Original Article

Testicular Cancer at the University of Port Harcourt Teaching Hospital: A 10-year Retrospective Review

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Abstract

Background: Testicular cancers are rare malignancies. They are however very common in males aged 15–40 years. Reports of increasing incidence of testicular cancer in western countries have been noted. Despite the increasing incidence, mortality has remained low in these countries. There are few publications on the management of testicular tumors in Nigeria. **Aim:** The aim of this study was to determine the hospital prevalence and highlight our experience in the management of patients with testicular cancer. **Materials and Methods:** This was a 10-year retrospective study on patients diagnosed with histologically confirmed testicular cancer from January 2009 to December 2018. The case records were retrieved. Data obtained included biodata, clinical presentation, investigations, treatment received and outcomes. Data analysis was carried out using SPSS version 20.0. **Results:** Eleven patients with testicular cancer were managed during the study period, constituting 0.01% of new cases seen in the hospital. Peak age was 20–29 years (54.55%), with a mean age of 29.27 ± 9.51yrs. The most common presentation was painless scrotal swelling, observed in nine (81.8%) patients. Nine (81.8%) patients presented six months or more after onset of symptoms with advanced disease. Distant metastasis was seen in two (18.2%) patients. Right sided disease was found in seven (63.6%) and left sided disease in four (36.4%). All had radical inguinal orchidectomy. The most common histological diagnosis was seminoma in 8 (72.7%) patients. All the subjects were offered four courses of chemotherapy with bleomycin, etoposide and cisplatin. However, only four (36.4%) completed the chemotherapy. A statistically significant association was observed between the duration of symptoms and the disease stage (P = 0.003), and between number of chemotherapy sessions and survival (P = 0.02). **Conclusion:** Testicular cancer was an uncommon condition in the catchment area of the University of Port Harcourt Teaching Hospital, affecting relatively young men. The commonest presenting complaint was painless scrotal swelling. Most patients presented with Stage II disease, with seminoma being the commonest histopathology. All had surgical treatment; adjuvant chemotherapy improved 5-year survival. Public education is necessary to surmount sociocultural barriers to effective management of testicular tumors in our environment.

Keywords: *Chemotherapy, inguinal orchidectomy, outcomes, testicular cancer*

Abstrait

Contexte: Les cancers testiculaires sont des malignités rares. Ils sont cependant très fréquents chez les hommes âgés de 15 à 40 ans. Des rapports d'incidence croissante de cancer testiculaire dans les pays occidentaux ont été notés. Malgré l'incidence croissante, la mortalité reste faible dans ces pays. Il y a peu de publications sur la gestion des tumeurs testiculaires au Nigéria.
Objectif: Déterminer la prévalence hospitalière et mettre en évidence notre expérience dans la prise en charge des patients atteints d'un cancer des testicules.
Matériaux et Méthodes: Il s'agissait d'une étude rétrospective de 10 ans sur des patients diagnostiqués avec un cancer testiculaire confirmé histologiquement de janvier 2009 à décembre 2018. Les dossiers ont été récupérés. Les données obtenues comprenaient les bio-données, la présentation clinique, les investigations, le traitement reçu et les résultats. L'analyse des données a été effectuée à l'aide de SPSS version 20.
Résultats: Onze patients présentant le cancer testiculaire ont été gerés pendant la période d'étude, constituant 0.01% de nouveaux cas vus dans l'hôpital. L'âge maximum était de 20–29 ans (54,55%), avec un âge moyen de 29,27 ± 9,51 ans. La présentation la plus commune était le gonflement scrotal indolore, observé sur neuf (81.8%) patients. Neuf (81,8%) patients sont examinés après six mois ou plus après début des symptômes avec la maladie avancée. On a observé la métastase à distance sur deux (18.2%) patients. On a observé la maladie du côté droit sur sept (63.6%) patients et la maladie du côté gauche sur quatre

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(36,4%) patients. Tous ont eu l'orchidectomie inguinale radicale. Le diagnostic histologique le plus commun était le seminome sur 8 (72.7%) patients. Tous les patients ont suivi quatre séances de chimiothérapie avec la bléomycine, l'étoposide et le cisplatine. Toutefois, quatre patients seulement (36,4%) ont terminé la chimiothérapie.
Une association statistiquement significative a été observée entre la durée des symptômes et le stade de la maladie (P = 0,003), et entre le nombre de séances de chimiothérapie et la survie (P = 0,02).
Conclusion: Le cancer testiculaire était une condition rare dans la zone du Centre Hospitalier Universitaire de Port Harcourt, affectant des hommes relativement jeunes. Le symptôme le plus commun observé était le gonflement scrotal indolore. La plupart des patients présentait la maladie de stade II, avec le seminome étant l'histopathologie la plus commune. Tous ont reçu le traitement chirurgical; la chimiothérapie adjuvant a amélioré la survie de 5 ans. La sensibilisation du public est nécessaire pour surmonter les obstacles socioculturels à une prise en charge efficace des tumeurs testiculaires dans notre environnement.

