INTRODUCTION

The South East Scotland Cancer Network (SCAN) for Gynaecological Cancer was formally established over 10 years ago. Our first task was to develop a consensus document on management protocols. This year we have reviewed our protocols taking into account the Royal College of Gynaecologists report on vulval cancer published in 2006. CT and MRI scanning are also becoming increasingly important in the management of patients with gynaecological malignancy and the update reflects this.

Patient pathways help patients, doctors, nurses and other members of the team to ensure that patients found to have gynaecological malignancy receive treatment in an appropriate and timely fashion. The clinical management protocols provide the evidence base on which to build these pathways. We are grateful for all the help that has been given by the members of SCAN in reviewing this document.

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Previous and current chair of SCAN Gynaecological Group
December 2009

Membership – SCAN Gynae Group
See www.scan.scot.nhs.uk
THE MANAGEMENT OF CANCER OF THE VULVA

Squamous cell carcinoma of the vulva is the most common malignant tumour, and accounts for approximately 4% of all gynaecological cancers. 80% occur after the menopause, especially in the 7th decade. Incidence approximate 2/100,000 women per year. Rarer malignancies include malignant melanoma, basal cell carcinoma, verrucous squamous carcinoma, Bartholin’s gland carcinoma and adenocarcinoma.

All patients, following a diagnosis of invasive carcinoma of the vulva, should be referred to the Edinburgh Combined Gynaecological Oncology Multidisciplinary Meeting for discussion regarding their further management. Patients with advanced disease will be seen by both the gynaecological oncologist and the clinical oncologist to discuss possible treatment options.

It is well recognised that women with vulval cancer have a variety of psychosocial, psychosexual 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.

1. DIAGNOSIS

1.1 Asymptomatic patients who may be at risk

Vulval Intra-epithelial Neoplasia Grade III (VIN III) is the main potentially pre-malignant condition of the vulva. Adequate conservative therapy (by local excision and/or laser or hyfrecator treatment) can reduce the individual risks of developing carcinoma. Topical treatment with Imiquimod and be useful in conservative management of VIN. In women over the age of 35 the risk of malignant progression is thought to be higher than in younger age groups but at any age the decision to treat depends upon the vulvoscopy appearances, particularly with regard to the possibility of microinvasive disease, and symptomatology (pruritis or pain).

Wart virus infection (especially HPV types 16 & 18) in immunosuppressed patients can lead to potentially pre-malignant conditions of the vulva. Adequate local treatment with long-term follow up is necessary.

Lichen Sclerosis of the vulva is found in association with squamous carcinoma in 3-6% of cases, but its true malignant potential is not known.

Patients should be offered support to stop smoking, including referral to smoking cessation clinics, as this is a well recognised risk factor.

Women with high grade VIN should be followed up in specialist multidisciplinary clinics or by gynaecology oncologists (RCOG recommendation)

1.2 Symptomatic patients

Patients with vulval symptoms such as pruritus vulvae, pain,
discomfort, bleeding, discharge, nodularity, or ulceration must be closely examined for lesions such as an ulcer, a suspicious warty growth, a fungating growth or a pigmented lesion. Patients with suspicious vulval lesions should be referred to a gynaecologist with a view to biopsy and treatment. The biopsy, which should preferably be incisional rather than excisional, can often be done at the first clinic visit under local anaesthesia. On examination, the lesion is characterised by colour, site, size and laterality, and it is assessed for evidence of spread to the urethra, vagina, anus and/or inguinal lymph nodes. Following biopsy to establish definitive diagnosis, the lesion is staged according to the FIGO classification (1988 Old; 2008 New).

1.3 **Advanced disease**

Patients with advanced disease may present with a fungating lesion which may cause pain, urinary retention or rectal bleeding and faecal incontinence, depending on its site. Joint consultation with a gynaecological oncologist, urologist, colorectal surgeon and plastic surgeon may be appropriate. Following biopsy to establish definitive diagnosis, the lesion is staged according to the FIGO classification.

2. **STAGING AND SPREAD OF DISEASE**

2.1a **Staging (FIGO)**

FIGO updated vulval staging in 2008. Both are represented here as previous patients will be staged in the older system.

**1988 FIGO (Old)**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>0</td>
<td>Carcinoma in situ (VIN3)</td>
</tr>
<tr>
<td>I</td>
<td>Tumour (\leq 2) cm in diameter confined to the vulva and/or perineum with no nodal metastasis</td>
</tr>
<tr>
<td>IA</td>
<td>A histological diagnosis in which the depth of stromal invasion is (\leq 1) mm (measured from the basement membrane of the nearest dermal papilla)</td>
</tr>
<tr>
<td>IB</td>
<td>IA but (&lt;) or = (2) cm diameter and confirmed to vulva/perineum with no nodal metastasis</td>
</tr>
<tr>
<td>II</td>
<td>Tumour (&gt;2) cm in diameter confined to the vulva and/or perineum with no nodal metastasis</td>
</tr>
<tr>
<td>III</td>
<td>Tumour of any diameter invading the lower urethra, vagina, or anus, and/or the presence of unilateral groin lymph node metastasis</td>
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</tbody>
</table>
Stage IVa  Tumour invasion of upper urethra, bladder or rectal mucosa, pelvic bone and/or bilateral regional lymph node metastases.

