VULVAL MALIGNANCY AT EDENDALE HOSPITAL FROM JUNE 1954 TO JULY 1963*

SOME POINTS OF POSSIBLE INTEREST IN A SMALL SERIES OF 28 CASES

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A total of 28 patients with vulval malignancy have been seen at Edendale Hospital since its opening in June 1954. If we accept that 600 cases of carcinoma of the vulva occur annually in England and Wales,[1] then, on a proportional population basis, about 180 cases probably occur among all races in South Africa each year. Of these, approximately 3 per year are seen at Edendale.

The total of 28 cases excludes 2 patients with chorionepithelioma who presented with haemorrhagic secondary deposits in the vulval area, but it does include: 1 case of *sarcoma vulvae* and 1 of *carcinoma urethrae* involving the urethral meatus.

The patient with sarcoma vulvae was a 13-year-old girl who was subjected to radical vulvectomy and bilateral groin dissection. She died with gross secondary deposits within 2 months of admission.

The carcinoma of the urethra was a tumour of the transitional cell type, and although it can justifiably be classified as a vestibular carcinoma, it has been excluded from the analysis which follows.

With the exclusion of the above 2 cases, we are left with 26 cases of frank vulval carcinoma which form the basis of this paper.

AGE INCIDENCE

From Table I it will be noted that the average age is considerably lower than the usual mean quoted in the literature: 59 years,[2] 60 years,[3] 62 years,[4] and 64·8.[5] The lowest mean that could be found in the literature was 53·4 years,[6] in which 62% of the patients were Negroes.

TABLE I. AGE OF PATIENTS GROUPED BY DECADES

Age group	*No. of patients*	
11 - 20	0	
21 - 30	2	
31 - 40	7	
41 - 50	8	
51 - 60	5	
61 - 70	3	(including 1 Indian)
71 - 80	1	(Indian)
Total	26	

Average age = 47·4 years.

AETIOLOGY

The possible pre-cancerous conditions are shown in Table II:

TABLE II. POSSIBLE PRE-CANCEROUS CONDITIONS

Condition	*No. of patients*	
Leukoplakia vulvae	1	(Indian)
Condylomata accuminata	3	
Syphilis	10	
Vulval tuberculosis	1	
Leprosy	1	
Pellagra	1	
Total	17	

Leukoplakia

The possible significant feature emerging from this series is the absence of leukoplakia in the African group. Palmer,[7] in a large series of 313 cases in which there were no women of Jewish or Negro origin, described a low incidence of 12%. Miller *et al.*[8] however, are of the opinion that leukoplakia is uncommon in Negroes. Most authors with predominantly European patients, have described a high incidence of leukoplakia — 38%,[5] 58%,[9] and 64%.[10]

Syphilis

The incidence of this disease is high. As the Wassermann reaction was not done in 9 of these cases, the incidence might be still higher. The high positive Wassermann rate (11·4%) among the women attending our antenatal clinic must, however, be borne in mind. Taussig[11] has pointed out that in the absence of syphilis, carcinoma of the vulva is ordinarily rare in Negroes, possibly because of the differences in skin histophysiology which do not favour the development of either leukoplakia or malignancy. Our cases lend support to the truth of this statement.

Lundwall,[12] in a series of 373 cases, found a low incidence of lues, viz. 7·2%. An interesting finding was that among these few patients a large number of tumours were anaplastic.

Pellagra

Mention must be made of severe pellagra in one case. It is just possible that the skin changes (parakeratosis, etc.) bore some relationship to the development of carcinoma.

Diabetes Mellitus

Some authors have pointed out a high incidence of diabetes in patients with vulval carcinoma. Macafee[13] found an incidence of 5·8%, Tompkins *et al.*[5] found it to be 6%, while Edsmyr[14] found an incidence of only 2·9%. In this series no cases of diabetes mellitus were found.

PATHOLOGY

Type of carcinoma. There were 2 adenocarcinomata in this series, the remaining 24 all being cases of squamous carcinoma.

