fragmented endometrial glands. Such cases were very few.

The most common pathology observed was estrogen dominance followed by anovulatory endometrium. The cases with estrogen dominance had spindly stroma and proliferative phase rounded to tubular glands along with thick walled blood vessels. This diagnosis was most common in 31-40 years age group. The anovulatory cases showed thin walled blood vessels in an edematous stroma with areas of hemorrhage and stromal breakdown. The glands were having attenuated secretory activity and were still in proliferative phase. This diagnosis was most common in 21-30 years age group. Disordered proliferative endometrium morphologically showed the presence of dilated branching irregular glands in proliferative phase with compact stroma. This diagnosis was most common in the age group of 41-50 years. Pill effect endometrial changes were seen in 15 cases and luteal

phase defect in 5 cases. These changes are due to imbalanced progesterone. All these diagnosis were related to abnormal hormonal balance in the patient which cause abnormal proliferation of the endometrial glands and stroma in some way.

Table-1: Number and Percentage distribution of patients by diagnosis

Diagnosis	Number of cases	%age of cases
Estrogen dominance	129	27
Anovulatory endometrium	40	8
Disordered proliferative phase	20	4
Pill effect endometrium	15	3
Luteal phase defect	5	1
Atrophic endometrium	10	2
Simple cystic hyperplasia	17	4
Endometrial hyperplasia without atypia	7	1
Atypical endometrial hyperplasia	8	2
Malignant neoplasm	4	1
Endometrial polyp	4	1
Endometritis	20	4
Inadequate	4	1
No pathology detected (normal Secretory or Proliferative phase endometrium)	202	41
Total	485	100%

The cases of chronic endometritis in the study group were characterized morphologically by having plasma cells in the stroma. There were 11 cases in which the endometrial tissue showed caseating granulomas with giant cells signifying the diagnosis of tuberculosis. One case of actinomycosis characterized by radiating colonies of filamentous bacteria was found. Splendorehoeppli phenomenon was also seen in this case. The remaining 8 cases did not have any granulomas or caseation. PAS stain also did not reveal any fungal hyphae. However in our settings chronic endometritis with plasma cells in the endometrial stroma is usually due to tuberculosis.

Atrophic changes were seen commonly in the age group of 40 -60 years of age. There was one case of endometrial atrophy with age of 36 years. Simple cystic hyperplasia was present in 17 cases. Endometrial polyps were found in 4 cases. Morphologically these were characterized by thick walled blood vessels, spindly stroma with fibrous character and dilated glands of various sizes.

Among the biopsies where the diagnosis of endometrial hyperplasia was made half of them were with atypia and rest without atypia. Both these diagnosis were most common in 40-50 years age

group. The malignant diagnoses were made in 4 cases. These included leiomyosarcoma, endometrioid adenocarcinoma, serous carcinoma and metastatic signet ring adenocarcinoma. All these four cases were later confirmed on hysterectomy specimens. All the patient with neoplastic diagnoses were in age group of 50-60 years.

Discussion

Abnormal uterine bleeding is one of the commonest presenting complaint in the gynecological clinic. It accounts for almost 25% of gynecological operations and 12-20% of outpatient visits.^{2,6} It is considered an important medical, social and financial burden to the society.⁷ The International Federation of Gynecology and Obstetrics published guidelines in 2011 to develop universally accepted nomenclature and a classification system for abnormal uterine bleeding.⁸ The American College of Obstetrics and Gynecology has given an update recommendations on evaluation of abnormal uterine bleeding and indications for endometrial biopsies.⁹ Endometrial biopsy is the most cost effective and diagnostically yielding investigation for such patients.⁷

