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Spectrum of Endometrial Hyperplasia in Abnormal Uterine Bleeding: A Descriptive Study in Tertiary Care Hospital Over 2 Years

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Abstract

Background: Unopposed estrogenic stimulation either due to exogenous or endogenous source is responsible for endometrial hyperplasia and is rare in women under the age of 30 years with an increasing incidence with age. Endometrial hyperplasia is a distinct clinical and pathologic entity and very closely related with abnormal uterine bleeding. Abnormal uterine bleeding is a relatively common gynecological condition that affects women in adolescent and perimenopausal age group due to anovulatory cycles or irregular maturation of follicles. *Objectives:* 1. To study the clinicopathological spectrum of endometrial hyperplasia in abnormal uterine bleeding above 40 years of age group. 2) To analyze the different patterns of endometrial hyperplasia and classify them according to WHO classification. *Methods:* The prospective study included 105 cases who histopathologically diagnosed various patterns of endometrial hyperplasia in patients of abnormal uterine bleeding above 40 years of age over the period of 2 years. The detailed clinical history was obtained. Specimens were routinely processed and H & E stained slides were studied. *Result:* A total of 105 cases of endometrial hyperplasia were studied. The most common age group presenting with endometrial hyperplasia was 40-50 years (74.28%) and most common presenting complaint was menorrhagia (72.38%).The commonest pattern was simple hyperplasia without atypia (77.14%) followed by complex hyperplasia without atypia. *Conclusion:* Endometrial hyperplasia is a common condition and usually associated with abnormal uterine bleeding above the age of 40 years. So it deserves special attention because of its relationship of progression to endometrial carcinoma. Early recognition and histopathological work up can prevent disease progression.

Keywords: Abnormal Uterine Bleeding; Endometrial Hyperplasia; Menorrhagia.

Introduction

Endometrial hyperplasia is a spectrum of morphologic alterations ranging from benign changes caused by an abnormal hormonal environment to premalignant disease [1]. Endometrial hyperplasia is the result of persistent, prolonged estrogenic stimulation of the endometrium due to anovulatory cycles [2]. Women at any age with unopposed estrogen from any source are at increased risk of endometrial hyperplasia but most often in older age group in the climacteric phase as they have commonly anovulatory cycles when ovarian activity declines and pronounced fluctuating estrogen production [3]. Hyperoestrogenic states may be due to exogenous or endogenous estrogen. The common cause of exogenous estrogen is postmenopausal estrogen replacement therapy. Endogenous estrogen is usually due to anovulatory cycles, polycystic ovarian syndrome, estrogen secreting ovarian tumor and obesity [4].

Endometrial hyperplasia is a precursor of endometrial carcinoma, the most common malignancy of female reproductive tract. The increased risk of endometrial hyperplasia and endometrial carcinoma is more evident in perimenopausal and postmenopausal women with abnormal uterine bleeding so careful screening for malignancy is imperative and should be treated promptly [5].

The classification of endometrial hyperplasia is

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currently debated but the WHO classification has been widely accepted and classified as simple hyperplasia without atypia, complex hyperplasia without atypia, simple atypical hyperplasia and complex atypical hyperplasia [1]. Simple hyperplasia is usually regressing if the source of estrogen is removed. Atypical hyperplasia often progresses to adenocarcinoma unless diagnosed or treated.

Herein, we study the different patterns of endometrial hyperplasia in detail with the help of clinical data.

Materials and Methods

The present descriptive study was conducted in the department of pathology ACPM medical college Dhule, India over a period of 2 years from June 2013 to June 2015. During this period, a total of 105 cases diagnosed as endometrial hyperplasia in patients presenting with abnormal uterine bleeding above 40 years of age were studied. The age of patients with abnormal uterine bleeding ranged from 40-54 years. Patients presented with complaints of menorrhagia, polymenorrhagia, polymenorrhea were included.

Eligibility Criteria Adopted in our Study

Inclusion Criteria

Endometrial curettage, biopsy and hysterectomy specimen were included in the study.

Exclusion Criteria

Inadequate endometrial samples, age below the 40 years and postmenopausal bleeding.

Relevant clinical data as age, menstrual history were noted. Specimens were fixed in 10% formalin and studied grossly and multiple sections from each were taken. All the endometrial specimens were processed in automated tissue processor and 4-5 micron thick paraffin embedded sections were taken and stained by Haematoxylin and Eosin. Each slide was carefully examined by two pathologists. All the histo-pathological endometrial patterns were recorded and classified according to the WHO classification.

