ENDOMETRIAL CARCINOMA — A SIX YEAR REVIEW

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SUMMARY

This is a retrospective analysis of the management of 91 patients of endometrial carcinoma in South Cleveland Hospital (SCH), Middlesbrough, United Kingdom. 82% per cent (75 cases) were adenocarcinomas, 10% (9 cases) were papillary adenocarcinoma, 4% (4 cases) were adenoacanthomas. The remaining 3.3% (3 patients) were adenosquamous carcinomas. There was no patient with clear cell carcinoma. In cases of adenocarcinoma, 52.17% were well differentiated, 30.34% were moderately differentiated and 17.39% were poorly differentiated at diagnosis 91.2% presented with postmenopausal bleeding and a definite diagnostic curettage and histology of the endometrium. 81.6% of the patients presented between the age of 51–800 years with uniform distribution through these three decades. 67% of the patients presented with stage I disease. 97% of the patients had total abdominal hysterectomy and bilateral salpingo-oophorectomy. Only one patient had a Wertheim's hysterectomy. 84.61% were given progesterone for a period of 12–18 months. Two cases had chemotherapy, one for recurrence with distant metastases and the other for a associated ovarian carcinoma. Cumulatively, of the 91 patients treated for the six year period, 76 were alive at the time of study. Except stage II disease, the management of endometrial carcinoma in SCH is up to the standard as the new staging would dictate.

INTRODUCTION

Endometrial carcinoma is a neoplastic condition of the endometrium which can be diagnosed in quite early stages and treated well in time to give good long term prognosis. It is mostly a disease of the perimenopausal and postmenopausal women and manifests itself by irregular and/or heavy periods, or postmenopausal bleeding, and endometrial curettage is of great help in the early diagnosis of the disease.

This paper presents study of 91 cases of endometrial carcinoma managed at South Cleveland Hospital (SCH), with a view to auditing their management and making recommendations for improvement in their care.

MATERIAL AND METHODS

The computer data and from the clinical notes of patients diagnosed as suffering from endometrial over a six year period from 1986-1991 were collected for analysis. Out of a total of 141 cases, 91 were available for study. Of the remaining 49, case notes of 32 were sent for microfilming, whilst 17 case notes had been transferred to peripheral hospitals as the patients had moved out of Middlesbrough.

RESULTS

The 75 cases of adenocarcinoma were graded as in the Table given below.

Because of the small number involved, the remaining tumour types were not analysed for grading.

The presentation of the patients were as follows.

There were two patients with suspicious cervical smears. One was just picked on routine smear and the other had postmenopausal bleeding at the time of presentation for the cervical smear. There were two patients with vaginal vault recur-

TABLE – I

Tumour Type	No. of patients	Percentage
Adenocarcinoma	75	82.32
Papillary Adenocarcinoma	09	09.89
Adenoacanthoma	04	04.40
Adenosquamous	03	03.30
Clear Cell Carcinoma	—	—

rence, out of which one presented with bleeding P/V and the other was found on follow up vaginal examination to be having some granular tissue in the vault which was biopsied and sent for histology.

The definitive diagnosis was made either by dilatation and curettage or laparotomy, except in the case of vaginal vault recurrence where the biopsy was taken from the local lesion, and one case of advanced carcinoma in which an endocervical polyp was avulsed and sent for histology.

All these patients presented after 40 years of age. The youngest patient was 43 years old and the oldest was 86 years old. The yearly distribution between 51 and 80 years was nearly the same.

As the histology reports and operation notes were available in the majority of cases, it was possible to stage all but three cases according to the FIGO 1988 classification.

As recommended by FIGO (Shepherd 1989), three patients who did not undergo surgery for various reasons were staged according to the old classification. Two patients were unfit for surgery because of ill health and one was considered to be a bad operative risk because of extreme obesity. 65 out of 91 patients, i.e., 67% of the patients presented in stage I of the disease. No of patient presented in stage IIIB.

TABLE – II

Grade	No. of patients	Percentage
Well differentiated	38	50.67
Moderately differentiated	23	30.67
Poorly differentiated	14	18.67

The stage at diagnosis and the type of treatment given is tabulated as follows.

None of the cases in the stage IIA were given radiotherapy, whereas 18 out of 25 in the earlier stage (IC) and 4 out of 5 in the later stage (IIB) were given it. The fifth patient in stage IIB refused it. The one case in stage IIA that received radiotherapy was two years later when she developed local recurrence.

TABLE – III

Presentation	No. of cases	Percentage
Postmenopausal Bleeding	83	91.20
Perimenopausal Bleeding	07	07.69
Suspicious Cervical Smear Report	01	01.11

On analysing the timing of radiotherapy, it was noted that four patients were given pre-operative radiotherapy in the form of viginal insertion of caesium. All the rest were given post-operative radiotherapy. 19 were given vaginal vault radiation with caesium and 38 were given external beam radiotherapy, the use of which was replacing vaginal caesium in the last there years of study.

