Protocol for Planning and Treatment

The process to be followed when a course of chemotherapy is required to treat:

CARCINOMA OF THE CORPUS UTERI

Patient information given at each stage following agreed information pathway

1. DIAGNOSIS

All patients who have undergone TAH and BSO which has confirmed a diagnosis of endometrial carcinoma should be registered at the Combined Gynaecological Oncology Clinic, for pathology review and to discuss whether adjuvant treatment is appropriate. Some patients may be referred following a pipelle biopsy or D&C which has revealed a diagnosis of endometrial carcinoma, for advice regarding optimal management.

It is well recognised that women with uterine cancer have a variety of psychosocial and informational needs. Patients will be provided with the opportunity to discuss their concerns and questions confidentially in a private area at all stages of the disease process. Written literature will be available to support verbal information. Referral to a Clinical Nurse Specialist will ensure continued support throughout the cancer journey.

Unlike carcinoma of the cervix, there is no established population screening programme for endometrial cancer. Available screening tools are invasive and of unproven efficacy. Their use is therefore limited to screening “high risk” individuals with a hereditary predisposition.

Presentation

- Post-menopausal bleeding is the commonest presentation, and all women with PMB warrant urgent investigation
- An abnormal smear suggesting a glandular abnormality or endometrial cancer - these patients should be seen at a Colposcopy clinic (some may have cervical cancer) or referred for urgent investigation
- Irregular bleeding on HRT or in the peri-menopausal patient may indicate sinister pathology and should be referred for endometrial sampling
- Postmenopausal discharge - blood-stained or purulent discharge should arouse suspicion of malignancy

Diagnostic curettage

Pipelle biopsy together with vaginal ultrasound has been shown to be as reliable as curettage for diagnosis in symptomatic women. The merits of diagnostic hysteroscopy remain unproven.

2. STAGING AND SPREAD OF DISEASE

Staging (FIGO 2009)

The FIGO staging system is surgical (unlike cervical carcinoma). The 1971 staging system applies to those who have not had surgery.

Stage I
Tumour confined to corpus (75% of all patients)
Ia Invasion of <1/2 of myometrial thickness
Ib Invasion >1/2 of myometrial thickness

Stage II
Tumour involving corpus and cervix

Stage III
Tumour outwith uterus (not bladder or bowel mucosa)/ +ve cytology
IIIa Tumour invades serosa/adnexa and/or positive peritoneal cytology
IIIb Vaginal metastases
IIIc Metastases to pelvic or para-aortic nodes

Stage IV
Tumour invading bladder or bowel mucosa/ distant metastases
IVa Mucosa of bladder and/or bowel invaded
IVb Distant metastases including intra-abdominal and/or inguinal nodes

All stages sub-grouped according to histological differentiation:

G1 Well differentiated adenocarcinoma
G2 Moderately differentiated adenocarcinoma with partly solid areas
G3 Poorly differentiated (predominantly solid) or entirely undifferentiated

Carcinoma

Spread of disease
i) Direct: through myometrium to cervix to one or both ovaries
ii) Lymphatic: to vagina e.g. vault, suburethral to pelvic lymph nodes, to para-aortic lymph nodes, to inguinal lymph nodes, to one or both ovaries
iii) Blood-borne: usually late, to liver, lungs, long bones

3. HISTOPATHOLOGY

Introduction
All tissue specimens removed at laparotomy are submitted for histopathological examination. Specimens are handled according to Standard Operating Procedures (SOPs) of the Department of Pathology, which cover fixation, dissection, block taking and reporting, and conform to national guidelines and minimum data sets (where available).

All cases are reviewed by consultant pathologists with a special interest in gynaecological pathology, and presented at the Combined Gynaecological Oncology Clinic Meeting prior to decision making about post-surgical management.

