

## PRIMARY CANCER OF THE SCROTUM IN SOUTH-SOUTHERN NIGERIA: FEATURES AND OUTCOME.

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### ABSTRACT

**Background:** In spite of sordid experiences of patients with primary scrotal cancer in Nigeria, little has been published about the disease in the country. **Aim:** To present clinico-pathological features and outcome of the disease in South Southern Nigeria. **Materials and Methods:** Consecutive patients that presented to the University of Port Harcourt Teaching Hospital (UPTH), Nigeria, with scrotal lesions between April 2004 and June 2018 were evaluated clinically and with relevant investigations including histology of incisional biopsies of the lesions. Data collected, which included histological reports, treatment methods and clinical photographs, were analyzed with simple statistics. **Results:** Five of a total of 7 patients seen during the period had confirmed histological diagnosis. Their ages ranged from 59 to 70 years (mean, 64.6 years). The patients presented for treatment with an average delay of 3.8 years after noticing an initial scrotal lesion. One patient (HIV- positive) presented with eccrine porocarcinoma (stage D) and 4 others stages C to D squamous cell carcinoma, all of the left hemi-scrotum. Each patient was treated with wide tumour excision, a method enhanced by centripetal scrotal distribution of the disease. One patient died 4 weeks after operation. The rest were lost to follow-up within 14 weeks of operation. **Conclusion:** Features were found similar to findings in patients with advanced scrotal squamous cell carcinoma elsewhere. There was no predilection for particular occupations and no additional synchronous primary malignancies were found. Prognosis was poor due to delayed presentation.

**KEYWORDS:** Primary scrotal cancer; features and outcome; south Southern Nigeria.

### INTRODUCTION

South-Southern Nigeria lies mostly in the Niger Delta belt of the country. Port Harcourt, the capital City of Rivers State, is a thickly populated cosmopolitan and industrial city, which also has a dense indigenous population of the Niger Delta communities of southern Nigeria. Primary cancer of the scrotum has worldwide distribution but literature on it is rare in the area like elsewhere in the country. The distribution, type, features and outcome of the disease varies in different regions of the world. Reports from various black communities in South and North America (the USA).<sup>[1,2]</sup> indicate that the most common histological variant of the disease is squamous cell carcinoma. This often has aggressive malignant features and poor prognosis (2). This contrasts with studies reported from the Far East including Taiwan (3), China,<sup>[4,5,6,7]</sup> South Korea.<sup>[8,9]</sup> and some parts of Europe.<sup>[10,11]</sup> In these latter reports, extra mammary Paget's disease of the scrotum (EMPDS) is the most common and tends to have better prognosis, especially in the early stages of the disease.

**Aim:** The aim of this study is to present clinical and pathological features and outcome of a series of primary cancer of the scrotum in Port Harcourt, and to compare the same with findings elsewhere.

### MATERIALS AND METHODS

Consecutive patients that presented to the Urology Division of the University of Port Harcourt Teaching Hospital (UPTH), Nigeria, with scrotal lesions between April 2004 and June 2014 were evaluated clinically and had relevant investigations. Data, which were obtained prospectively in two and retrospectively in five, included personal data, history of presence or absence and duration of previous scrotal lesions, occupational history, family history of cancer, social history, other symptoms and signs of disease, full blood count, serum electrolyte, urea and creatinine, fasting blood sugar levels, liver function tests, urine microscopy culture and sensitivity tests, HIV screening, wound microscopy, culture and sensitivity, abdominal ultrasonography, plain chest X-ray studies and electrocardiography. Incisional biopsy of

malignant scrotal and groin ulcers, histological reports and treatment methods were recorded. Pre-operative, intra-operative and immediate post-operative clinical photographs were taken. The Ray and Whitmore Staging System,<sup>[12]</sup> (reproduced below) was used to stage the tumours. Data collated were analysed with simple statistics.

