Clinicopathological Correlation of Ovaries and Endometrium in Dysfunctional Uterine Bleeding

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Summary: A prospective and retrospective study of DUB was made to correlate the menstrual abnormality with endometrial histopathology in 520 cases, which was found to be statistically highly significant ($p<0.001$). In 164 cases menstrual patterns were correlated in ovarian and endometrial histopathology. Stromal cell hyperplasia was found in 23% cases. Relationship of stromal cell hyperplasia with menstrual abnormality did not show statistical significance ($p>0.05$).

Introduction

The greatly accepted definition of 'dysfunctional uterine bleeding", (DUB) applies to abnormal bleeding from the uterine endometrium unrelated to gross uterine lesions. But it is restricted to those in which, basis is a disturbance in the rhythmical production of hormones by the ovary (Jeffcoate, 1981).

The defined cause of this problem is functional disturbance affecting hypothalamus-pitutary-ovarian pathway controlling endometrial bleeding. As ovary is most accessible organ in this pathway, this study was carried out to correlate the ovarian and endometrial histopathology in DUB.

Material & Methods

The study was carried out in the Deaprtment of Obstetrics & Gynaecology at MGIMS, Sevagram, in cases of DUB. The analysis included the cases (prospective as well as retrospective) admitted for menstrual abnormalities without any uterine lesions. There were 7206 gynaecological admissions during the study period from 1981 to 1991 amongst whom 520 cases were of DUB representing an incidence of 7.22%. Of these 520 cases, 164 underwent hysterectomy with bilateral salpingoopherectomy and the reports of ovarian and endometrial histopahology were obtained for study. An attempt was made to correlate the menstrual abnormality with ovarian and endometrial histopathology in these cases.

Observation and Discussion

The incidence of DUB in the present study was 7.22%. The incidence reported by various authors ranged from 15 to 20 percent (Devi & Sutaria, 1964; Dawn, 1995; Sanfilippo & Pabon, 1996).

All the cases were above 38 years of age, and 28 cases presented with postmenopausal bleeding (PMB). Purandare & Lalitha (1993) had reported that all their patients to be above the age of 35 and more than 65% fell in the group of 40-50 years.

Table I shows the different abnormal menstrual patterns in 520 cases of DUB. The analysis had shown that maximum number of 208 (40.0%) cases presented with menorrhagia followed by 110 (21.15%) cases with continuous bleeding. Gleeson (1994) reported higher endometrial tissue plasminogen activator activity during menses in women with menorrhagia. Smith et al (1981) have implicated inverse correlation between the endometrial PGF2 a / PGE_2 and the amount of menstrual loss.

There were 28 (5.38%) cases who had PMB. The endometrial histopathology of these cases showed hyperplasia in 2.11%. Previously it was believed that hyperplasia could rarely persist for more than a year or two after menopause but the concept of postmenopausal function by adrenal, ovary and other sites could be of oestrogen leading to hyperplasia. Mitra (1964) reported that the ovaries are stimulated by pituary gonadotrophins even after menopause leading to ovarian stromal cell hyperplasia.

Procope (1969) had reported surgically removed ovaries showing stromal hyperplasia causing significant reduction in urinary excretion of oestrogen showing the possibility of association of stromal hyperplasia with various endometrial hyperplasia in postmenopausal women. Analysis of specific menstrual abnormalities showed 40%

Table I

Different abnormal menstrual patterns

Abnormal menstrual pattern	Number of cases	Percentage
Menoorhagia	208	40.0
Polymenorrhoea	9	1.73
Polymenorrhagia	79	15.19
Metrorrhagia	25	4.81
Continuous bleeding	110	21.15
Postmenopausal bleeding	28	5.38
Amenorrhoea followed by bleeding	61	11.74
Total	520	100.00

Table-II

Correlation between different menstrual patterns and endometrial histopathology

n=520

	Endometrial Pathology and No. of cases							
Menstrual pattern	PP	SP	HI	E	HO	AH	IS	NE
Menorrhagia	69 (13.27)	57 (10.96)	44 (8.46)	4 (0.77)	25 (4.8)	4 (0.77)	1 (0.19)	5 (0.96)
Polymenorrhoea	3 (0.57)	3 (0.57)	2 (0.38)	- -	1 (0.19)	- -	- -	- -
Polymenorrhagia	24 (4.62)	18 (3.46)	22 (4.23)	2 (0.38)	10 (1.92)	1 (0.19)	- -	2 (0.38)
Metrorrhagia	8 (1.54)	5 (0.96)	4 (0.77)	- -	- -	6 (1.15)	2 (0.38)	- -
Continuous bleeding	37 (7.11)	13 (2.5)	16 (3.07)	7 (1.34)	26 (5)	3 (0.57)	4 (0.77)	3 (0.57)
Postmenopausal bleeding	5 (0.96)	2 (0.38)	3 (0.57)	1 (0.19)	11 (2.11)	- -	- -	6 (1.15)
Amenorrhoea followed by bleeding	18 (3.46)	- -	13 (2.5)	2 (0.38)	25 (4.8)	2 (0.38)	- -	1 (0.19)
Total 520 100%	164 (31.54)	98 (18.85)	104 (20)	16 (3.07)	98 (18.85)	16 (3.07)	7 (1.35)	17 (3.27)