Ovarian Cancer
Histopathology reports on ovarian cancer cases include the following:

Summary of clinical history
Macroscopic description of all specimens including dimensions of ovarian tumours, status of capsule, cyst contents

Microscopic description (synoptic report available) including:
- Histological tumour type (WHO classification)
- Grade
- Status of capsule
- FIGO stage

Endometrial Cancer
Histopathology reports on endometrial biopsy specimens (Pipelle or curettage) will include:
- Histological tumour type. If the tumour type is one recognised to have an aggressive clinical course (such as papillary serous carcinoma or clear cell carcinoma), a comment to this effect will be made in the report.
- Grade

Histopathology reports on cases of hysterectomy for endometrial carcinoma will include the following:
- Summary of clinical history

Macroscopic description of specimens including:
- Dimensions of tumour
- Apparent extent, including depth of myometrial invasion, cervical involvement, adnexal involvement

Microscopic description (synoptic report available) including:
- Histological tumour type (WHO classification)
- Grade
- Extent of myometrial invasion
- Presence or absence of lymphatic/vascular space invasion
- Presence or absence of cervical mucosal or stromal involvement
- Presence or absence of adnexal involvement including fallopian tubes and ovaries
- FIGO stage

Cervical Cancer
LETZ specimens showing microinvasive carcinoma are reported using a template format, which will include the following:
- Depth of invasion in mm (measured by ocular micrometer)
- Horizontal extent of invasive lesion (measured by ocular micrometer)
- Focality of invasive lesion(s)
- Presence or absence of lymphatic invasion
- Status of excision margins

- Presence of concurrent CIN or CGIN. In early invasive adenocarcinoma, it is recognised that measurement of depth of invasion may be difficult or impossible.

Reports on diagnostic biopsy specimens of frankly invasive carcinoma will include:
- Histological tumour type
- Grade
- Presence or absence of lymphatic invasion.

Histopathology reports on Wertheim's hysterectomy cases include the following:
- Summary of clinical history

Macroscopic description of specimens, including dimensions of tumour, extent of local spread, distance from vaginal resection margin

Microscopic description (synoptic report available) including:
- Histological tumour type (WHO classification)
- Grade
- Presence or absence of lymphatic/vascular space invasion
- Depth of invasion and horizontal extent (measured in mm by ocular micrometer) of microinvasive or early invasive squamous carcinomas
- Status of original and paracervical surgical excision margins
- FIGO stage

Vaginal cancer
The histopathological report will include the following:
- Summary of clinical information provided, including reasons for biopsy
- Specimen type
- Macroscopic description, including accurate measurement of specimen, tumour and distance from resection margins

Microscopic report including:
Histological tumour type
- Accurate measurement (optical micrometer) of depth and lateral extent of early invasive tumours
- Proximity to lateral and deep excision margins
- Presence or absence of lymphatic/vascular space invasion

Vulval cancer
The histopathological report will include the following:
- Summary of clinical information provided, including indications for biopsy
- Specimen type
- Macroscopic description, including accurate measurement of specimen, tumour and distance from resection margins

Microscopic report including:

- Histological tumour type
- Accurate measurement (optical micrometer) of depth and lateral extent of early invasive tumours
- Proximity to lateral and deep resection margins
- Presence or absence of lymphatic/vascular space invasion
- Description of adjacent vulval skin
- Total number of lymph nodes in each submitted group
- Total number of involved lymph nodes in each submitted group

4. INVESTIGATIONS

i) History
ii) Pipelle biopsy and USS
iii) Hysteroscopy (in some cases)
iv) EUA, D&C (in some cases)
v) CXR
vi) FBC, U&E, Creatinine, LFTs
vii) Patients may also require cystoscopy, sigmoidoscopy, IVU, Ba enema, CT/MRI scan

5. TREATMENT

All patients will have an opportunity to discuss their condition and will be given a full explanation of the aims and possible side effects of treatment, before giving their written informed consent to treatment.

Stage I and II
Surgery is the preferred option.

Surgery
Total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal washings for cytology, and pelvic/para-aortic lymph node sampling in selected cases. Lymphadenectomy has not in the past comprised part of the standard surgical approach

There may be circumstances in which a Wertheim's hysterectomy and pelvic lymphadenectomy may be considered.

Vaginal hysterectomy may be considered where major abdominal surgery is contra-indicated.

6. RADIOTHERAPY

Indications for post-operative radiotherapy
Combination of:

- Grade 3 tumours
- Myometrial invasion > 1/2
- Stage II or more disease
- Nodal involvement
- LVI

Radiotherapy technique
a) External beam therapy to whole pelvis:
3 or 4 field 'brick' using 9 or 16 MeV photons (as for carcinoma of cervix)
Dose: 4500cGy in 20 fractions over 4 weeks

b) Vaginal caesium using the 'line source'
Dose: 3000cGy to the vaginal mucosa. Insertion time approximately 8h.