## RESULTS

Seven patients with primary cancer of the scrotum were treated in UPTH during the study period. Five had confirmed histological diagnosis and were analysed. Two patients were too ill for any invasive intervention and had conservative supportive treatment only. They died shortly on admission of overwhelming disseminated disease. They were not included in this analysis because confirmatory histological diagnosis could not be made. A summary of the five cases with confirmed diagnosis is presented below:

### Patient No 1

The first patient was a 70-year-old trade-medicalist who presented to the hospital with complaints of an ulcer on the left side of the scrotum of 5 years duration. The ulcer was antedated by an itchy popular lesion that developed spontaneously at the same site. The lesion broke down into the presenting ulcer during scratching.

He was elderly, ill-looking, and afebrile, weighed 55kg, and had supra-pubic and perineal oedema with moderate-to-severe pallor. There were multiple masses of matted enlarged left inguinal lymph nodes, each 1-3cm in greatest dimension.

He had an ulcer in the left hemi-scrotum. The ulcer had raised everted edges, sero-purulent discharges, with necrotic floor. The surrounding skin was hyper-pigmented. The dimensions were 5cm x 6cm. It was non-tender and the base indurated. A clinical diagnosis carcinoma of the left hemi-scrotum made.

His haemoglobin level was 8.3g/dl, erythrocyte sedimentation rate (ESR) 28mm/first hour (WesterGreen) and serum electrolyte, urea and creatinine levels normal. His wound culture showed evidence of infection. He was sero-negative for HIV I & II and had plain radiographic evidence of pulmonary metastases. Histology reports of incisional biopsy of the ulcer showed that he had poorly differentiated squamous cell carcinoma of the scrotum. His malignancy was staged C.

He was given supportive treatment, left hemi-scrotectomy and transposition of the testis to the contralateral hemi-scrotum, wound closure and selective left inguinal lymphadenectomy. He was discharged 22 days post operation and was lost to follow up in spite of medical advice.

### Patient No. 2

A 67-year old peasant fisher man who presented to UPTH with complaints of a persistent wound at the scrotum of over one year duration. It persisted in spite of previous treatment and dressings. He first had a pruritic papule at the same site at the left hemi-scrotum; it broke down into an ulcer during scratching about 1 year before presentation. The small ulcer became persistent.

He was chronically ill-looking pale with enlarged ulcerated matted left inguinal nodes, with scrotal, perineal and supra-pubic oedema. He had a clinically malignant ulcer at the left hemi-scrotum. His PCV was 28%, serum electrolyte, urea and creatinine levels were within normal limits. He was sero-negative for HIV I & II. Histology report of incisional biopsy of the scrotal wound confirmed clinical diagnosis that he had squamous cell carcinoma of the scrotum (Stage C).

He had wide excision of the ulcer with 3-5 cm margin and reconstitution of the scrotum. The testis with the spermatic cord was preserved. Selective inguinal lymphadenopathy was done for clinically suspicious nodes. He recovered satisfactorily and was discharged after the 14<sup>th</sup> post-operative day on admission. He was followed up for 14 weeks during when he was worked up for cytotoxic chemotherapy. He was lost to follow-up.

### Patient No 3

This was a 65-year old ex-soldier, farmer and accounts clerk who presented to UPTH with complaints of an ulcer in the left side of his scrotum of 6 months duration. The scrotal lesion started as a small pruritic scrotal papule 10 months before presentation, ulcerated on scratching and had progressive non-healing growth.

He was chronically ill – looking, pale with a fungating ulcer about 10cm x 10cm in the left hemi-scrotum. The ulcer had raised everted edges, and involved the ventrum of the proximal fourth of the phallus. The base of the ulcer was granular, exophytic, bleeding freely on contact and indurated. There were bilateral enlarged and ulcerated inguinal nodes. His two testes were atrophic. A clinical diagnosis of carcinoma of the scrotum was made.

His haemoglobin concentration was 8.3g/dl; serum electrolyte and urea and plain chest radiographic examinations had normal findings. He was sero-negative for HIV I & II. Histology reports of incisional biopsy of the ulcer confirmed the diagnosis of squamous cell carcinoma. This was staged D.

The patient had supportive treatment, near-total scrotectomy, scrotal reconstruction with rotated upper thigh flaps and bilateral selective inguinal lymphadenectomy. The inguinal defects were covered with rotated pedicled supra-pubic flaps.

