Types and Frequencies of Pathologies in Endometrial Curettings of Abnormal Uterine Bleeding

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Introduction: Abnormal uterine bleeding is one of the most frequently encountered and perplexing condition in adult women. Its causes include a wide spectrum of diseases. An important diagnostic method is endometrial curettage. It provides information regarding specific and nonspecific infections and malignancy. Histological evaluation can also highlight the incidental findings of organic causes as polyps or malignancy in cases in which no organic cause of bleeding was initially suspected.

Objective: The objectives of the study were to determine the types and frequencies of pathologies in endometrial curettings of abnormal uterine bleeding & compare different endometrial pathologies in patient groups made according to age, presenting complaints and parity.

Study Design: It was a comparative study.

Setting: Histopathology department, Pakistan institute of Medical Sciences (PIMS), Islamabad.

Material and Methods: H&E slides of endometrial curettings of 25 patients were evaluated. Diagnosis was made by correlating the morphological findings with the clinical history over a period of one year i.e 14th Oct. 2004 to 14th Oct. 2005

Results: The most common complaint was polymennorrhagia 36% (18/50) followed by mmenorrhagia 30% (15/50). There were two cases of oligomenorrhoea (2%) and five cases of post menopausal bleeding (10%). Frequencies of endometrial pathologies was Estrogen dominanace pattern 42% (21), Anovulatory endometrium and chronic endometritis 24% (12) each, atrophic endometrium and endometrial carcinoma 2% (1) each and 6% (3) cases of pill effect endometrium.

Conclusion: Our study on endometrial curettings in abnormal uterine bleeding revealed clustering of cases around perimenopausal age. There was relative estrogen excess termed as Estrogen Dominance Pattern (EDP) over Progesterone leading to specific changes such as clusters of thickened blood vessels, spindly stroma, weak or absent secretory changes in the glands and stroma with or without polyp formation. We also noted frequent anovulatory pattern in the old age.

Key words: Frequency, Endometrial curettings, Abnormal uterine bleeding.
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The study spanned from 14th Oct. 2004 to 14th Oct. 2005. It was a comparative study based on convenience (non-probability) sampling. Data were collected according to proforma. Relevant history and biopsy were supplied by the MCH centre PIMS. Ultrasound examination had been done, the endometrial curettages were received in 10% formalin and gross descriptive details like color, weight etc. were noted. Approximately 3 mm. thick sections were taken. Slides were stained by routine hematoxylin and eosin stains. The trainee and the supervisor made the final diagnosis after correlating histopathological findings with the clinical data.

All women undergoing curettage for the reason of abnormal uterine bleeding were included while those with systemic or pelvic causes of bleeding, without adequate history, without adequate samples and unfixed specimen were excluded.

All data were entered into SPSS version 10. Frequencies of various pathologies like hyperplasia, hormonal imbalance, endometritis, malignancy etc. were calculated. Chi square test was used to compare the different pathologies among the said patient groups.

Results

A total of 416 curettage specimens were submitted for histopathological examination during the study period. Out of 416 cases, 50 samples were selected which fulfilled the inclusion criteria for the study. Twenty four patients had undergone hysteroscopic examination in addition to conventional dilatation & curettage. Also ultrasound examination had been done in all cases. Specimen were received as multiple soft tissue fragments ranging in weight from 0.5g to 2g. The frequencies of various types of endometrial pathologies observed are given in the Table I.

Among 50 cases of endometrial curettage only one case had malignancy i.e. endometroid adenocarcinoma (Figure 2) while in the rest there was either hormonal imbalance (55%) or infection (24%). Estrogen dominance pattern of the endometrium was dominant accounting for 42% (21/50) of cases. This was characterized by spindly stroma, discrepancy between glands and stroma, glandular hyperplasia, formation of polyps and clusters of thick walled vessels. (Figure 3). Anovulatory cycle accounted for 24% (12/50) cases. There were inactive or weakly proliferative glands in stroma showing numerous thin walled, telangiectatic vessels having fibrin thrombi and stromal breakdown. (Figure 4). An equivalent number of cases of chronic endometritis were seen (Figure 5) This was followed by pill effect endometrium seen in 6% (Figure 6) cases and a single case of atrophic endometrium (2%). The distribution of cases in different age groups and according to presenting complaints is given in Table II. Correlations of Age to diagnosis and Presenting complaints to diagnosis are given in Tables III and IV.
Discussion

Endometrium is a dynamic, hormonally sensitive and responsive tissue which constantly and rhythmically undergoes changes in the active reproductive life. The pathological changes can be easily evaluated by microscopy. Dysfunctional Uterine Bleeding is very commonly observed in clinical practice. The endometrium is a sensitive bioassay for estrogen and progesterone whose actions are mediated by acting on specific receptors.

