

Vulval Cancer

by Dr Trudy Smith

Principal Specialist – Department of Obstetrics & Gynaecology and Medical School of University of Witwatersrand, Johannesburg

Although cancer of the vulva is rare, it is primarily a disease of elderly women, although it is observed in premenopausal women as well. There is prevailing evidence that favours persistent human papillomavirus (HPV) infection as the principle causative factor in genital tract carcinomas and vulval cancer is no exception. HPV is not the only prerequisite as 4% of women with lichen sclerosus are also at risk of developing vulval cancer.

The labia majora are the commonest site of involvement and accounts for about 50-60% of cases, the labia minora 15% to 20% whilst the clitoris and Bartholin glands account for the rest of the cases. Naturally, however as the tumour spreads it can ultimately involve the peri-anal, anal areas and even the buttocks.

Squamous cell carcinoma accounts for more than 90% of cases. Of the rest, about 2% are malignant melanoma, 2% are basal cell carcinoma, 2% are sarcomas including leiomyosarcomas, rhabdomyosarcomas, angiosarcomas, neurofibrosarcomas, and epithelioid sarcomas. True Bartholin gland cancers are very rare and include adenocarcinomas, squamous cell carcinomas and even more rarely, transitional cell carcinomas. Adenocarcinoma of the vulva is very rare, occurring in about 1% of cases, and if they do occur, they are most likely to arise within the Bartholin glands.

Squamous carcinoma of the vulva is generally a local malignancy with a predilection for sequential nodal involvement. Distant metastases are uncommon in the absence of advanced local disease, although lymphatic embolization to regional lymph nodes may occur early. The pattern of spread appears to be influenced by the histology. Well-differentiated lesions tend to spread along the surface with minimal invasion, while anaplastic lesions are more likely to be deeply invasive. Spread beyond the vulva is either to adjacent organs such as the vagina, urethra, and anus, or via the lymphatics to the inguinal and femoral lymph nodes and finally to the deep pelvic nodes. Haematogenous spread appears to be uncommon.

The International Society for the Study of Vulvar Disease has classified the histological disorders of the vulva. Some of these are malignant precursor lesions.

Non-neoplastic epithelial disorders of skin and mucosa

Lichen sclerosus (lichen sclerosus et atrophicus).

Squamous cell hyperplasia (formerly hyperplastic dystrophy).

Other dermatoses.

Classification of vulvar intraepithelial neoplasia (VIN)

Mild dysplasia (formerly mild atypia).

Moderate dysplasia (formerly moderate atypia).

Severe dysplasia (formerly severe atypia).

Carcinoma in situ.

Paget disease of the vulva

Other histologies

Basal cell carcinoma.

Verrucous carcinoma.

Sarcoma.

Histiocytosis X.

Malignant melanoma

Presentation

The most common presentation in postmenopausal woman is a vulval mass and or a history of chronic recurring vulval pruritus. Diagnoses of vulval disease are often delayed because of patient procrastination and embarrassment, professional omission or neglect, and ineffective treatment. It is quiet common to have women who have visited several practitioners and have been given a variety of creams for topical application to the vulva before the diagnosis is finally made. A persistent mass of the vulva or chronic recurring pruritis vulvae always warrants further investigation. Dystrophic changes are found in the adjacent skin to the tumours in more than 50% of patients with invasive vulvar cancer. Higher grades of vulval intraepithelial neoplasia (VIN 2 and 3) are premalignant conditions, but the proportion of cases that progress to invasive cancer is not definitely known. VIN 1 is no longer considered a premalignant condition and is, to all intense and purposes, a flat warty lesion consisting of HPV infection only and even if left alone is very unlikely to progress to invasive vulval cancer.

At presentation, about 10% of patients will already have lymph node metastases. The most frequent nodes involved are the inguinal nodes and in stage 1 lesions 15% will be positive. If the depth of the lesion is less than 1mm then the risk of lymph node metastases is practically nil. Verrucous carcinoma is a locally invasive slow growing tumour that is characterized by a cauliflower-like, or verrucoid, growth pattern. It also affects predominantly postmenopausal women. Radiotherapy may cause anaplastic transformation of this tumour and is contraindicated. Surgery is the treatment of choice.

Contributory or predisposing factors

Risk factors for the development of invasive squamous cancer include chronic inflammatory diseases of the vulva, some vulval dystrophies, poor hygiene, and age greater than 70 years. Multiple sexual partners, abnormal results on pap smear, anogenital HPV infection or neoplasm, smoking, and immunosuppression also increase the risk for invasive vulval cancer. About 22% of vulval cancer patients may also have a coincident secondary primary malignancy, most commonly cervical cancer. For this reason it is prudent that any patient with vulval pathology must also have a pap smear.

Staging

Staging is based on an adaptation of the T N M classification adopted by FIGO.