He had satisfactory wound healing and post-operative recovery. He was discharged 4 weeks post-operation,

followed up at Urology outpatient clinic and was being worked up for adjuvant cytotoxic chemotherapy but he was lost to follow-up after another 8 weeks.

#### Patient No 4

A 62-year old brick layer, referred from a specialist hospital in Port Harcourt to UPTH, presented with Left-sided scrotal ulcer of more than 1 year duration. The lesion started as a small painful scrotal papule which progressively increased in size. No history of scrotal trauma. The lesion ruptured into an ulcer 6 months before presentation. The ulcer which bled freely on contact was non-healing and became associated with progressive weight loss, lethargy and waist pain. He was married to two wives and had 12 children.

He was chronically ill-looking, middle aged, and pale, febrile with bilateral inguinal lymphadenopathy. The inguinal nodes were matted together, forming masses in both groins with supra-pubic, scrotal and perineal oedema.

His pulse was 88 beats/minute and blood pressure 120/80mmHg. The heart sound 1 & 2 were normal with no murmurs.

He had a fungating ulcer at the left hemi-scrotum involving parts of the right hemi-scrotum and the median raphe. The floor was necrotic, had recent haematoma; the edges were raised and everted, and the floor bleeding freely on contact. A clinical diagnosis of carcinoma of the scrotum, which was staged D, was made.

His fasting blood sugar level was 5.4mMol/L, and packed cell volume 26%. He was sero-positive for HIV I & II but sero-negative for hepatitis B surface antigen (HBsAg). Histology reports of incisional biopsy of the scrotal ulcer showed he had eccrine porocarcinoma of the scrotum.

He was given supportive treatment including blood transfusion and antiretroviral therapy. He had near-total scrotoectomy, selective inguinal lymphadenectomy. His condition was too severe for extensive exploration. He had a tortuous post-operative recovery and died on admission 4 weeks post-operatively.

#### Patient No. 5

This patient was a 59-year old petty patent drug trader who presented with complaints of a wound at the scrotum and masses in the left groin first noticed 10 months before presentation. The scrotal ulcer started as a black painless papule in the left hemi-scrotum became painful about 6 months before presentation and ulcerated 4 months after onset of pain. He had progressive lethargy and weight loss. He had no known family history of scrotal cancer or cancer generally. He smoked an average of 5 cigarettes daily for 15 years. He also took an average of 4 bottles of beer (about 3000ml) at a time

frequently a week for 39 years. He was married to a wife and had 4 children.

He was middle-aged, chronically ill-looking with an ulcerated mass in the left hemi-scrotum. The ulcer had sero-purulent discharges, proud granulation tissues and raised everted edges. There was oedema of the surrounding tissues, induration and oedema of the mons pubis with masses of matted bilateral inguinal nodes. A clinical diagnosis of carcinoma of the scrotum was made.

His PCV was 26%. He had normal results of serum electrolyte, urea, creatinine, fasting blood sugar assays and plain chest radiographic examinations. His malignancy was confirmed histologically and staged D.

He had wide excision of the wound with 2-3cm margins, selective inguinal lymphadenectomy and inguinal wound closure with rotated supra-pubic flaps. He was discharged the 20<sup>th</sup> day post-operation, scheduled for cytotoxic chemotherapy after preparation during outpatient clinic reviews. He was lost to follow-up 10 weeks later.

#### Table 1: The Ray and Whitmore Staging System (12) with Post-Operative Status of the Patients.s

The Ray and Whitmore Staging System.<sup>[12]</sup>

Patient/Post Operative Status

Stage A

A1 - Disease localized to scrotum

A2- Locally extensive disease Involving adjacent structures (Penis, perineum, testis, and/or Cord structure, pubic bone) by Continuity but without evident Metastasis

Stage B - Regional metastasis (inguinal or Ilio-inguinal), resectable

Stage C - Regional metastasis, nonre-1 Discharged, LTFU 3<sup>RD</sup> WK Post-OP

Sectable 5 Discharged, LTFU16<sup>TH</sup> WK Post-OP

Stage D Distant metastases 2 Discharged, LTFU 8<sup>TH</sup> WK Post OP 3 Died 4 weeks Post OP