Stage IVb  Any distant metastasis including pelvic lymph nodes

2.1b 2008 FIGO (New)

Stage I  Tumour Confined to the Vulva

IA Microinvasive Carcinoma  Lesions ≤2cm, confined to vulva or perineum and in which the depth of stromal invasion is ≤1mm (measured from the basement membrane of the nearest dermal papilla). No nodal metastases

IB  Tumour >2 cm in diameter or with stromal invasion > 1.0mm, confined to the vulva and/or perineum with no nodal metastasis

Stage II  Tumour of any size with extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus) with negative nodes

Stage III  Tumour of any size with extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus) with positive inguino-femoral lymph nodes

IIIA (i)  With 1 lymph node metastasis (≥5 mm) or
IIIA (ii)  1-2 lymph node metastasis(es) (< 5mm)
IIIB (i)  With 2 or more lymph node metastases (≥5 mm), or
IIIB (ii)  3 or more lymph node metastases (<5mm)
IIIC  With positive nodes with extracapsular spread

Stage IV  Tumour invades other regional (2/3 upper urethra, 2/3 upper vagina) or distant structures

Stage IVa  Tumour invades any of the following:

(i) Upper urethral and/or vaginal mucosa, bladder mucosa, rectal mucosa, or fixed to pelvic bone, or
(ii) Fixed or ulcerated inguino-femoral lymph nodes

Stage IVb  Any distant metastasis including pelvic lymph nodes

2.2 Spread of disease

i) Direct: vagina urethra anus bladder, rectum
3. STAGING INVESTIGATIONS

i) Examination with or without anaesthetic and vulval biopsies
ii) Rectovaginal examination (site dependent)
iii) CXR
iv) FBC, U&E, Creatinine, LFTs (In advanced disease)
v) In advanced disease an MRI scan of the abdomen and pelvis may be helpful for assessment of local spread and measurement of tumour volume. MRI is probably more helpful than CT for the demonstration of lymph node enlargement, but is not always reliable. Any patient being considered for primary chemoradiotherapy should have pretreatment pelvic MRI and CT scan Chest/Abdomen.
vi) PET-CT is useful in assessing advanced or recurrent disease and is mandatory prior to exenterative surgery.

vii) Consider HIV testing if clinically indicated

4. HISTOPATHOLOGY – see Appendix 2

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.

The aim of treatment is to excise disease with a 1 cm margin of clearance on all sides.

5.1 Primary Lesions Confined to Vulva and/or Perineum

5.1.1 Surgery is the treatment of choice. The aim of treatment is to excise disease with ≥1 cm margin of clearance on all sides

Micro-invasive carcinoma

Lesions <2 cm in surface extent and ≤1 mm in depth of invasion should be treated by wide local excision. Groin node dissection is not required.
Stage I

Lesions ≤2 cm in surface extent and >1 mm in depth of invasion should be treated by radical vulvectomy and unilateral or bilateral groin lymphadenectomy through separate incisions.

Unilateral, ipsilateral groin node dissection should be reserved for well lateralised lesions ≤2 cm in diameter, which do not involve the labia minora – a lesion is “well lateralised” if the 1cm medial margin of clearance does not cross the midline. Large, anterior (clitoral/ labia minora) lesions, and those which cross the midline, tend to metastasise bilaterally.

Stage II

Lesions ≥ 2 cm in surface extent and >1 mm depth of invasion should be treated by radical vulvectomy and bilateral groin lymphadenectomy. The role of sentinel node biopsy is to guide selection of patients requiring full groin node dissection or post operative radiotherapy. This may limit post-operative morbidity where it is not indicated. Sentinel node biopsy is being undertaken in some trained centres and being evaluated through prospective multicentre trials. This may become standard management in the future.

(In medically unfit elderly patients these guidelines may have to be modified.)

5.1.2 Indications for post-operative radiotherapy

A) Indications (Depending upon patient fitness and wishes):
   1. Positive or close surgical margins (0.8cm)
   2. ≥2 nodes (either or both sides) with microscopic disease
   3. single macroscopically involved node
   4. extra-nodal spread

Consider whole pelvic radiotherapy if

1. 3 or more unilateral nodes involved
2. Bilateral nodal involvement

Radiotherapy is usually 4500 cGy in 25 fractions given over a 5 week period. Full radiotherapy protocols are found on the Edinburgh Cancer Centre Quality Assurance Documents (OOQS).

5.2 Locally advanced disease

Treatment should be individualised.

5.2.1. Surgery

Ano-vulvectomy or exenterative surgery, with reconstruction should be considered for lesions involving the rectum, vagina or
bladder, together with groin and/or pelvic lymphadenectomy. Myocutaneous flaps may be required to cover the surgical defect. Surgery is likely to involve a multidisciplinary team of gynaecology oncology specialists with input from urologist, coloproctologist surgeon, and plastic surgeon as required.

5.2.2. Chemo-irradiation

Radiotherapy +/- chemotherapy should be considered.