The majority of patients 38% in this study were in the reproductive age group of 31-40 years. This is also supported by a local study where presentation of abnormal uterine bleeding was seen in reproductive age group in 41% and 49 % of cases respectively.^{10,11} In other studies the majority of the patients were in perimenopausal 41-50 years age group.^{12,13} Normal secretory endometrium or proliferative endometrium was seen in 41% cases in our study. Abid et al found 34% cases of normal endometrium¹⁰ and Abdullah et al found 45% cases as normal,¹⁴ however Tariq et al found normal endometrium in 81 % of cases¹⁵ which is considerably higher than the current findings. Out of these cases with normal endometrium 17% cases remained undiagnosed. The increase number of cases with normal secretory or proliferative endometrium is due to the fact that endometrial biopsy is routinely done in all patients with AUB even if they have an organic cause on ultrasound.

Hormonal imbalance is one of the common causes of abnormal uterine bleeding. Most of the cases are due to estrogen excess relative to progesterone. This reflects on different morphological patterns in the biopsy. These include estrogen dominance pattern, anovulatory endometrium, disordered proliferative endometrium and luteal phase defect. These comprised 40% of the study group, which is in

contrast with 28% of hormone related diagnosis made in another study.¹⁶

The most common morphological pathology found in this study was estrogen dominance pattern followed by anovulatory endometrium. Estrogen dominance in perimenopausal women is the major cause of anovulatory cycles and abnormal uterine bleeding.¹⁷ Timely endometrial sampling in these patients and their management of hormonal abnormality can prevent evolution towards neoplastic transformation. The most frequent diagnosis made in various studies was different. A study done in Tehran showed that the disordered proliferative endometrium was the most common cause of abnormal uterine bleeding in women, followed by polyps.¹² Similarly another study also had the same findings.¹⁸ However a local study showed estrogen dominance pattern as the most common finding similar to our study.¹⁹ Asynchronous endometrial glands have aberrant hormone receptors expression and this is related to defective epithelial maturation leading to menorrhagia.²⁰ Abnormalities in hormonal status leads to abnormal uterine bleeding.

Diagnosis of Endometrial polyps on biopsy is a challenging one and this entity is usually over looked. Four cases of endometrial polyps 1% were diagnosed in this study. In another study polyps comprised 2 % of the diagnosis for abnormal uterine bleeding.¹²

Chronic endometritis is not so uncommon in our settings. Next to the pathologies related to hormonal disturbances, chronic endometritis is the common cause of abnormal uterine bleeding. Chronic endometritis was diagnosed in 4% cases, which also included a case of Actinomycoses. In another study the percentage of chronic endometritis was 5%.¹⁴ The percentage of cases with this diagnosis was found higher (12%) by abid et al.¹⁰ and 7% in another study.¹⁴ Endometrial sampling helps to exclude these cases and they effectively respond to antibiotic therapy.

The neoplastic cases comprising of hyperplasia and endometrial malignancies comprised 4% of cases. These were most common in perimenopausal and post menopausal ages. Similar findings were seen in another study.¹⁴ Endometrial malignancies were found in older age group which is similar to the findings in the study by Pessoa et al.²¹

The present study showed that secretory and proliferative endometrium are the most common endometrial histopathological patterns identified in endometrial samples obtained for abnormal uterine bleeding in our region. The hormonal disturbances are amongst the major causes of abnormal uterine

bleeding, The most common one being the estrogen dominance pattern. This finding is most common in perimenopausal age group.