Situation of the tumour. As the exact macroscopic appearances were not always described in the clinical notes, no reliable information can be given on this point.

Tumour differentiation. Although the pathologist did not always report on the degree of differentiation of the tumour, for the most part they were moderately to well differentiated carcinomata. In 3 cases only was distinct anaplasia demonstrated.

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Gland involvement. The inguino-femoral group of glands were involved positively in 10 out of the 26 cases, and almost certainly in 3 further cases, making a total of 13 out of 26. This represents a 50% incidence. Way,[15] Bibby,[16] Green *et al.*,[9] Collins,[17] Macafee,[13] and Tompkins *et al.*[5] report positive nodes in 61%, 60%, 34%, 38·3% and 30% respectively.

Surprisingly, in 3 gross stage-III carcinomata, in which the vagina, perineum and anus were involved, the glands contained no metastatic deposits. Presumably the co-existing regional adenitis had blocked the path for metastatic travel. Isaacs and Topek[18] believe that the combination of neoplasm and inflammation generally has a better prognosis.

Size of Tumour and Staging

Using a slight modification of the system suggested by Stenning and Elliott[19] the staging is reflected in Table III.

TABLE III. STAGING OF CASES

Stage		*Number of cases*
0	Carcinoma-*in-situ*	1
I	Growth less than 2·5 cm.	1
II (*a*)	Growth greater than 2·5 cm. No spread to glands	6
(*b*)	Spread to inguino-femoral glands	4
III	Spread to intrapelvic nodes and/or involvement of vagina or anus, or large movable groin mass	12
IV	Bone or distant metastases or ulcerative fixed groin mass	2
	Total	26

The conclusion drawn is that the majority of cases were of a very advanced variety.

Associated Carcinoma

Merrill and Ross[2] and Gosling *et al.*[10] found incidences of associated carcinoma elsewhere in the body of 16% and 1·5% respectively. In this series no associated carcinomas were detected.

PRESENTING SYMPTOMS

The chief symptoms encountered are presented in Table IV.

TABLE IV. PRESENTING SYMPTOMS

Symptom	*Number of cases*	
The lesion itself. Ulcer or swelling	24	
Plus pain or discomfort on walking or sitting	6	of
Plus bleeding	3	the
Plus itching	2	above
Discharge. This was usually associated with the above and was of a yellow, sanguineous or watery character	9	
Dysuria. (With urethral involvement)	2	
Painful defaecation. (With rectal involvement)	2	
A Mass in the groin.	2	
Bloody diarrhoea. (Plus tuberculous fistula-*in-ano*)	1	

It will be noted that, contrary to the findings of most other writers, pruritus is not a leading symptom in this series. The leading symptom in the non-White appears to be almost always the lesion itself.

Delay Period

That there is often a long delay period between the onset of symptoms and the commencement of treatment has been pointed out by many authors. This delay period was over 1 year in 11 out of the 26 cases, i.e. in over 40%. It is significant that in this time many of the patients stated that they had attended regularly for treatment at hospitals, clinics or private medical practitioners, but without any improvement in the lesion. It would thus appear that delay by the physician occurs almost as often as delay by the patient.

Operability Rate

Twenty-three out of the 26 cases were operated upon. This indicates an operability rate of 88·4%. One patient died of gross carcinomatosis within 6 hours of admission and another 2 refused operative treatment altogether.

TREATMENT

Louw,[20] in a paper on carcinoma of the cervix, has indicated that only by early diagnosis will any improvement be noted in the overall results of treatment of that disease. The same remarks and reasoning apply equally well, one feels, to cases of vulval carcinoma.

Prophylaxis and Early Diagnosis

This may be conveniently discussed under 3 headings:

1. Education

(*a*) *The patient.* Cancer propaganda in general among the non-Whites, especially in regard to the early reporting of symptoms, should be undertaken. A knowledge of general hygiene, especially of the genital tract, and a knowledge also of the general principles of nutrition should be fostered in all schools. The lack of vitamin A and the B-Complex group may play a significant part in the pathogenesis of the disease under discussion.