4 Discharged, LTFU,13 WKS post OP

LTFU=lost to follow up; WK= week. OP=operation



**Figure 1: Squamous Cell Carcinoma of the Scrotum in Port Harcourt, Southern Nigeria, Patient No. 3**  
**Note:-Raised everted edges involving anterior parts of the scrotum, ventrum of proximal fourth of the phallus. There is contact bleeding. Note also ulcerated, enlarged and matted left inguinal nodes. There is oedema of proximal parts of both thighs and groins from lymphadenopathy and malignant infiltration.**



**Figure 2: Intraoperative photograph of the lesion (Figure 1) at the stage of skin cover. The phallus was retained, ulcerated nodes excised and skin closed with rotated flaps.**

Average age at presentation = 64.6 years, range =59-70 years.

Average duration of illness before presentation = 3.8 years.

All the tumours were squamous cell carcinomas except the eccrine poro carcinoma recorded in an HIV positive patient.

One patient (4) died 4 weeks post-surgery the rest were lost to follow- up after 8 to 12 weeks of Surgical Out-patient Clinic review.

The tumours observed at surgery were more distributed at the fascio-cutaneous layers of the scrotum, outside the internal spermatic fascia. A distinct layer of areolar tissue, which macroscopically appeared tumour-free, existed between the testis, pampiniform plexus and the spermatic cord. Involved inguinal nodes were easily stuck to the pubic bone and the inguinal vascular structures. Three cases had bilateral malignant inguinal lymphadenopathy.

## DISCUSSION

UPTH, Port Harcourt is a major treatment Centre for malignant and other diseases in South Southern Nigeria, especially the Niger Delta States, and receives referrals from several states in the region. The finding of 5 histologically confirmed cases of primary cancer of the scrotum of a total of only 7 clinically diagnosed cases in 15 years attests to the rarity of this disease in this region, and partly explains the dearth of literature on it in the country. The study also brings to the fore features that were common to the patients, natural history of the disease, histological variant and its prognosis.

Clinical features of the disease were found consistent with those recorded elsewhere.<sup>[13, 4, 5]</sup> in patients with squamous cell carcinoma of the scrotum. The ages at presentation for treatment (average of 64.6years; range 59-70years) agree with observations from eastern Nigeria<sup>[15]</sup> and those from black populations of the USA,<sup>[2]</sup> Barretos, Saopaulos Brazil.<sup>[1]</sup> and extra-mammary Paget's disease of the scrotum(EMPDS) in Shanghai, China.<sup>[16,17,18]</sup> and Japan.<sup>[14]</sup> However the ages are lower than those of patients with extra mammary Paget's disease of the scrotum (EMPDS) observed in several studies in the USA.<sup>[19]</sup> Nanjing.<sup>[20]</sup> and Chengdu,<sup>[21]</sup> in China, Venezuela<sup>[22]</sup> and the Netherlands.<sup>[23]</sup> It appears squamous cell carcinoma of the scrotum affects patients at lower ages than EMPDS, but this comparison requires a global multi-centre comparative study.

The study did not reveal any predominant occupational aetiology for scrotal cancer but the occupational distribution of the 5 patients revealed that all the patients were of low socio-economic and educational backgrounds. It is common knowledge that these handicaps are frequently associated with poor health education, ignorance and poor personal hygiene. We may surmise that those factors facilitated the development of malignancy in the patients. However, it is preposterous to make absolute inferences in this study because of the small sample size. The rarity of the tumour, even in developing countries including Nigeria,<sup>[15]</sup> suggests that the absolute cause of primary cancer of the scrotum transcends only low socio-economic factors. This is because in most developing societies the poor currently

form the majority of the population.<sup>[24]</sup> The disease therefore should be very common. Secondly in the State of New York (the USA) Weinstein et al<sup>[25]</sup> observed that managerial or professional staff of establishments, assumed to have had higher socioeconomic status, developed non-melanoma scrotal skin cancer almost as frequently as skilled, semi-skilled or unskilled workers. Again, of primary scrotal cancer (SCC) in the USA generally, Mastoso et al<sup>[13]</sup> stated that the disease “currently affects white-collar professionals.” What is however plausible is that these adverse socio-economic factors played a role in the neglect of the initial scrotal lesions and delayed presentation for treatment which are typical features of the disease and its patients in Port Harcourt. The patients delayed for an average of 3.8 years (range 10 months to 10 years) before presentation for treatment after noticing an initial scrotal lesion.