References

1. Rafique N, Al-Sheikh MH. Prevalence of menstrual problems and their association with psychological stress in young female students studying health sciences. *Saudi Med J.* 2018 ;39(1):67-73.
2. Kai J, Middleton L, Daniels J, Pattison H, Tryposkiadis K, Gupta J. Usual medical treatments or levonorgestrel-IUS for women with heavy menstrual bleeding: long-term randomised pragmatic trial in primary care. *Br J Gen Pract.* 2016;66(653):e861-70.
3. Wagaarachchi PT, Sirisena J. Efficiency of Pipelle device in sampling endometrium. *Acta Obstet Gynecol Scand.* 2000;79(9):793-5.
4. Singh P. Abnormal Uterine Bleeding- evaluation by Endometrial Aspiration. *J Midlife Health.* 2018;9(1):32-5.
5. Sanam M, Majid MMK. Comparison the Diagnostic Value of Dilatation and Curettage Versus Endometrial Biopsy by Pipelle--a Clinical Trial. *Asian Pac J Cancer Prev.* 2015;16(12):4971-5.
6. Goldstein SR. Menorrhagia and abnormal bleeding before the menopause. *Best Pract Res Clin Obstet Gynaecol.* 2004 ;18(1):59-69.
7. Cooper NAM, Barton PM, Breijer M, Caffrey O, Opmeer BC, Timmermans A, et al. Cost-effectiveness of diagnostic strategies for the management of abnormal uterine bleeding (heavy menstrual bleeding and post-menopausal bleeding): a decision analysis. *Health Technol Assess.* 2014 ;18(24):1-201, v-vi.
8. Fraser IS, Critchley HOD, Broder M, Munro MG. The FIGO recommendations on terminologies and definitions for normal and abnormal uterine bleeding. *Semin Reprod Med.* 2011;29(5):383-90.
9. Matthews ML. Abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol Clin North Am.* 2015 ;42(1):103-15.
10. Abid M, Hashmi AA, Malik B, Haroon S, Faridi N, Edhi MM, 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 Womens Health.* 2014;14:132-7

11. Vaidya S, Lakhey M, Vaidya S, Sharma PK, Hirachand S, Lama S, et al. Histopathological pattern of abnormal uterine bleeding in endometrial biopsies. *Nepal Med Coll J.* 2013 ;15(1):74-7.
12. Soleymani E, Ziari K, Rahmani O, Dadpay M, Taheri-Dolatabadi M, Alizadeh K, et al. Histopathological findings of endometrial specimens in abnormal uterine bleeding. *Arch Gynecol Obstet.* 2014 ;289(4):845-9.
13. Doraiswami S, Johnson T, Rao S, Rajkumar A, Vijayaraghavan J, Panicker VK. Study of endometrial pathology in abnormal uterine bleeding. *J Obstet Gynaecol India.* 2011 ;61(4):426-30.
14. Abdullah LS, Bondagji NS. Histopathological pattern of endometrial sampling performed for abnormal uterine bleeding. *Bahrain Med Bull.* 2011;33(4):195.
15. Tariq MU, Idrees R, Raheem A, Kayani N. Spectrum of Histopathological Findings in Postmenopausal Bleeding. *J Coll Physicians Surg Pak.* 2015 ;25(11):794-7.
16. Muzaffar M, Akhtar KA, Yasmin S M-U-, Rehman, Iqbal W KM. Menstrual irregularities with excessive blood loss: a clinicopathological. *J Pak Med Assoc.* 2005;55(11):496-89.
17. Sweet MG, Schmidt-Dalton TA, Weiss PM, Madsen KP. Evaluation and management of abnormal uterine bleeding in premenopausal women. *Am Fam Physician.* 2012 ;85(1):35-43.
18. Akram. Histopathological Pattern of Abnormal Uterine Bleeding in Endometrial Biopsies. *J Basic Appl Sci.* 2012;8(1):74-7.
19. Khan P, Baloch FA, Khalid A. Spectrum of Histological Changes in Endometrial Biopsies with Abnormal Uterine Bleeding. 2015;13(3):108-14.
20. Stewart CJR, Bharat C, Leake R. Asynchronous glands in secretory pattern endometrium: clinical associations and immunohistological changes. *Histopathology.* 2015 ;67(1):39-47.
21. Pessoa JN, Freitas ACL, Guimaraes RA, Lima J, Dos Reis HLB, Filho AC. Endometrial Assessment: When is it Necessary? *J Clin Med Res.* 2014;6(1):21-5.

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