(P-<0.001)

Number in parenthesis indicates the percentage

PP - Proliferative phase
SP - Secretory phase
HI - Hormonal imbalance
E - Endometritis
HO - Hyperoestrogenism (hyperplasia)
AH - Atypical hyperplasia
IS - Irregular shedding
NE - No endometrium

Table III

Ovarian histopathology and type of menstrual pattern

n = 164

Type of bleeding	Ovarian histopathology								
	GCH	TCH	SCH	SC	UnR	LC	Hy	PSC	Total
Menorrhagia	6	2	12	13	26	2	1	-	62
	(3.65)	(1.22)	(7.32)	(7.93)	(15.85)	(1.22)	(0.6)	-	(37.8)
Polymenorrhoea	1	-	-	-	-	-	-	-	1
	(0.6)	-	-	-	-	-	-	-	(0.6)
Polymenorrhagia	2	-	3	4	15	-	-	1	25
	(1.22)	-	(1.83)	(2.44)	(9.14)	-	-	(0.6)	(15.24)
Metrorrhagia	-	-	-	3	4	-	-	-	7
	-	-	-	(1.83)	(2.44)	-	-	-	(4.26)
Continuous bleeding	1	1	9	5	15	-	-	-	31
	(0.6)	(0.6)	(5.48)	(3.04)	(9.14)	-	-	-	(18.9)
Postmenopausal	1	-	5	3	7	-	-	-	16
bleeding	(0.6)	-	(3.04)	(1.83)	(4.26)	-	-	-	(9.75)
Amenorrhoea followed	1	-	9	5	6	-	1	-	22
by bleeding	(0.6)	-	(5.48)	(3.04)	(3.65)	-	(0.6)	-	(13.41)
Total	12	3	38	33	73	2	2	1	164
	(7.32)	(1.83)	(23.17)	(20.12)	(44.51)	(1.22)	(1.22)	(0.6)	(100%)

p>0.05

Number in parenthesis indicates the percentage

GCH-granulosa cell hyperplasia
TCH-theca cell hyperplasia
SCH-stromal cell hyperplasia
SC-serous cyst
UnR-unremarkable
LC-luteal cyst
Hy-Hyalinised tissue
PSC-Papillary serous cyst adenoma

of cases had menorrhagia and had 21.15% continuous bleeding. Similar incidence has been reported by Sagar (1980). Anovulatory endometrium in patient with menorrhagia was seen in 13.27% (Table II). This association stresses the fact that probably anovulation leads commonly to menorrhagia. Sanfilippo and Pabon (1996) reported anovulatory DUB in 90% cases. Menorrhagia and continuous bleeding force the distressing women to seek early medical advice. In the present study proliferative endometrium indicating anovulation was observed in maximum number of cases.

It was observed that the frequent anovulation occurs after 40 years of age which may be due to various reasons like:

a) depletion of follicles with declining concentrations of inhibin like material causing a rise in FSH levels,
b) decreased sensitivity of the hypothalamus-pitutary axis to the feedback of oestrogens and
c) relative resistance to gonadotrophin stimulation of the remaining oocytes after depletion of oocytes with normal responsiveness (Menon et al 1980). Cases in our study were mostly above 40 years (68%).

On correlating the menstrual patterns with endometrial patterns it was observed that out of 164 (31.54%) cases proliferative pattern was seen in 69 (13.27%) presenting with menorrhagia, 37 (7.11%) with continuous bleeding, 18 (3.46%) with amenorrhoea followed by bleeding and 5(0.90%) with PMB (Table II). This abnormality in menstrual pattern could be due to persistent oestrogen predominance and resultant endometrial proliferation in the absence of progesterone. Inadequate cycling with progesterone causes structural instability (increased vascularity, hyperglandularity and lack of stromal support)

Table IV

Correlation between ovarian histopathology and endometrial histopathology n = 164