Stage 0:	carcinoma in situ, VIN 3
Stage I:	lesions 2cm or less confined to the vulva or perineum. No lymph node metastases
Stage IA:	lesions 2cm or less in size confined to the vulva or perineum with stromal invasion no greater than 1mm and no nodal metastases
Stage IB:	lesions 2cm or less in size confined to the vulva or perineum and with stromal invasion greater than 1mm and no nodal metastases
Stage II:	tumour confined to the vulva and/or perineum or more than 2cm in the greatest dimension with no nodal metastases
Stage III:	tumour of any size arising on the vulva and/or perineum with adjacent spread to the lower urethra and/or the vagina, or the anus; and/or unilateral regional lymph node metastases
Stage IVA:	tumour invading any of the following: upper urethra, bladder mucosa and rectum
Stage IVB:	any distant metastasis including pelvic lymph nodes

Treatment Goals

Complete resolution is obviously the ultimate goal. The 5-year survival after surgery is 90% for stage I disease, but decreases to 70% when all stages are considered. Preservation of sexual function is particularly important to the young patient, particularly with view to sexual activity and preservation of the clitoris, although genital anatomy should also be conserved in the elderly. The concept of incorporating wide excision of the vulval tumours or, if not feasible, simple vulvectomy, does allow retention of vaginal function and sexual activity, particularly if the clitoris is not removed. Leaving the clitoris in situ as part of treating vulval cancer is an acceptable option provided the clitoris is clear of disease.

Therapeutic options

Treatment must be individualised and depends on tumour stage. Standard treatment for vulval cancer is surgery in stages I and II disease. For those with more advanced stages, surgery may be combined with radiation and/or chemotherapy. Radiation and chemotherapy may also be used as primary therapy.

The previously performed, traditional “butter fly” radical vulvectomy, has been shown to have major psychosexual consequences and is commonly associated with a high morbidity. As a result, surgical options offered today are significantly more conservative than that performed previously. En bloc radical vulvectomy and a bilateral inguinal lymphadenectomy, as performed previously, is rarely undertaken today and the surgical strategy offered at present is a simple vulvectomy or wide excision of the vulval tumour with a 2 cm disease free border and bilateral inguinal lymphadenectomy through three incisions. There are no head to head trials but the triple incision method has a lower morbidity with less breakdown and infection. Complications of this surgery include lymphoedema in 14 to 21% of patients, lymphocoele formation and deep vein thrombosis. Radiotherapy is not without its own complications as the skin in this area is very thin and sensitive. Acute erythema with moist desquamation is seen with lower doses in this area than when radiation is used in other areas.

Since invasive and preinvasive neoplasms may be HPV induced and the carcinogenic effect widespread close follow-up is mandatory for detection of recurrent or second tumours developing.

Treatment by stage of disease.

Stage 1

Treatment is confined to wide local excision of the lesions where the stromal invasion is less than 1mm. Inguinal-femoral lymphadenectomy is not necessary in these patients. Lesions that have >1mm stromal invasion (stage 1b) should undergo ipsilateral inguinal-femoral lymphadenectomy for lateral lesions and bilateral lymphadenectomy for central lesions which cross the midline and hence may lead to metastases to the ipsilateral lymph nodes. If surgical margins around the vulval tumour do not have more than 1-2cm of disease free border, or if two or more inguinal nodes that have metastatic disease, adjuvant radiotherapy to the vulva and inguinal nodes should be given.

Stage 2

Selected cases of stage II disease may be treated with wide excision and bilateral lymphadenectomy although the vast majority will require a simple vulvectomy and bilateral inguinal-femoral lymphadenectomy. Patients with more than one positive lymph node require pelvic and groin irradiation.

Stage 3 and 4

Patients with advanced vulval lesions involving the urethra, anal sphincter, or vagina would require radical primary surgical intervention which may necessitate a colostomy or exenterative procedures. This carries significant morbidity and mortality and alternative options including neoadjuvant chemotherapy and radiation on its own or followed by surgery as described above.

Future Trends

Patients who have been successfully treated for premalignant disease of the cervix need to be monitored for a field effect of the ano-genital tract and may well be at risk for developing vulval cancer at a later date. This scenario is of particular concern amongst HIV positive patients who will require constant observation as they are at greater risk of developing vulval cancer, particularly if there is concurrent or a past history of cervical pathology. The new quadrivalent HPV vaccine has been shown to decrease the incidence of vulvar cancer and will hence play a important role in combating the disease.

The role of inguinal lymph node mapping is becoming more defined in managing vulval cancer. Pre-operative intra lesion or peri-lesional injection of dyes or radioactive material allow identification of sentinel nodes which can then be removed individually and sent for histology thus avoiding all the complications that are associated with the conventional inguinal lymphadenectomy that are commonly being performed. Incorporating this initiative into present day management of vulval cancer should minimise even further disease associated morbidity.

A recent Cochrane review has shown that combination chemo radiation improves the chance of surgical excision in patients that are initially assessed as inoperable. There is however a need to develop a less toxic chemotherapeutic drug as this is a disease of the elderly.

The incidence of HIV is increasing and it would appear that ARVs do not have an effect on the acquisition of HPV. This may increase the incidence of Vulval cancer. Alternatively the introduction of the qaudravalent vaccine may result in a decrease in this rare disease.

References on request

Diagnoses of vulval disease are often delayed because of patient procrastination and embarrassment, professional omission or neglect, and ineffective treatment