Mots-clés: *Cancer testiculaire, orchidectomie inguinale, chimiothérapie, résultats*

Introduction

Testicular cancers comprise a number of different neoplasms, depending on the cell of origin and the typical age at presentation.[1,2] Testicular cancers are relatively rare and account for approximately 1% of all male cancers globally.[3,4] However, in many countries they are the most commonly diagnosed malignancy among men between 15–40 years.[5] Studies from Ile-Ife,[6] Kano,[7] Enugu[8] and Tanzania[9] attest to its relatively low incidence in Africa. The incidence of testicular cancer has been noted to be increasing, especially in industrialized countries.[10-12] Genetic and environmental factors appear to play a role in this rise.[11]

Testicular cancers can be subdivided into germ cell and non-germ cell tumors. Ninety-five percent of all testicular tumors are germ cell tumors.[11] Germ cell tumors are classified into seminomatous and non-seminomatous germ cell tumors.[1] Non-seminomas are further subdivided into teratomas, yolk sac tumor, embryonal carcinoma, choriocarcinoma, and mixed tumors.[13]

The risk factors for developing testicular cancers include young age, Caucasians and family history.[14] Other risk factors include undescended testes,[15,16] personal history of testicular cancer,[17-19] and premalignant conditions.[17]

Differential diagnosis of testicular cancers includes epididymo-orchitis, torsion, testicular cyst and testicular hematoma.[20,21]

This study was designed to determine the hospital prevalence and describe our experiences in managing testicular cancers, highlighting the presentation, investigations, treatment and outcome.

Patients and Methods

This was a retrospective study carried out at the University of Port Harcourt Teaching Hospital (UPTH), a tertiary hospital located in Port Harcourt, the capital city of Rivers State, Nigeria. It receives referrals from all parts of the state, as well as from communities in neighboring states in the country.

All patients with histologically confirmed testicular cancer diagnosed between January 2009 and December 2018 were included in the study. The case notes of patients were retrieved. The age, educational status, occupation, presentation, duration of symptoms before presentation, risk factors, side involved, results of investigations, treatment received and outcomes were evaluated. Patients with features of testicular cancer without histological confirmation and those with incomplete information were excluded.

The data was entered using Microsoft Excel ® version 2010 and transferred into the Statistical Package for Social Sciences (SPSS) version 20 for analysis. Categorical data was presented in the form of frequencies and percentages using tables, graphs or pie charts. Continuous variables were presented in Means, Median and standard deviation.

Results

The total number of new cases that presented to the hospital in the study period was 111,797. Eleven patients were diagnosed with testicular cancer within the study period, constituting 0.01% of new cases seen. This was after excluding eight patients from the study: five patients who could not afford a computerized axial tomography (CT) scan and were excluded because the disease could not be staged appropriately, and three patients whose case notes could not be found even though they were recorded in the ward register as testicular carcinoma cases.

The 11 patients included in the study had an age range between 17–53 years; the mean age was 29.27 ± 9.51 with a median of 27 years. Most of the patients (6, 54.5%) were within the 20–29 years age group. Majority of the patients (9, 81.8%) had had at least secondary education and most of them (7, 63.6%) were single. Students, 5 (45.4%), formed the largest group [Table 1].

Clinical presentation

Nine patients (81.8%) presented with painless scrotal masses, one (9.1%) with multiple, non-tender, firm abdominal masses and one (9.1%) as Fournier's gangrene after a scrotal orchidectomy as treatment for a testicular mass.

The duration of symptoms before presentation ranged from 4 months to 22 months [Table 2]. Only two patients presented less than 6 months from onset of symptoms; the mean duration from onset of symptoms to presentation was 10.3 ± 5.0 months.

Median duration of symptoms was 10 months. Seven (63.6%) of the tumors were right sided and four (36.4%) were left sided. No patient presented with a painful scrotal mass.

The patient who presented with multiple abdominal masses had been scheduled for exploratory laparotomy before the correct diagnosis of testicular cancer was made by the urologists. The patient that had scrotal orchidectomy had done an incisional biopsy for a testicular mass in another hospital before presentation; there was associated ipsilateral inguinal lymphadenopathy.

Patient evaluation

No identifiable risk factors were found in nine (81.8%) patients. Two (18.2%) patients had undescended testes with orchidopexy having been performed before puberty. All patients had tumor markers done. Alpha-fetoprotein (AFP) alone was elevated in 2(18.2%) patients, human chorionic gonadotrophin (HCG) alone was elevated in 5(45.5%), both HCG and AFP were elevated in 1(9.1%), and lactate dehydrogenase (LDH), HCG and AFP were all elevated in one patient. Two patients had normal tumor marker levels.

All the patients had ultrasound scan, which suggested testicular malignancy in each case. They all also had abdominal computerized tomography (CT) scan and chest x-ray to stage the disease. All the patients could not afford a chest CT scan in addition to an abdominal CT scan because of the added cost.