Another factor that may be important as a risk factor of primary scrotal cancer is cigarette smoking. Although cigarette smoking has been associated with various malignancies,<sup>[26,27,28]</sup> confirmatory evidence linking it with aetiology of primary scrotal cancer is lacking in the literature. Most of the studies recording cigarette smoking were institutional case reports with small sample sizes. However two of the five patients in this index study were moderately heavy cigarette smokers, one smoking 5 cigarettes per day for 15 years, and the second 2 per day for 50 years before presentation. Saunders S et al<sup>[29]</sup> recorded history of heavy cigarette smoking (15-20 cigarette per day lifelong) in a 55-year old patient with primary scrotal cancer who was also exposed to mineral oils for a long time. In that report prominence was given to the prolonged contact with mineral oils. Cigarette smoking may induce scrotal malignancy either due to its carcinogenic contents or its depression of immunity, or a combination of these and other factors.<sup>[30,31]</sup>

A limitation of this study was the challenge encountered in the investigation of the patients, including the two that died on admission. They were too poor to provide for many tests especially staging investigations, e.g. CT – scanning and MRI studies which were available in the hospital. The result of this was that the distinction between stage C and D had to be made mostly on clinical grounds. Secondly local circumstances did not favour intra-operative use of frozen-section histology that could probably have improved tumour-free margins. The Ray and Whitmore staging (Table 1) reproduced herein gave a convenient adaptation of a staging method to difficult clinical situations.

The preponderance of squamous cell carcinoma in the series agrees with the reports of Azike JE et al,<sup>[15]</sup> in eastern Nigeria and findings in various black communities in the USA,<sup>[2]</sup> and Brazil.<sup>[1]</sup> This variant of scrotal cancer has been reported in various studies to be associated with poorer prognosis,<sup>[2]</sup> than observed in patients with EMPDS.<sup>[16,17]</sup>

There were no additional primary synchronous malignancies in the series. There are reports in the literature citing studies with observation of additional extra-scrotal primary malignant tumours occurring with primary carcinoma of the scrotum. McDonald<sup>[32]</sup> reported that 4 of 12 patients with squamous cell carcinoma treated by him had respectively additional parotid tumour, squamous cell carcinoma of the oropharynx, sub-bungal squamous cell carcinoma in the fingers, and in the fourth, multifocal SCC in the body. Other additional tumours were reported in different studies to involve the gastrointestinal tract, extra-scrotal cutaneous sites, T-cell lymphoma and the lungs.<sup>[33,34,35,36,37]</sup> Dean was reported as the first to report cases of additional primary malignancies in patients with primary scrotal cancer.<sup>[38]</sup> McDonald reasoned that non-cutaneous additional primary malignancies were either “coincidental”, developed as an expression of “generalized proneness to malignancy”, occurred consequent upon immunopaenia, or as a result of “exposure to carcinogens active in different parts of the body”. Although the issues of under-diagnosis (especially since we could not do all investigations) and under-reporting elsewhere in Nigeria might have been limitations, additional synchronous primary malignancies in patients with primary cancer of the scrotum are extremely rare in Southern Nigeria. We suggest that genetic factors and high immunity may have a role.

The aim of treatment was palliation, with reduction of the bulk of loco-regional disease to facilitate the effects of adjuvant systemic cytotoxic chemotherapy. Facilities for radiotherapy were not available in the hospital. Radiotherapy was available about 1000km from Port Harcourt. Considerations of cost of radiotherapy, low patients’ performance status, poverty and inability of the patients to undertake long distance travels and provide accommodation at the Radiotherapy Centre were hindrances to our choice of palliative radiotherapy. Squamous cell carcinoma of the scrotum has however not shown substantial sensitivity to both radiotherapy and cytotoxic chemotherapy.<sup>[32]</sup> Andrews et al.<sup>[39]</sup> observed that patients with advanced stages of scrotal SCC, similar to findings in this study, had no improved survival advantage with adjuvant radiotherapy. Usami and Kotake,<sup>[40]</sup> on the other hand, found that a combination of methotrexate, bleomycin and cisplatin was effective as primary mode of treatment for these cases with involvement of inguinal lymph nodes.