Primary radical radiotherapy

A) Indications (depending upon patient wishes and fitness):

- Locally advanced squamous cell carcinoma of the vulva where exenterative surgery is being considered.

B) Technique

Radiotherapy is given in 2 phases over a possible 7 weeks according to the Edinburgh Cancer Centre protocol on OOQS.

Phase 1: 4500 cGy is given in 25 fractions over 5 weeks. Radiosensitizing chemotherapy is given as weekly cisplatin in selected patients.

Phase 2:
Response is first assessed (4 weeks after starting radiotherapy) and should be rediscussed at the MDM.

- ≥ 50% response proceed to Phase 2
- <50% response to consider surgical resection

In phase two 2000cGy is given in 10 fractions over 2 weeks with no chemotherapy

6. FOLLOW-UP POLICY

6.1 After surgery

3-monthly for 1 year, 6-monthly for 1 year, then yearly to 5 years. Discharge at 5 years if well.

6.2 After chemo irradiation

Patients will be reassessed 6-8 weeks post chemo-irradiation, and if there has been an unsatisfactory response will be re-evaluated regarding surgical options. Follow up as clinically indicated - usually 3 monthly for first 18 months, 6 monthly up to 3 years, then yearly to 5 years. Discharge at 5 years if well. Vaginal dilators will be offered to all patients.

6.3 Emotional support

Vulval cancer is particularly distressing and patients may often feel lonely and isolated. Contact with Gynaecological oncology nurse specialist and/or pelvic dysfunction clinic is available where necessary at follow-up clinic.
7. **TREATMENT OF RECURRENT / METASTATIC DISEASE**

Palliative radiotherapy may be helpful to control bleeding and/or ulceration from vulval recurrence and should be tailored to patient fitness, symptoms and wishes. Maximum dose of 3000 cGy in 10 fractions.

Palliative chemotherapy may be considered with cisplatin according to patient wishes and fitness.

8. **OTHER RARER MALIGNANCIES**

Basal cell carcinoma and verrucous squamous carcinoma – these tumours metastasise only very rarely. Wide local excision is usually adequate.

Malignant melanoma – wide local excision is usually performed aiming for ≥1 cm clearance at all margins. Palpable groin nodes may be excised but in the absence of signs of clinical involvement groin lymph nodes are not routinely removed. CT scans are performed for staging disease.

Bartholin's gland and adenocarcinoma – treatment is similar to that for invasive squamous carcinoma of the vulva. Adenoid cystic carcinoma of Bartholin's gland is prone to perineural invasion and a much wider area than macroscopically involved will require treatment.
References

- Online Oncology Quality System (OOQS) - Edinburgh Cancer Protocol for vulval cancer, Edinburgh Cancer Centre
- McCall AR. Cancer, 75, 2286-8, 1995.
- http://www.nci.nih.gov/cancertopics/pdq/treatment/vulvar/HealthProfessional/page1
- Barnes EA, Thomas G, Semin Radiat Oncol 16:168-176
Appendix 1 – Summary of recommendations (RCOG 2006)

- Women with high grade VIN, Paget’s disease and melanoma in situ should be followed up in specialist multidisciplinary clinics or by gynae oncologists (C)
- Women with an unexplained vulval lump should be referred urgently (C)
- Women with pain bleeding pruritis and ulceration should be referred routinely if symptoms persist (C)
- Vulval cancer should be managed in cancer centres/networks by multidisciplinary teams (B/C)
- Women should be seen and managed according to national directives on waiting times and time from diagnosis to treatment
- Radical treatment should not be undertaken without biopsy to confirm malignancy (C)
- Wide local excision of the primary with a minimum margin of 15mm is often sufficient (C)
- Groin node dissection should be omitted in stage 1a, melanoma, basal cell, verrucous tumours (B)
- Surgery is the treatment of choice for groin nodes, in women unfit for surgery XRT may be used (A/B)
- Groin node surgery can often be carried out through separate incisions – in early disease skin bridge recurrence is rare (B)
- Superficial groin node dissection alone should not be performed (B)
- In lateral tumours, ipsilateral groin node dissection should be performed, if nodes are positive, contralateral is required (B)
- Preservation of long saphenous vein reduces groin wound and lower limb problems (C)

Grade of recommendations:

**Grade A:** Based on randomised controlled trials (RCTs).

**Grade B:** Based on other robust experimental or good observational studies.

**Grade C:** More limited evidence but the advice relies on expert opinion and has endorsement of respected authorities.
Appendix 2 - Histopathology

Introduction

All tissue specimens removed surgically 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 confirm 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 Multidisciplinary Meeting prior to decision making about post-surgical management.

Vulval cancer

- Vulvectomy specimens should be submitted to pathology pinned to cork (provided by Pathology Department, preferably with coloured pins to aid orientation.)

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

Macroscopic photographs are helpful in many cases and will be taken as appropriate.

Microscopic report including:

- Histological tumour type
- Grade of tumour
- Accurate measurement (optical micrometer) of depth and lateral extent of early invasive tumours
- Proximity to nearest vaginal, vulval 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