Virtually nothing is done in the above regard for the African at the moment, although conditions appear to be showing some improvement. The vast majority of the non-White masses in South Africa are completely ignorant of these vital issues. In this area of Natal the ex-Chief Native Commissioner, Mr. Turton, has been most helpful in disseminating knowledge among tribal chiefs, particularly in regard to antenatal care. This avenue of approach to the problems connected with Bantu obstetrics and gynaecology should be more fully explored and exploited.

(*b*) *The undergraduate student.* It would appear that medical students receive only a very sketchy training in the recognition of vulval pathology. The number of patients who have been under prolonged treatment by general practitioners without the nature of the disease being recognized is quite alarming.

(*c*) *The postgraduate student.* Cases of vulval pathology should be shown to postgraduate classes from time to time and the points in early diagnosis stressed. This is particularly important with regard to the refresher courses for general practitioners which are held annually by many medical schools.

2. The Establishment of Vulval Clinics at Leading Hospitals

Collins[21] has pioneered the way in New Orleans. Here gynaecologists, dermatologists and pathologists cooperate

fully in elucidating the correct diagnosis and in deciding on the appropriate therapy for each case.

3. Prophylactic Vulvectomy

All chronic dermatoses presenting as irritative lesions and affecting the vulva, should be most carefully investigated and followed up. It is as rational to submit the aged person with the symptom of pruritus with external vulval manifestation to skin biopsy as a *sine qua non* of investigation, as it is to perform diagnostic curettage for postmenopausal bleeding.[19] Particularly in women over 40, where any atypical epithelium is demonstrated histologically, prophylactic vulvectomy has much to commend it.

Curative Treatment

In this institution 2 principles have been borne in mind in the treatment of carcinoma of the vulva:

1. The patient is treated firstly and the disease secondly. A high operative mortality is unacceptable and a surgical procedure consistent with the physical and emotional status of the patient is undertaken wherever possible. As stated by Isaacs and Topek[18] the plan of therapy must be one of individualization. Macafee[12] has stressed the importance of adequate pre-operative explanation to the patient so that psychological re-adjustment may be more readily achieved. In this unit a fellow sufferer who has already undergone radical surgical treatment was, whenever possible, demonstrated to the patient to show her that the ultimate result is not as mutilating as it at first sounds. She is encouraged to discuss her disease and the operation with this patient.

2. 'Metastatic disease cannot be chased with the knife'[22] is a maxim which is firmly upheld. In keeping with the views of Bibby,[16] and lately with the altered opinion of Way,[15] iliac lymphadenectomy is seldom performed in cases of carcinoma of the vulva. McElvey[23] found that results were equally good without iliac node dissection, and Graber[22] believes this step to be completely illogical. It is felt that Louw[20] would also be ready to support this viewpoint. From his studies with carcinoma of the cervix he has concluded that when glands are involved the prognosis tends to be uniformly poor, in spite of a well-executed technical procedure.

The fact must be accepted that once the tumour has metastasized it will destroy the host. The length of time it takes to do this depends on the basic resistance of the host and the predetermined invasiveness of the cancer cell. The operation performed or the type of other therapy dispensed really does little to alter or modify the natural course of the disease once distant spread has taken place.

It is only necessary to study two sets of figures, e.g. given by Collins[17] in New Orleans and Green *et al.*[9] in New England, both great advocates of deep-node dissection, to grasp the real meaning of the maxim quoted above. Collins quotes only an 18% 5-year survival in patients with node metastases, while Green *et al.* report an 8% survival if there is bilateral deep-node involvement and 33% if there is unilateral involvement.