Result

The present study included 105 cases of endometrial hyperplasia diagnosed by morphological examination on endometrial specimens. Age group of patients ranged from 40-54 years and again categorized into 40-50 years (74.28%) age group and 51-54 year (25.71%) age groups (Table 1).

Majority of cases of endometrial hyperplasia were observed in the age group of 40-50 years. The most common clinical symptoms were menorrhagia in 71cases (72.38%) followed by polymenorrhoeain 24 cases (16.19%) and only 12 cases (11.42%) presented as polymenorrhagia. The histopathological examination showed simple hyperplasia without atypia (Figure 1) as the predominant finding in 81 cases (77.14%). We observed 16 cases (15.23%) of complex hyperplasia without atypia (Figure 2) and only 8 cases (7.61%) of complex atypical hyperplasia (Figure 3) (Table 2). We did not find any case of endometrioid carcinoma in associated with complex atypical hyperplasia.

Table 1: Age wise distribution of patients

Age group of patients in years	No of cases (%)
40-50	78 (74.28%)
51-54	27 (25.71%)
Total	105

Table 2: Different pattern of endometrial hyperplasia in 40-50yrs and 51-54 yrs age groups

Histopathological findings	40-50 yrs	51-54 yrs
simple hyperplasia without atypia (81cases)	64	17
complex hyperplasia without atypia (16 cases)	9	7
complex atypical hyperplasia (8 cases)	3	5
Total cases (105)	76	29

Table 3: Comparison of results of various studies

Types of hyperplasia	Present study (2015)	Takreem A (2009)	Baral R (2011)
simple hyperplasia without atypia	81 (77.14%)	10 (66.6%)	27(72.97%)
complex hyperplasia without atypia	16 (15.23%)	3 (20.0%)	3(8.10%)
complex atypical hyperplasia	8 (7.61%)	2 (13.3%)	7(18.91%)
Total cases	105	15	37

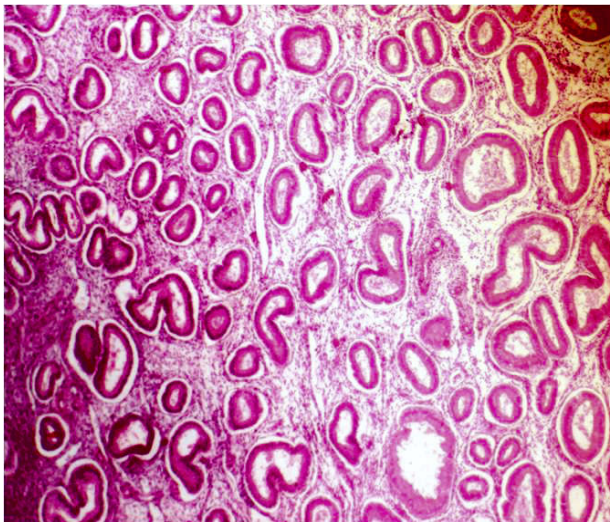

Fig.1: Microphotograph of simple hyperplasia without atypia showing few cystically dilated glands.[H & E,x 100]

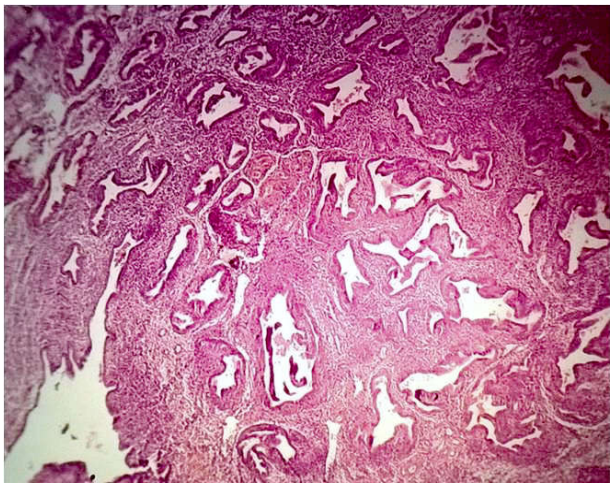

Fig. 2: Microphotograph of complex hyperplasia without atypia showing irregular glands with absence of cytological atypia.[H & E,x100]

