ADENOCARCINOMA OF THE ENDOMETRIUM—A CLINICO PATHOLOGIC STUDY

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Introduction

Increased life expectancy and exposure to estrogenic compounds has steadily increased the population at risk for carcinoma of the endometrium (Hulka *et al*, 1980). However, the incidence of endometrial adenocarcinoma in India and other Afro-Asian countries is low as compared to the western countries (Ogunbode and Aimakhu, 1974; and Randhawa, 1977). Very few studies are available from India on endometrial carcinoma (Randhawa, 1977). We present herewith the clinical features along with cytohistological study with respect to international staging of 25 cases of adenocarcinoma of the endometrium who underwent hysterectomy.

Material and Methods

Twenty-five cases of endometrial adenocarcinoma who underwent hysterectomy between 1969 and July 1980 form the basis of this study. The clinical features, diagnostic procedures, type and staging of the tumour, and treatment given are analysed. Staging used was based on that established by the International federation of Obstetricians and Gynaecologists in 1970 (Kottmeier, 1971).

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Observations

Stage of disease

Nineteen patients had stage I disease and 3 each were in stages II and III (Table I). Stage I patients were further subdivided so that 8 were in stage Ia and 11 in stage Ib.

Age of patients: Maximum number of patients were between the ages of 50-59 years (52%). Only 3 were below 45 years of age (Table I). The mean age of patients was 52.2 years. No difference in age incidence was seen with respect to the clinical stage of the disease.

Menstrual Status: Of the 25 cases, 14 were postmenopausal for more than 2 years and rest were menstruating (Table II). The menstruating and post menopausal patients were equally divided in respect to clinical stage of the disease.

Presenting Symptoms and Their Duration

Fourteen of the cases presented with post menopausal bleeding, while the rest complained of irregular menstrual disturbance. Ten of the patients had symptoms for more than 1 year duration. Only 6 had sought medical advise within 3 months of the onset of symptoms (Table III). No relation was seen between the

TABLE I
Age Incidence and Stage of the Disease

Age in Years	Stage									Total
	IA			IB			II	III	IV	
	G1	G2	G3	G1	G2	G3				
30-39	-	1	-	-	-	-	-	-	-	1
40-49	1	-	-	3	1	-	1	1	-	7
50-59	4	1	-	2	3	1	-	2	-	13
60-69	1	-	-	1	-	-	-	-	-	2
70-79	-	-	-	-	-	-	2	-	-	2
Total	6	2	0	6	4	1	3	3	0	25

TABLE II
Menstrual Status

Stage	Total Patients	Mens-truating	Menopausal 2-5 Yrs	>5 Yr
IA	8	4	1	3
IB	11	5	2	4
II	3	1	—	2
III	3	1	1	1

TABLE IV
Parity

Parity	No. of patients*
0	4
1-2	9
3-4	5
5 or more	6

* In one case parity not known.

stage of disease and the duration of symptoms.

Parity: All the patients were married. Four of them were nulliparous and 9 were para 2 and less. The remaining 11 were multipara, with 6 of them having 5 or more children (Table IV). The low fertility index generally seen in these patients was not observed in the present series.

Associated conditions like diabetes mellitus and hypertension were noted in 1 and 2 patients respectively. Intramural leiomyomas were present in 3 cases.

Pathologic findings

Gross Appearance of Tumor: Diffuse involvement of the endometrium by the tumor was seen grossly in 20 cases (Table V). This was seen either as multiple polypoidal projections or as diffuse ulceration and necrosis of the whole endometrial surface. Of the remaining 5

TABLE III
Duration of Symptoms Versus the Stage of the Disease

Stage	Total Patients	Duration of Symptoms 0-3 months	4-6 months	7-12 months	> 1 year
IA	8	1	2	1	4
IB	11	3	2	2	4
II	3	1	—	—	2
III	3	1	1	1	—

TABLE V
Gross Appearance of Tumor

Stage	Total patients	Diffuse	Focal
IA	8	4	4
IB	11	10	1
II	3	3	—
III	3	3	—

uteri with focal lesions, a polypoidal mass projecting from the fundus or the cornua of the uterus was seen in 4 and 1 had a focal, ulcerated and necrotic endometrium. All these 5 cases belonged to stage I. Gross myometrial infiltration was observed in two cases.

Microscopic: Several sections were examined and graded according to Malkasian *et al* (1977) as G1, G2 and G3. G1 were high differentiated adenomatous carcinomas, G2 differentiated adenomatous carcinomas with partly solid areas and G3 predominantly solid or entirely undifferentiated carcinomas. Of the stage IA, 6 tumors were classified as G1 and 2 as G2 (Table I). In stage Ib, 6 tumors were G1, 4 as G2 and 1 as G3 (Table I). Histologic grading of tumors in clinical stage II was G1-2 and G3-1 and in clinical stage III was G1-1, G2-1, and G3-1. Three of the 25 tumors showed a predominant papillary pattern and in 1 case large areas of metaplastic squamous epithelium was identified and the tumor classified as adenoacanthoma.

Table VI depicts the depth of myometrial invasion seen on microscopic examination by the tumor. The upper 1/3 of myometrium was invaded in 18 cases and middle 1/3 of myometrium in 6 cases. Only in 1 case, no myometrial involvement was detected.

Metastases: The pelvic lymph nodes showed tumor metastasis in 2 cases belonging to clinical stage II. Ovarian metastasis were identified in another 2 cases.