Lundwall,[12] in his magnificent review of the subject, believes that an inguino-femoral node dissection painstakingly performed is more important than a doubtfully radical iliac-node dissection. He believes that the increased operative mortality may entail the loss of patients without pelvic (or groin) metastases, while it is very doubtful if anything is gained once metastases are scattered in the pelvic nodes.

By these means this unit has achieved, with a *nil operative mortality*, a reasonable chance of cure in 12 relatively early cases, and has obtained fair to satisfactory palliation in the remaining group of late cases. Death within one month of operation is the definition used here for operative mortality. Way's[15] mortality in 45 cases with positive nodes was 33%. He states that the hospital staphylococcus problem was most serious at the time. Ulfelder[21] records a 5% mortality in his 53 cases.

Types of Operation Performed (See Table V)

Whenever possible a one-stage operation has been performed. The staged procedure, however, especially in the poor-risk case, or when 2 operating teams are not available, is a safe and satisfactory operation. Two obvious drawbacks must be noted when one is dealing with the non-White section of the population. The first is the refusal of the patient to agree to the groin excision once her main complaint or lesion is removed. This occurred in 2 of our cases. The second is the longer period of hospitalization required and the concomitant worry about bed shortage. The one-stage operation, therefore, is considered the one of choice.

TABLE V. TYPES OF OPERATION PERFORMED

Type of operation	No. of cases
1. Biopsy excision	1
2. Simple vulvectomy with no groin dissection. (1 case refused 2nd-stage groin dissection)	2
3. Palliative perineo-ano-vulvectomy without groin dissection	1
4. Radical vulvectomy with regional inguino-femoral lymphadenectomy (bilateral)	
(*a*) One-stage operation	5
(*b*) Two-stage operation	2
5. Radical vulvectomy with bilateral inguino-femoral and iliac lymphadenectomy. Two-stage operation	2
6. Transverse colostomy, perineo-ano radical vulvectomy and bilateral inguino-femoral lymphadenectomy. (One-stage operation)	1
7. Perineo-ano radical vulvectomy plus bilateral inguino-femoral lymphadenectomy	
(*a*) One-stage operation	2
(*b*) Two-stage operation	2
8. One-stage radical vulvectomy with bilateral inguino-femoral lymphadenectomy plus modified anterior exenteration with cystorectoplasty	1
9. Colostomy, radical vulvectomy and bilateral inguino-femoral lymphadenectomy plus posterior exenteration. (One-stage operation)	2
10. Colostomy, radical vulvectomy and bilateral inguino-femoral lymphadenectomy plus posterior exenteration and modified anterior exenteration with ileo-urethroplasty. (One-stage operation)	1
11. Ipsilateral inguino-femoral lymphadenectomy only	1
Total	23

Pre-operative Preparation

The usual basic laboratory and X-ray investigations, as for any major cancer case, are done. The bowel is

emptied as a routine and sterilized, commencing 2 days before the date fixed for operation.

OPERATIVE TECHNIQUE

The operation itself. The Stanley-Way[25] operation as opposed to the Ulfelder[21] modification is preferred for the late case. Parry Jones'[22] suggestion of limiting the incision to the labiocrural fold would have been possible in only 6 of our cases. The growth had encroached too near the fold for safety or had spread to the perineum and/or anus in the remaining cases. In the latter instances some skin on the medial thigh was excised as suggested by both Way and Jones.

Position on the table. The patient is placed usually in a modified lithotomy position in Lloyd-Davies supports, with the hips and knees only slightly flexed.

Blood. Two intravenous drips, with 15-gauge needles, are inserted into the arms. A formalin-sterilized blood administration set complete with pumping unit is available for emergency femoral artery pressure transfusion if necessary. This procedure proved life-saving in one case.

Six pints of blood are cross-matched as a routine for the operation, but only 2-3 units are used on the average.