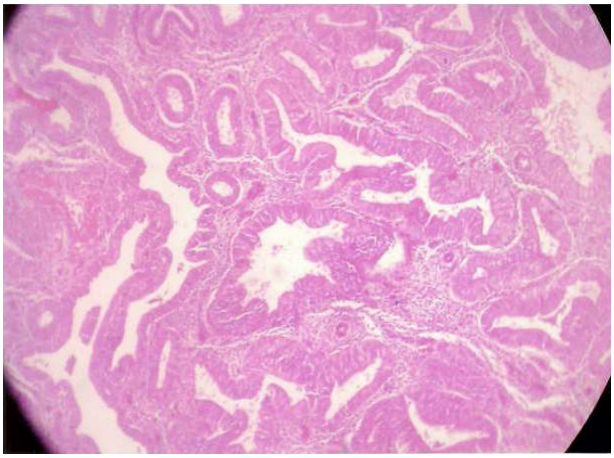

Fig. 3: Microphotograph of complex atypical hyperplasia showing intense crowing of glands with loss of polarity and cytological atypia.[H & E,x100]

Discussion

Abnormal uterine bleeding is the most common presenting symptom of endometrial hyperplasia. Unopposed estrogen from exogenous use or anovulatory cycles results in a hyperplastic endometrium with subsequent breakthrough bleeding. Endometrial hyperplasia occurs in abnormal uterine bleeding due to uninhibited, prolonged and excessive oestrogen secretion in the absence of growth limiting progesterone with endometrium attaining an abnormal height and vascularity. The endometrium outgrows its blood supply and hormonal support and collapses, resulting in prolonged, excessive and irregular bleeding [6].

In 1850, Recamier first introduced the terminology of endometrial hyperplasia and then it was classified in many ways [7]. In Nineteenth century 'Cullen' suggested an association between endometrial hyperplasia and endometrial carcinoma and his view was subsequently supported by Taylor, Novak and Yui [8]. For many years, endometrial hyperplasia has been a diagnostic problem for pathologists because the condition comprises a spectrum of histological changes from simple exaggeration of the normal proliferated state at one extreme to changes that are difficult to distinguish from carcinoma at the other end of the spectrum [9].

WHO classification is the most widely accepted classification of endometrial hyperplasia. According to WHO the endometrial hyperplasia are classified by their degree of architectural complexity as simple or complex (adenomatous) and by their cytological (nuclear) features as typical or atypical hyperplasia [1].

Who Classification of Endometrial Hyperplasia [1]

Hyperplasia (Typical)

1. Simple hyperplasia without atypia
2. Complex hyperplasia without atypia (adenomatous without atypia)

Hyperplasia (Atypical)

1. Simple atypical hyperplasia
2. Complex atypical hyperplasia (adenomatous with atypia)

Simple hyperplasia is also known as cystoglandular or mild hyperplasia. It is a diffuse abnormality of the endometrium characterized by variability in gland size with a normal gland/ stroma ratio. The glands are tubular although frequently cystic

or angular and show minor epithelial budding. The lining is pseudostratified with cells displacing regular, elongated nuclei lacking atypia similar to those of proliferative endometrium. These lesions uncommonly (only 1%) progress to adenocarcinoma and largely reflect a response to persistent estrogen stimulation. Complex hyperplasia is a proliferation of endometrial glands which displays extensive complicated architectural changes represented by irregular epithelial budding into both lumina and stroma and a typical cytology with pseudostratified but uniform, elongated and polarized glandular nuclei, no atypia, and produces the 'finger-in-glove' pattern. There is a paucity of intervening stroma producing back-to-back arrangement of groups of glands [1].

Atypical hyperplasia is characterized by the atypical cytology of the glandular lining as represented by loss of axial polarity, unusual nuclear shapes that are often rounded, irregularity in the nuclear membranes, prominent nucleoli and cleared or dense chromatin. The inter- glandular stroma is diminished but remains present. The assessment of cytological atypia is the key problem in assigning individual cases to one of the four different WHO categories [1].

In current study, 105 cases of abnormal uterine bleeding above the age of 40 years were evaluated to find out the age related incidence of endometrial hyperplasia in tertiary care hospital. The age incidence of endometrium hyperplasia was more in 40-50 years (74.28%) of age group in our study because of irregular and anovulatory cycles. This was very much in alliance with Takreem A et al [10] (86.66%) and very much higher than that reported by Muzaffar M et al [11]. Menstrual cycles often become irregular due to the decreased number of ovarian follicles and their increased resistance to gonadotrophic stimulation, resulting in a low level of estrogen, which cannot keep the normal endometrium growing [12]. In present study we found each type of hyperplasia was more common in 40-50 years of age group. This was in concordance with Schroder et al [13].