Wide surgical excision of the scrotal tumour, as observed from different centres,<sup>[41,4,18,42]</sup> remains the mainstay of the treatment of loco-regional disease in our Centre. This practice has been reinforced by our intra-operative findings that, in spite of the extent of local disease, in all operated cases, the tumour was almost all virtually macroscopically distributed to the fascio-cutaneous layers of the scrotal wall mainly outside the internal spermatic fascia, separated from the deeply lying testis and spermatic cord structures by a cleavage plane

of loose fatty and areolar tissue. This plane seemed in all cases macroscopically free of malignancy and could be exploited to free the testis, epididymis and cord of the disease and ensure reasonable tumour-free margins.

The non-involvement of the testis in the five advanced scrotal malignancies in this study agrees with observations of Southam et al,<sup>[43]</sup> who reported that the testis was rarely involved in the spread of primary squamous cell carcinoma of the scrotum. In their study, they had only 6 (4.2%) of 141 cases of primary squamous cell carcinoma involving the testis. This suggests that, as expected the spread of the tumour in the scrotum is mainly centrifugal, involving more of the areas of blood supply and lymphatic drainage of the scrotum<sup>[44]</sup> than centripetal spread which can easily involve the testis and spermatic cord structures.

Groin lymphadenopathy which was bilateral in 3 cases became a major challenge. Extensive groin disease, supra-pubic and perineal oedema, and involvement of the pubic bone in two cases made achievement of tumour-free margins and adequate skin cover difficult. In two patients delayed primary skin cover and later use of rotated vascularized local upper thigh and supra-pubic flaps, respectively, were most useful.

Involved nodes were very obvious especially in the patients with malignant lymph node ulceration and matting together of the nodes. Although Dean and others<sup>[38]</sup> advised that prior nodal biopsy and histological confirmation of malignant lymphadenopathy should be made before inguinal lymphadenectomy in primary squamous cell carcinoma of the scrotum, we preferred selective lymphadenectomy in these patients based on clinical observations. Complaints from the patients, increased cost of treatment and local delays in obtaining histological reports in our setting were some of the factors we relied upon to justify presumptive lymphadenectomy on clinical grounds. We did not observe immediate post-operative lymphoedema and unexpected wound infections which could complicate lymphadenectomy.

We considered extensive pelvic dissection of little therapeutic value to the patients because of the experiences of others,<sup>[32]</sup> low performance status of the patients, and the high burden of loco- regional and distant metastatic disease. It was not possible to make timed survival or prognostic calculations since 4 of the 5 patients did not comply with follow-up schedules. We attributed this attitude to ignorance and inability to sustain cost of continued supportive therapy and evaluation for proposed adjuvant treatment. Mortality in three out of seven suspected to have primary squamous cell carcinoma of the scrotum smacks of very poor prognosis.

## CONCLUSION

Primary cancer of the scrotum was found rare in South-southern Nigeria. Patients presented late for treatment with an average delay of 3.8 years. Average age at presentation was 64.6 years with a range of 59 to 70 years. Almost all cases were squamous cell carcinomas, stages C and D and affected the left hemiscrotum. Wide local excision was done in each case, a procedure that was enhanced by a characteristic centripetal spread of the tumour. Inguinal malignant lymphadenopathy was advanced and became a challenge at dissection. Rotated pedicled flaps were appropriately used for skin closure. The use skin grafts was not considered likely to be of better advantage to close the extensive wound surfaces.

One patient, who also had human immunodeficiency virus infection died 4 weeks post operation. Four were lost to follow-up and did not comply with treatment schedules. The findings were similar to those with same stages of the disease elsewhere.

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