Anaesthetic. Pentothal, gas, oxygen and curare are used for the older women, while pentothal and halothane are used for the younger patients. Halothane has a hypotensive effect, and when combined with slight Trendelenberg tilting of the table, definitely reduces the blood loss during the operation. No hibernation technique, as used by Bibby[16] has been attempted. The advice of McElvey,[28] who uses ilio-inguinal plus pudendal block, and Hesseltine,[27] who uses continuous spinal anaesthesia, has not been followed. Recently, however, 2 operations have been performed under epidural anaesthesia with good results and minimal bleeding.

Operating team. Two teams, if available, commence with a simultaneous inguino-femoral groin dissection, preserving an *en bloc* specimen. One team then retires, leaving the other to complete the vulvectomy.

Diathermy. This is used as a routine for control of haemorrhage. Transfixion sutures of silk are employed to secure the larger vessels, e.g. long saphenous vein and pudendal vessels.

Operating time. This varies from 2½ to 4 hours, depending on the extent of the procedure. The average time in Ulfelder's[24] series was 3½ hours, and in Currie's it was 50 minutes.[16]

GENERAL REMARKS ON RADICAL VULVECTOMY

Since Way's[25] description of the sartorius transplant to cover the femoral vessels, this step has been performed as a routine.

The same surgeon's suggestion of massive full-thickness thigh flaps, by incising well down the thigh in order to cover the large raw vulval surface, has been abandoned owing to the excessive amount of sloughing which has occurred. Primary skin grafting, as suggested by Schaeffer *et al.*[25] has not been attempted.

If fixed inguino-femoral glands are present, a surgeon skilled in vascular technique should be on hand as a member of the operating team.

Substantial amounts of fat are removed from the ischiorectal fossae, but this is never completely cleared, as suggested by Collins *et al.*[29]

Nodal smears and frozen section[25] are not done at this hospital. Cloquet's gland is always sought for but not always found in the position described. The femoral canal is carefully obliterated to prevent subsequent herniation.

The skin, after cleansing with ether and tincture of 'hibitane', is sprayed with 'nobecutane'. It is felt that this does help to seal the septic fungating lesion.

Polybactrin spray is used before closure, and finally polythene catheters are placed under the flaps for drainage by continuous suction. These tubes are led out through stab incisions in the thigh, secured with a suture, and each drains into a bottle under the patient's bed on her return to the ward.

Postoperative Care

Nothing out of the ordinary is ordered. The patient is usually given a broad-spectrum antibiotic for the first week. Careful control is kept of fluid balance, and parenteral feeding is conducted for 2-3 days. Early breathing exercises are important. Following the advice of Way[25] the patients are now nursed with the legs adducted and the knees slightly flexed. This places less tension on the suture lines.

Convalescence

This has varied from 6 weeks to 3 months at Edendale. Ulfelder's[24] cases required hospitalization for 33 to 44 days.

POSTOPERATIVE COMPLICATIONS

Five complications have caused some concern.

1. *Wound separation, sloughing and infection.* This complication has been present in varying degrees in most cases treated by radical excision. This is expected, however, and after clearing of sloughs and sepsis, skin grafting is undertaken after about a month. On the whole the results of grafting have been very pleasing.

2. *Lymphoedema.* This has proved troublesome in 2 cases. A collection of lymph in the mid-thigh required repeated aspiration in one, while the other resolved on 'varidase' therapy.

3. *Secondary haemorrhage.* This occurred in 1 patient only, an elderly Indian, who died after a series of brisk haemorrhages from the femoral artery.

4. *Deep-vein thrombosis of the calf.* This occurred in 1 patient only and was readily controlled with anticoagulants.

5. *Scar contracture in the groin.* This proved annoying in 2 patients. After physiotherapy one patient walked with little disability at the time of discharge, although she had a limited range of abduction of the thighs. The other required excision of scar tissue and a skin graft.

Femoral hernia and stress incontinence have not been encountered.

SEQUELAE

As so few cases have been seen for complete follow-up, little information can be given.