Endometrial histopathology	Ovarian histopathology								
	SCH	GCH	TCH	SC	PSC	HY	LC	UnR	Total
Proliferative	9	2	1	5	-	2	-	37	56
	(5.48)	(1.22)	(0.60)	(3.04)	-	(1.22)	-	(22.56)	(34.14)
Secretory	3	2	-	3	-	-	1	10	19
	(1.83)	(1.22)	-	(1.83)	-	-	(0.60)	(6.09)	(11.58)
Hormonal	9	4	2	12	-	-	1	7	35
imbalance	(5.48)	(2.44)	(1.22)	(7.32)	-	-	(0.60)	(4.26)	(21.34)
Hyperplasia	15	4	-	10	1	-	-	12	42
	(9.14)	(2.44)	-	(6.09)	(0.60)	-	-	(7.32)	(25.60)
Endometritis	1	-	-	1	-	-	-	1	3
	(0.60)	-	-	(0.60)	-	-	-	(0.60)	(1.83)
Irregular	-	-	-	-	-	-	-	-	-
shedding	-	-	-	-	-	-	-	-	-
Atypical	-	-	-	1	-	-	-	5	6
hyperplasia	-	-	-	(0.60)	-	-	-	(3.04)	(3.66)
No endometrium	1	-	-	1	-	-	-	1	3
	(0.60)	-	-	(0.60)	-	-	-	(0.60)	(1.83)
Total	38	12	3	33	1	2	2	73	164
	(23.17)	(7.32)	(1.83)	(20.12)	(0.60)	(1.22)	(1.22)	(44.51)	(100%)

$p<0.001$

Number in parenthesis indicates the percentage

GCH-granulosa cell hyperplasia
SCH-stromal cell hyperplasia
UnR-unremarkable
Hy-Hyalinised tissue
TCH-theca cell hyperplasia
SC-serous cyst
LC-luteal cyst
PSC-Papillary serous cyst adenoma

and irregular shedding from the thickened lining of the endometrium (Sanfilippo and Pabon 1996).

In the present study of 520 cases, 104 (20%) had hormonal imbalance. In these cases of hormonal imbalance fault lies in the corpus luteum as reported by Jeffcoate (1981). However, Brewer & Jones (1948) believed that the endometrium was at fault and stressed that the bleeding usually occurs from localised regions of nonfunctioning endometrium while rest of the endometrium shows secretory changes in normal response to corpus luteum.

On analysis hyperplastic endometrium was found in more than 18.85% of cases (Table II), who presented with menorrhagia and amenorrhoea followed by bleeding. The failure of ovulation is the most common cause of DUB. The physiology of anovuation relates to failure of the feedback mechanism in which rising oestrogen levels result in a decline in FSH with subsequent decline of oestrogen. Thus oestrogen secretion continues resulting in endometrial proliferation with subsequent unstable g... and incomplete shedding (Hillard 1996).

We had 16 cases of atypical hyperplasia. The presence of atypia with abnormal proliferation is associated with increased risk or progression to endometrial carcinoma (Hillard 1996). In one study only 2% of 122 patients with hyperplasia without atypia progressed to carcinoma. Whereas 23% of those with atypical hyperplasia subsequently developed carcinoma (Kurman et al 1985). We believe that atypical endometrial hyperplasia in postmenopausal women should be treated enthusiastically. Follow up is not available in the present series.

On statistical analysis, the correlation between various menstrual patterns and histopathological picture of en-

dometrium was found to be highly significant ($p < 0.001$) Table II

Table III shows correlation of ovarian histopathology with menstrual pattern. We had 164 cases of DUB where bilateral salpingoopherectomy was done. More than 56% had positive ovarian pathology. Stromal cell hyperplasia was present in 38 (23.1%) cases, serous cyst in 20% and granulosa cell hyperplasia in 12 (7.32%).
Stromal hyperplasia refers to abnormal proliferation of ovarian stroma. The transitional cells of cortex produce steroid hormone in stromal hyperplasia. The stroma is an androgenic compartment of ovary. Oestrogen changes when present may result from peripheral conversion of excessive androstenendione to oestrogen. (Young and Scully 1995).

We had association of serous cyst in 20% cases with DUB. It is not unusual to find associated pathology. Mitra (1964) reported incidence of such cysts in 6.4% cases.

Ovaries with follicular cysts and granulose cell predominance characterises the syndrome of metropathia haemorrhagica (Schroders diseases) associated with production of oestrogen. This is the commonest type of cyst of ovary and some are associated with hormonal dysfunction. (Jeffcoate, 1981, Dawn, 1995). Our study shows 7.3% GCH (Table IV).

An attempt was made to correlate ovarian histopathology with menstrual pattern which is depicted in Table III. The statistical analysis did not show any significant correlation between the type of bleeding and ovarian histopathology ($p>0.05$).

Correlation of ovarian and endometrial histopathology was found to be statistically significant with $p < 0.01$ (Table IV).

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