Progesterone was given to all the patient except 14. Seven of them had either an associated malignancy like carcinoma cervix, ovarian cancer, mixed Mullerian tumour or stromal sarcoma. In the remaining seven, no factor could be identified.

TABLE – VI

TREATMENT PROVIDED

Stage of Dx	No. of cases	TAH & BSO	Radiotherapy	Hormone	Chemotherapy
IA	04	04	0	04	
IB	36	35	27	30	01
IC	25	25	18	23	
IIA	04	04	01	02	01
IIB	05	04	04	04	
IIIA	04	03	04	04	
IIIB	0	0	0	0	
IIIC	07	07	06	06	
IVA	01	01	02	01	
IVB	02	02	01	02	
UNSTAGED	03	03	02	02	

TAH = Total abdominal hysterectomy

BSO = Bilateral salpingo-oophorectomy

Two patients received chemotherapy. One patient in stage IIA was given carboplatin when she developed distant metastases within a few months after receiving radiotherapy for vaginal recurrence. The other woman received the drug for her associated ovarian cancer.

DISCUSSION

In endometrial carcinoma, the stage and grade of the tumour are of primary importance in working out the type of treatment needed and the prognosis.

The staging of endometrial cancer was changed from clinical to surgical staging in 1988 under the auspices of the International Federation of Gynaecologists and Obstetricians (FIGO) (Shepherd, 1989). FIGO in 1988 also revised the grading of the tumour as follows.

Grade 1 (G1): 5% or less of non-squamous or non-morular solid growth pattern.

Grade 2 (G2): 6–50% of a non-squamous or non-morular solid growth pattern.

Grade 3 (G3): More than 50% of a non-squamous or non-morular solid growth pattern.

According to the new FIGO staging recommendations, all those patients who can withstand surgery have to undergo it for proper staging of the disease and to evaluate

TABLE – V

Age Range	No. of cases	Percentage
41 – 50	08	08.79
51 – 60	25	27.47
61 – 70	25	27.47
71 – 80	27	29.67
80 years	06	06.59

TABLE – IV

Definite Dx	No. of cases	Percentage
D & C	82	90.11
Laparotomy	06	06.59
Local Lesion Biopsy	03	03.30

the type of treatment required. This means that total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO), peritoneal cytology study and pelvic and para-aortic lymph node biopsies have to be performed on every patient as the first line of action. Where the cervix is involved, a Wertheim's hysterectomy is preferred.

David (1991) and Chen (1989) suggest that for patients with stage I endometrial cancer with no extra corporal spread, a TAH and BSO gives as good results as the same procedure with radiotherapy. However, according to the Gynaecologic Oncology Group (GOG) study, there is a 7.7% recurrence rate for stage Ib and Ic.

STAGING SYSTEM FOR ENDOMETRIAL CARCINOMA

Stage		Criteria
Ia	G123	Tumour limited to the endometrium
Ib	G123	Invasion to less than one-half of the myometrium
Ic	G123	Invasion to more than one-half of the myometrium
IIa	G123	Endocervical glandular involvement only
IIb	G123	Cervical stromal invasion
IIIa	G123	Tumour invades serosa and/or adnexa and/or positive peritoneal cytology
IIIb	G123	Vaginal metastases
IIIc	G123	Metastases to pelvic and/or para-aortic lymph nodes
IVa	G123	Tumour invasion of bladder and/or bowel mucosa
IVb	G123	Distant metastases including intra-abdominal and/or inguinal lymph nodes

Although pelvic radiation reduced the incidence of pelvic recurrence, its effects on overall survival for the stage are not significant (Edward, 1991). David (1991) conducted a study in the light of the new surgical grading and found no statistical difference in the survival rates for patients with different substage of stage I disease after TAH and BSO. He rather suggested that all the substages should be eliminated and only called as stage I disease when it is confined to the uterus only.

In my study, it was noted that collectively all patients with stage I disease had TAH and BSO. No patient was given radiotherapy in stage Ia of the disease, but 27 out of 36 patients were in stage Ib, and 18 out of 25 patients in stage Ic were given radiotherapy. It was also noted that in the year 1991, no patient in stage Ib was given radiotherapy, but in stage Ic radiotherapy was given in higher histological grades. The FIGO 1988 grading is very god if all the criteria could be fulfilled for the stage. But practically speaking, there will be cases which are unfit for surgery and which cannot be surgically staged. Secondly, there would be cases where the patient had TAH and BSO but no nodes were sampled and/or no peritoneal washing taken. In such cases, it is preferable to go by the grade of the tumour and invasion of the myometrium. In such cases, Piver and Hempling (1990) suggest that for grades 1 and 2 disease with less than 50% of myometrial involvement, TAH and BSO should be enough, and additional radiotherapy is of no benefit.