1. *Dyspareunia* from fibrous contracture and stenosis of the introitus has not been a feature in the cases seen in

the late postoperative period. If coital difficulty is encountered, however, various plastic procedures for the relief of this condition are described.[20]

2. *Frigidity* in the sense of failure to achieve orgasm, from the loss of the clitoris, might be a major complaint. However, the answer to this question is not given in the literature or by any of the cases in this series. Charlewood,[21] in his series, looked for this complaint but did not encounter the problem.

3. *Dystocia* in a future pregnancy may be met with; this arises from fibrous contracture of the introitus. Gemmel and Haines,[22] in their report on 10 cases, believe that caesarean section is necessary only if extensive scarring is present. The only pregnant patient in this series was delivered normally *per vaginam* after bilateral episiotomies.

OTHER METHODS OF TREATMENT

Radiotherapy. This was employed as a late method of treatment in 2 cases. One of these had a simple vulvectomy performed for 'carcinoma-*in-situ*' and she presented 3 years later with massive fixed fungating glands in one groin. These were successfully excised together with a large single iliac gland. The tumour was completely radioresistant. The other case was an adenocarcinoma which also proved radio-resistant.

Radiotherapy as a whole appears to offer little hope to the late carcinoma vulvae cases. Andersen,[33] in Sweden, could only show a 4·1% 5-year survival rate with deep X-ray therapy in his series of late cases. Nolan,[34] on the other hand, states that occasionally the results of radiation may be gratifying.

Drug therapy. Cytostatic agents were tried in only 2 late cases. In the one it was given intramuscularly and in the other by aortic perfusion. In neither case was any improvement noted.

Electrocoagulation. This is a valuable palliative procedure and was used with good effect in 2 cases with vulval and vaginal recurrences in this series.

Combined therapy. In the Scandinavian countries the most favoured method of treatment is electrocoagulation of the vulva followed by radiation to the inguinal regions and lymphadenectomy if there is evidence of nodal involvement.[12,14,35,36] Five-year cure rates vary from 35·5%[14] to 51%.[36]

Lundwall,[12] in reviewing the literature and from the results obtained in 290 patients at the Radium Centre, Copenhagen, however, has come to the conclusion that radical surgery is the most efficacious method of treatment.

SURVIVAL RATE

Nine out of the series of 26 patients are known to be dead. Good palliation, however, was afforded to 6 of these patients, who each lived about 2½ years, and 1 for 7 years. Ten patients are known to be alive and well. Seven cannot be traced. Of this number 3 can confidently be expected to be alive and well and 4 to have died of metastatic disease. This prediction is based on the fact that a satisfactory operation was performed and that no glands were involved at the time of operation in 3 of the patients.

PROGNOSIS

This is related to 7 main factors.

1. Site and size of the tumour. Spread to urethra, vagina or rectum generally has a poor prognosis.[2,4]

2. Histological grading of tumour. The presence of 'giant cells'[15] carries an unfavourable outlook.

3. The presence of lymph gland involvement.

4. The presence of associated lymphadenitis, blocking metastatic spread.[18]

5. Associated pathology, e.g. heart disease, diabetes, liver disease or the presence of another carcinoma.

6. The delay period before treatment.

7. The type and scope of treatment.

In the small series under review not much could be hoped for in view of the late picture in the majority of cases.

SUMMARY

1. A brief sketch of carcinoma of the vulva in so far as it affected 24 African and 2 Asiatic patients in the Midlands of Natal is given. The high incidence of syphilis and the virtual absence of leukoplakia in the African patients are emphasized. The disease possibly has a lower age incidence than in Whites.

2. The cancer for the most part presented in an advanced form and consequently a palliative procedure was often performed.

3. In general a policy of individualization is advocated for carcinoma vulvae cases.

4. Stress has been laid on the fact that metastatic disease cannot be cured with the knife, and for this reason deep iliac-node dissections have been omitted from the standard operation.

5. A scheme of prophylaxis has been outlined and the point made that early diagnosis, before the stage of glandular involvement is reached, is the only method by which any worth-while results will be achieved.

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