Rao Shalini studied to determine the nature and outcome of proliferative lesions of the endometrium during 16 years period. They studied 1778 cases and found 74 patients of endometrial hyperplasia and 5 cases of benign endometrial polyp. The predominant age for all types of hyperplasia was 41-50 years. Out of 74 cases, 59 cases of simple hyperplasia, 10 cases of complex hyperplasia without atypia and 5 cases with atypia were observed. They also showed progression, regression, and persistence of lesion [14]. Similarly in our study, the commonest age group is 40-50 years and also found that simple hyperplasia is the commonest endometrial pattern. Similar findings were also noted by Kurman et al [15].

Gargi R et al studied the clinical and the histomorphologic features of different types of endometrial hyperplasia over a period of 1.5 years. They revealed 46.5% of endometrial hyperplasia in 41-50 years of age group. Menorrhagia was the commonest clinical presentation and 95.6% of cases were in simple hyperplasia without atypia. They also studied gland-stroma ratio, gland architecture and the presence and extent of atypia[16]. Similarly in our study, menorrhagia was the commonest clinical complaint and simple hyperplasia without atypia was the commonest endometrial hyperplasia.

The menstrual disorder increases with advancing age. Endometrial hyperplasia with abnormal uterine bleeding presented as menorrhagia, intermenstrual bleeding, polymenorrhoea and polymenorrhagia. In our study the most common symptom was menorrhagia (72.38%). These observations were also noted by Takreem A et al (53.33%) and Muzaffar M et al (56.8%) [10, 11]. Takreem A observed 40.19% of polymenorrhoea but in our study we found only 16.19% of polymenorrhoea [10].

In present study, total of 105 cases of endometrial hyperplasia were evaluated; of these, a vast majority comprised of simple hyperplasia without atypia 81 cases (77.14%). We observed 16 cases of complex hyperplasia without atypia and only 8 cases of complex atypical hyperplasia. Muzaffar M et al observed 41 cases of endometrial hyperplasia and Bhatta S observed 10 cases of endometrial hyperplasiaout of 48 cases of abnormal uterine bleeding [11,17].

The study conducted in Pakistan by Takreem A found 15 patients of endometrial hyperplasia in100 cases presenting with polymenorrhagia/ menorrhagia in perimenopausal women. They noted 66.6% of simple hyperplasia, 20.0% complex hyperplasia and 13.3% of complex atypical hyperplasia [10]. Baral R et al conducted 3 years study in Nepal and showed 37 cases of endometrial hyperplasia in 40-55 years of age group. Incidence of simple hyperplasia was 72.97%, complex hyperplasia 8.10% and 18.91% of atypical hyperplasia [18] (Table 3).

When endometrial hyperplasia is diagnosed then those women should be investigated for endometrial and ovarian carcinoma to look for any endogenous source of estrogen.

In our study the commonest hyperplasia was simple hyperplasia (77.14%) and this is because of anovulatory cycles. Failure of ovulation with persistence of unripe follicles exposes the endometrium to an abnormally excessive and

prolonged estrogenic action. Bleeding is prolonged and excessive because of massive tissue available for bleeding and random breakdown of tissue resulting in exposure of vascular channels.In patients of simple hyperplasia bleeding is heavy but cycle is regular, while bleeding pattern is irregular in complex and atypical hyperplasia. In the present study majority of patients presented with simple hyperplasia with complaints of menorrhagia. Endometrial hyperplasia of any type must be considered as an alarming sign that an endometrium is non-cycling and therefore susceptibleto neoplastic events. So careful screening for malignancy is imperative and should be treated promptly.

Several studies have reported a close relationship of endometrial hyperplasia and endometrial carcinoma. The more severe the hyperplasia the more likely it is to be followed by invasive carcinoma. McBride studied cystic hyperplasia for a period ranging up to 24 years and found that less than 0.4% developed carcinoma [19]. Chamlian and Taylor, in a long term study, found that 14% adenomatous and atypical hyperplasia subsequently developed into carcinoma [20]. Endometrial hyperplasia without atypia may be treated medically or surgically with simple hysterectomy, while the atypical endometrial hyperplasia requires extensive treatment.

Conclusion

We conclude that in our study simple hyperplasia without atypia was the commonest type while complex atypical hyperplasia appeared to be very low. All women with abnormal uterine bleeding above the age of 40 years require endometrial sampling with careful screening for endometrial hyperplasia and carcinoma. Histopathological examination along with clinical history can help for definitive diagnosis. If detected early and treated in time, incidence can be reduced and it will help in further management and life expectancy also.

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