In ovulatory cycles it is shed in a cyclic, predictable fashion. The adequate synthesis of progesterone receptors in the endometrial epithelial cells by the estrogen in the follicular phase is essential for the formation of secretory endometrium, so that progesterone alone without the estrogen priming effect will not cause endometrial bleeding when its levels decline.
Without ovulation and subsequent progesterone production, a state of "unopposed" continuous estrogen secretion occurs. This stimulates excessive dilation of the spiral arterial supply and abnormal endometrial growth without adequate stromal support. The endometrium outgrows its blood supply. The consequence is spontaneous breakage and sloughing of the endometrium with unpredictable bleeding. Close to menopause there is aberrant follicular recruitment, decreased level of estradiol and shortened proliferative phase.

Fluctuating estrogen levels results in irregular bleeding and eventually ovulation completely stops. Therefore in anovulatory cycles, the estrogen levels can either be high as in hyperplasia or low as in atrophic endometrium.9

**Table II: Distribution of cases in different Age groups**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Diagnosis</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30 years</td>
<td>Estrogen dominance</td>
<td>2</td>
<td>28.8</td>
</tr>
<tr>
<td></td>
<td>Anovulatory</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Chronic Endometritis</td>
<td>3</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>Pill effect</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>7</td>
<td>100</td>
</tr>
</tbody>
</table>

**Table III: Age versus Diagnosis**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>&lt;40 years</th>
<th>&gt;40 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen dominance</td>
<td>7</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>Anovulatory</td>
<td>2</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Chronic Endometritis</td>
<td>5</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Endometrial Carcinoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

**Table IV: Presenting complaint versus diagnosis**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cyclic</th>
<th>Acyclic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen dominance</td>
<td>15</td>
<td>6</td>
<td>21</td>
</tr>
</tbody>
</table>
Anovulatory  8  4  12  
Chronic Endometritis  9  3  12  
Endometrial Carcinoma  1  1  
Others  3  1  4  
Total  35  15  50  

Although the withdrawal or decline of both estrogen and progesterone results in sloughing of the endometrium but the mechanisms are different. The progesterone withdrawal causes spasmodic constriction of the spiral arterioles, which become prominent under its effect, followed by ischemia and desquamation of the endometrium. The marked increase in the PGF2α by progesterone in the luteal phase seems to be responsible for it. PGF2α is a potent vasoconstrictor while PGE2 is a vasodilator. The critical ratio of PGF2α and PGE2 is responsible for vasoconstriction of spiral arterioles of the endometrium. In anovulatory uterine bleeding only estrogen is present, progesterone being absent. The pattern of bleeding in anovulatory cycle thus depends entirely on the duration and level of estrogen stimulation on the endometrium. In the absence of progesterone, the markedly decreased ratio of PGF2α to PGE2 may account for the nature of uncontrolled bleeding seen in these conditions. Sometimes, in evident ovulation, abnormal uterine bleeding occurs, because of disturbance in the delicate estrogen progesterone balance responsible for maintaining endometrial integrity. The blood vessels start to develop in late proliferative phase and continue to do so in luteal phase and become especially prominent on day twenty three of the menstrual cycle when they are surrounded by predecidua. At time of menstruation these vessels contract and then relax resulting in seepage of blood. The vessels of functional layer lack elastin and cannot stay contracted for long. They are shed with the functionalis and fail, therefore, to contribute to uterine hemostasis. The hemostasis is brought about by constriction of basal arteries in denuded basal layer and radial and arcuate arteries in the myometrium. But when there is hormonal imbalance i.e. estrogen is relatively higher than progesterone the vessels do become thick and form clusters, but the surrounding stroma remains spindly and no decidual changes are present. Such endometria may remain flat or form pseudopolyps. These vessels are not totally sloughed at the time of menstruation as in normal cycle. The remaining sprouts continue to persist in the next cycle and as they are not easily blocked so increased bleeding occurs. We termed such hormonal imbalance as Estrogen Dominance Pattern of endometrium (EDP). When long standing it can lead to various types of hyperplasias. If hormonal imbalance is such that progesterone is completely absent then the vessels fail to develop and under the constant estrogen influence they remain thin and telangiectatic. Such vessels are easily thrombosed and there is continuous seepage of blood into the stroma. This condition is commonly known as hemorrhagic or anovulatory endometrium.