Vaginal cytology

Preoperative cytology smears were available in 12 cases only. In 3 cases, cytology was reported as positive for adenocarcinoma. Two of these patients belonged to stage II and I to stage Ib. Five smears were called suspicious and showed fragments of atypical endometrial cells. All these cases belonged to clinical stage I. One of the smears from a patient showed marked hyperoestrin effect and was considered abnormal. Smears were reported as unsatisfactory in the remaining 3 patients.

Treatment: All the patients were treated by total hysterectomy with bilateral salpingo-oophorectomy. Post operative irradiation was given to patients with advanced disease.

Discussion

Very few clinico-pathologic studies on endometrial carcinoma from India are available (Randhawa, 1977). In present series of 25 cases, maximum number of patients were in the age group 50-59 years

TABLE VI
Depth of myometrial invasion

Stage	Total	None	Upper 1/3	Middle 1/3	Deep 1/3
IA	8	1	7	—	—
IB	11	—	8	3	—
II	3	—	2	1	—
III	3	—	1	2	—

and the mean age was 52.5 years (Table I). This finding is in accordance with Randhawa's (1977) study who found the mean age to be 51.6 years. However, the mean ages reported from western countries are higher than ours —58.7 years by Malkasian *et al* (1977) and 60.4 years by Sall *et al* (1970). In recent years, the incidence of endometrial cancer is steadily increasing in younger women in the western countries (Ramzy, 1979). In our series, only 3 patients were below 45 years of age.

Post-menopausal bleeding is considered to be the major clinical presenting complaint. Carmichael and Bean (1967) had reported this in 89.2 per cent of cases. In our patients, post menopausal bleeding was seen as the presenting complaint in fewer patients (56%). Incidence of post menopausal bleeding reported by Milton and Metters (1972) and Randhawa (1977) was 69.5 and 71.4 per cent respectively.

Infertility or low fertility is not the major finding in the present series of patients. Only 16 per cent were nulliparous and 36 per cent were para 1 or 2. Twenty-four per cent of the patients had 5 or more children (Table IV). These findings are different from those reported by other workers. Sall *et al* (1970) reported 42 per cent of patients to be nulliparous and Malkasian *et al* (1977) found 42.6 per cent to be nulliparous. Only 3.1 per cent of patients had 5 or more pregnancies (Malkasian *et al*, 1977). Randhawa (1977) had found 33.3 per cent of patients to be nulliparous and another 33.3 per cent to be having 1 or 2 children only.

Only 2 patients (8%) in our series had diabetes mellitus. This finding is similar to that of Milton and Metters (1972) who found diabetes mellitus in 4.6 per cent of their cases. Randhawa (1977) had reported a higher incidence of 22.2 per cent of diabetes mellitus in her cases.

A large majority of our patients (76% or 19 cases) were in clinical stage I and 12 per cent each were in clinical stages II and III (Table I). In Milton and Metter's series (1972), 67.7 per cent of patients were in stage I. On the other hand, only 55.5 per cent of Randhawa's (1977) patients belonged to stage I and 28.8 per cent to stage II.

Only 5 (20.0%) of the tumours were focal and rest had involved the endometrium diffusely (Table V). We also found no correlation between the histologic grade of the tumor and the clinical stage of the disease. The incidence of lymph-node involvement is related to the degree of differentiation of the tumor and the depth of myometrial invasion (Lewis *et al*, 1970), and correlates well with other prognostic factors (Creasman *et al*, 1976). In the present series, only 2 patients showed lymph node metastasis and they belonged to the clinical stage II. Because of the small number of cases, it is difficult to correlate lymph nodal metastasis with myometrial invasion and tumor differentiation in the present series.

Variable figures are reported for the pick up rates for endometrial carcinoma on vaginal smears. Milton and Metters (1972) were able to pick up tumor in only 11.9 per cent cases.

Randhawa (1977) could diagnose tumor in only 2 cases out of a total of 15 who had preoperative cytology smears examined. Frick *et al* (1973) studied vaginal smears from 193 proven cases of endometrial carcinoma and reported tumor in 64 cases (33%) only. Their false negative rate was 67 per cent. Cohen and Gusberg (1975) and Popkin (1976) have reported that endometrial carcinoma can be detected on vaginal pool material in 50-75 per cent of cases. Vuopala (1977) reported an accuracy of 56.8 per cent and after rescreening this went upto 77.3 per cent. Accuracy

of cytological detection of endometrial carcinoma can be increased by examination of endometrial aspirate or jet wash specimens. Vuopala (1977) picked up 98 per cent of endometrial carcinomas on cytological examination of jet wash specimens. In our patients, tumor cells were reported in 3 out of 9 satisfactory vaginal smears. In rest of the 6 cases, cytology was reported as suspicious either because of presence of atypical endometrial cells or hyperoestrin effect. Thus, in all the 9 cases where satisfactory smears were available, cytology was either diagnostic or suspicious for malignancy. We recommend that vaginal cytology should be done in all cases suspected to be having endometrial carcinoma.

Summary

Twenty-five cases of endometrial adenocarcinoma who underwent hysterectomy have been studied. Maximum number of patients were in the age group 50-59 years (mean age 52.5 years). Postmenopausal bleeding was seen as the presenting complaint in 56 per cent of cases. Only 52 per cent of the patients were either nulliparous or having one-two children. Twenty four per cent of the patients had more than five children. Seventy six per cent of the patients belonged to stage I. Satisfactory vaginal vaginal cytology smears were available in nine cases. Cytology was reported positive in three and suspicious for malignancy in six cases.

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