Those cases with either grade disease or grade 1 or 2 disease with deep (more than 50% myometrial invasion, should have post-operative pelvic radiation).

For serous papillary carcinoma of endometrium, Holley et al (1989) have suggested the use of platinum based chemotherapy for stage I of the disease, along with surgery because of the highly aggressive nature of this type of disease.

Those patients with positive peritoneal washings for the disease are given progesterone treatment for a period of one year. All patients in whom no peritoneal washing were obtained for cytology should be given progesterone for a period of one to one and a half years. The drug is quite safe for use in women and its side effects can be controlled by varying the dose of the drug and prolonging its period of treatment. In my study, 57 out of 65 patients in all grades of stage I were given progestogen therapy for 12–18 months.

On the literature review of the subject, it was noted that nothing more decisive has been written about the management of stage II endometrial carcinoma.. Boronow (1990) has mentioned a five years survival rate of 58.5% for patients receiving combined surgery and radiotherapy, 66.1% for patients treated by surgery alone and 77% for patients treated with irradiation only.

As noted from the age distribution table, the mean age for carcinoma endometrium is 65 years when patients are neither very fit for extensive surgery, nor is their tolerance to radiotherapy very good. In this study none of the four cases in stage IIa were given any form of radiotherapy initially. These patients had TAH and BSO lymph node sampling. One of them developed vaginal recurrence after two years and was given radiotherapy. The patients in stage IIa in my study seem to have been under treated.

If this stage is to treated like stage Ia2 of carcinoma of the cervix, then it should be treated by radical surgery alone (if she can withstand it), and it has good prospects of cure. Otherwise, she should have post-operative pelvic radiotherapy.

In stage IIb disease, a Wertheim's hysterectomy may be appropriate provided the patient is fit enough to withstand the extensive surgery, and the surgeon is well versed with the procedure otherwise, the usual TAH and BSO, followed by pelvic radiation, should give good prospects of disease control and even cure.

For all stage III and higher stages, surgery and radiotherapy is considered to be the treatment of choice, These days, pre-operative radiotherapy is falling into disfavour because the diseased uterus is otherwise going to be removed surgically for proper staging of the disease, and besides, pre-operative radiotherapy makes it difficult to grade the tumour histologically, and lastly, vaginal caesium insertion is associated with more vaginal scarring and stenosis, creating more problems in the patient's sexual life and difficulty in follow up for vaginal recurrences.

In the first three years of this study it was noted that vaginal caesium insertion was much favoured, but probably because of more post-radiation vaginal complications, it has been given up in favour of external beam radiation. Both external and internal radiation give significant radiation cystitis and proctitis and have similar cure rates, but the vaginal complications are much less with external bean radiotherapy. Patients with intra-abdominal metastases were given extended field radiation.

According to Partrodge (1991), patients with multiple metastatic sites, or with clear cell or serous papillary adenocarcinomas, should be considered for whole abdominal radiation or other systemic therapy.

Those patients who are considered unfit for surgery are treated with radiotherapy alone.

Cases with central local recurrence of endometrial carcinoma are treated with exenteration, if fit for surgery.

Radiotherapy may be given if not previously treated by this mode of the disease. Hormone therapy and chemotherapy may also be considered in cases of recurrent disease and/or with distant metastases.

In this study, it was noted that 80% of the patients were given progesterone for a period of 12–18 months. This probably controls the peritoneal spread of the malignant disease it is a well known fact that progesterone down regulated the estrogen and progesterone receptors in adenocarcinoma.

The prognosis of the disease also rests on the type of endometrial carcinoma. Adenocarcinoma which comprise approximately 60% of the disease (Christopherson, 1986) has a five year survival rate of 75% for this subtype in this study it comprised 82% of the endometrial carcinoma.

Prognosis-wise subtype adenoacantoma forms 20% of the disease with 87.5 five year survival rates. In this study it was present in 4.4% of the population suggesting some local variation. Adenosquamous carcinoma comprising about 10% of the disease (3.3% in my study) has a survival rate as low as 20% and serous papillary endometrial carcinoma (SPEC) are considered to be more aggressive with a 26–50% five year survival rate (Jeffrey et al, 1986). Cleare cell carcinoma, a very small proportion of the disease (none is my study), has a 33–55% survival rate (Christopherson, 1988).

CONCLUSION

The traditional teaching that PMB should always be considered as endometrial carcinoma until proven otherwise by histology cannot be over emphasised. Those cases diagnosed as endometrial carcinoma should be referred to an experienced gynaecologist for proper surgical staging and management. If the patient needs radiotherapy that may also be arranged as necessary.

This six year review has shown that management of endometrial carcinoma in South Cleveland Hospital over the period has essentially been satisfactory, except for some doubts over stage II disease management, using FIGO 1988 recommendations as a reference point.

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