Primary radiotherapy for Stage I or II disease
Patients unfit for surgery may be treated with primary radiotherapy, usually using intracavitary caesium with radical intent, given in two insertions a week apart (see Cervix protocol).

Stages III and IV
Radiotherapy is the preferred treatment. Chemotherapy may also be considered. Treatment is individualised and usually given for best palliation. When extension beyond the uterus is discovered at the time of operation, it may be appropriate to continue with TAH and BSO and to give post-operative radiotherapy as for Stage I and II disease.

Palliative radiotherapy
Intra-cavitary caesium in a single insertion will normally control bleeding. See carcinoma of cervix protocol.

Adjuvant chemotherapy
Taxol/Carboplatin 4 cycles for high grade disease.

Management of malignant mixed mesodermal tumours
As per grade 3 endometroid.

7. FOLLOW UP

Patients should not routinely be given HRT but this may be appropriate in selected cases.

After surgery
Patients may be seen, by the referring gynaecologist, for a post-operative check at six weeks. Oncological review thereafter is 3-monthly for the first year, 6-monthly for the second year and annually thereafter to 5 years, in the Combined Gynaecological Oncology Clinic or locally by the referring Gynaecologist. Discharge after 5 years if well. Vault smears are not indicated in the review assessment of patients who have been treated for endometrial cancer.

After radiotherapy
On completion of radiotherapy, all patients will be given a vaginal dilator to use until the vaginal epithelium is healed (usually 1st month post-treatment) to prevent vaginal stenosis.

Follow-up 1 month post-treatment in the Oncology clinic, then some patients are sent back to the referring gynaecologist to be seen 3 monthly for 2 years, then 6 monthly for up to 5 years. Discharge after 5 years if well, with no treatment-related morbidity, for written follow-up by GP questionnaire.

TREATMENT OF RECURRENT/ METASTATIC DISEASE

Recurrent disease may occur at the vaginal vault, within the pelvis or abdomen, or distally. Treatment will be individualised: surgery, radiotherapy, hormone therapy and/ or chemotherapy may all have a role.

Local recurrence may be amenable to surgical intervention, and exenteration may be appropriate. Patients without prior radiotherapy should be considered for radiotherapy.

Solitary vault recurrence
Following TAH and BSO, this is often suitable for treatment with vaginal caesium using the Edinburgh line source.

Prescribed dose: 5000cGy to vaginal mucosa in a single insertion.

SYSTEMIC THERAPY

Hormonal therapy
The use of hormonal therapy in early stage disease is unproven. A Mirena coil may be useful to control bleeding in patients unfit for surgery.

In advanced disease, response rates to hormonal therapy are approximately 30%.
Dose: medroxyprogesterone acetate 100mg TDS.

Chemotherapy
Adjuvant chemotherapy is recommended for endometrial cancer of serous papillary type: Taxol/Carboplatin. (see carcinoma of ovary protocol, for dosing information).

Chemotherapy for recurrent/metastatic disease:
Taxol/Carboplatin 3 weekly or weekly if retreat/platinum resistant

SCREENING FOR PATIENTS AT HIGH RISK

Female individuals from hereditary non-polyposis colorectal cancer (HNPCC) families may have up to a 30% lifetime risk for the development of endometrial cancer, (with a 10% lifetime risk for ovarian cancer).

The following groups of women may therefore be offered screening:

- Women in a family where hMLH1, hMSH2 or other predisposing gene has been identified
- Untested first degree relatives of gene carriers
- Female gene carriers

Screening comprises the following annual investigations:

- Pelvic ultrasound scans (usually transvaginal) with measurement of endometrial thickness
- Pipelle endometrial sampling
- (Ovarian assessment at USS and CA125 measurement for ovarian cancer screening)

Prophylactic surgery (TAH & BSO) may be considered in particularly high-risk cases

Author: …… Signature: …….. Date: ……

Chair: …… Signature: …….. Date: ……
(on behalf of OHMMG)

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