In 50 cases we studied five patterns of endometrial abnormalities were observed among the benign cases. The most frequent observation in almost all age groups was related to high estrogenic state termed as Estrogen Dominance Pattern of endometrium. In our cases of hyperplasia only simple typical hyperplasia was noted. This is similar to a study from Italy by Garuti et al which showed 51% cases of simple hyperplasia, 15% cases of complex hyperplasia and 7.7% cases of atypical hyperplasia, thus making simple hyperplasia the most common type.

Anovulatory cycles was the second most frequent diagnosis in our study. 8/12 (66.6%) cases of anovulatory endometrium were in age group 41-50 years. This is in accordance with the observation made by Kailas who explains perimenopause as the transition from normal ovulation to anovulation which then eventually leads to permanent loss of ovarian function. Farquhar et al in their study of 1033 cases had 46 cases of hyperplasia and 5 of carcinoma. The risk factors for endometrial hyperplasia in premenopausal women with abnormal menstrual bleeding were body weight >/=90 kg, age >/=45 years, infertility, family history of colonic carcinoma, and nulliparity. According to Phutkarzade and Chomakhashvili endometrial hyperplasia is associated with shortened and prolonged persistence of ovarian follicles and it is not a separate nosological phenomenon and effectiveness of its treatment strongly depends on the condition of ovary and hormone systems. Bender has recommended
the use of hysteroscopy along with dilatation and curettage in evaluation of perimenopausal bleeding.\textsuperscript{17} In a study from Karachi on 328 patients with postmenopausal bleeding showed hyperplasia and atrophic endometrium as common causes of bleeding. Endometrial carcinoma was present in 10.6\% of their cases.\textsuperscript{18} In our study the patient (20\% of patients with postmenopausal bleeding) with endometrial adenocarcinoma was 65 years old and had been menopausal for last 13 years and had presented with repeated episodes of bleeding over the past two weeks. Iatrikis et al have also shown that repeated episodes of postmenopausal bleeding are most probably associated with carcinoma.\textsuperscript{19}

In our study there were 24\% (12/50) cases of chronic endometritis. Two of which were diagnosed as chronic granulomatous inflammation. The diagnosis of chronic endometritis is made on the basis of presence of plasma cells. The morphologic features found to be of value in diagnosing this condition are superficial stromal edema, spindly stroma, difficult to date endometrium and stromal inflammatory infiltrate dominated by lymphocytes in the absence of plasma cells. Crum has used immunoperoxidase\textsuperscript{21}, Bayer used Syndecan –1\textsuperscript{22}, Yorukoglu has used methyl green pyronin for this purpose and claims that it helps in distinguishing the stromal cells from plasma cells.\textsuperscript{23} A study from India showed 2.6\% cases of infertility were due to tuberculous endometritis.\textsuperscript{24} A study from Rawalpindi showed 10\% out of 50 infertile patients as having tuberculous endometritis.\textsuperscript{25}

\section*{Conclusion}
Our study on endometrial curettage histopathology in abnormal uterine bleeding revealed that most cases are clustered around the perimenopausal age. Our study showed that there was relative estrogen excess termed as Estrogen Dominance Pattern (EDP) over progesterone leading to specific changes such as clusters of thickened blood vessels, spindly stroma, weak or absent secretory changes in the glands and stroma with or without polyp formation. We also noted frequent anovulatory pattern in the older age.

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