They were staged using the American Joint Committee on Cancer (AJCC) staging criteria. The distribution of the tumor stages is shown in Table 3, with most of the patients (7, 63.6%) presenting with stage II disease. There was no significant difference in duration of symptoms between patients who presented with stages I and II disease; however, those who presented with stage 3 disease had significantly longer duration of symptoms than those who presented with stage I or II disease [Table 4].

Table 1: Socio demographic characteristics

Characteristics	Frequency (n = 11)	%
Age		
<20	1	9.09
20–29	6	54.55
30–39	3	27.27
≥40	1	9.09
Level of education		
No formal education	1	9.1
Primary	1	9.1
Secondary	5	45.5
Tertiary	4	36.3
Marital status		
Single	7	63.6
Married	4	36.4
Occupation		
Student	5	45.4
Artisans (painter, mechanic)	2	18.2
Engineer	2	18.2
Business man	1	9.1
Banker	1	9.1

Treatment

All the patients had radical groin exploration and inguinal orchidectomy. The commonest histological type was seminoma (8, 72.7%); there were 2 (18.2%) cases of embryonal carcinoma and one (9.1%) of yolk sac tumor.

They were all offered 4 courses of bleomycin, etoposide and cisplatin chemotherapy. The patient's performance status was assessed before each treatment cycle. Each cycle consisted of cisplatin 20 mg/m^2 IV days 1–5, etoposide 100 mg/m^2

Table 2: Duration of symptoms

Characteristics	Frequency (n = 11)	%
Duration of symptoms (months)		
<6	2	18.18
6–12	7	63.64
13–18	1	9.09
19–24	1	9.09
Mean	10.30 ± 5.0 months	

Table 3: Distribution of stage of disease at presentation

Stage of disease	Frequency (n = 11)	%
I	2	18.18
II	7	63.64
III	2	18.18

Table 4: Mean duration of symptoms and stage of disease at presentation

Stage of disease	Duration of symptoms (months)	ANOVA (P value)
	Mean ± SD	
I	5.50 ± 3.54	12.03 (0.003)
II	9.28 ± 2.06	
III	18.50 ± 4.95	

Post hoc analysis (Tukey HSD): I vs II, P = 0.268; I vs. III, P = 0.0041; II vs. III, P = 0.0084

Table 5: Distribution of number of Chemotherapy cycles

No. of chemotherapy cycles	No. of patients (n = 11)	%
0	3	27.27
1	2	18.18
2	2	18.18
4	4	36.36

Table 6: 5-year survival of patients with testicular cancer

Status	Frequency	%
Survived	7	63.6
Died	4	36.4

Table 7: Tumor stage, mortality, and 5-year survival in patients

Stage	Number of patients	Mortality at 5 years	Number alive at 5 years	5-year survival %
I	2	0 (0%)	2	100
II	7	2 (28.6%)	5	71.4
III	2	2 (100%)	0	0

Table 8: Comparison of mean number of chemotherapy cycles between survivors and deaths at 5 years

Outcome	Number of chemotherapy sessions	*t*-test (*P* value)
Survived	2.9 ± 1.5	2.85 ($P = 0.02$)
Died	0.5 ± 1.0	

IV days 1–5, and bleomycin, 30 units IV, days 2, 9, and 16. A cycle lasted 21days. Two patients with stage 3 disease had neoadjuvant chemotherapy to downstage the tumor before radical orchidectomy. One patient who presented with wound breakdown following previous scrotal orchidectomy before referral to us, had repeated debridement for Fournier's gangrene, whereas another had bilateral chest tube inserted for bilateral pleural effusion.

Three patients refused chemotherapy despite adequate counseling. Two presented with stage II disease and one patient presented with stage I disease. Only 4 patients completed 4 courses of chemotherapy. One patient presented with stage I disease and three patients presented with stage II disease [Table 5].

Outcomes

The 5-year survival rate was 63.6% (7 out of 11). All patients with stage I disease were alive at 5 years, whereas all with stage III disease had died. Five of the 7 patients with stage II disease were alive. Those who had survived to 5 years had had significantly higher number of chemotherapy cycles than those who had died [Tables 6–8].

Discussion

Testicular cancer is a rare malignancy in Africans as observed in this study with eleven cases in 10 years and constituting 0.01% of new cases seen in the hospital during that period. Previous African studies have also noted the rarity of the disease.[6-9] This is at variance with other European and North American studies which reported higher prevalence and increasing incidence.[10-12] Numerous factors have been mentioned to explain this increase in the developed world.[14-17] Comparing older African studies[22-24] with more recent ones reveals no appreciable increase in incidence.[6-9] The low incidence of cryptorchidism in Africa may be a cause for the rarity on the continent. Cryptorchidism is the most characteristic risk factor for testicular cancer.[11] The 20 – 29-year age range had the highest number of patients in our study; other studies have reported similar findings.[6-9]

Most of our patients presented with stage II and stage III disease. The mean duration from onset of symptoms to presentation was 10.27 ± 5 months. A common cause of diagnostic delay, defined as the time interval from the onset of the first symptom to confirmation of diagnosis, is late presentation.[25-29]Late presentation ultimately leads to delay in treatment. An association was noted between the duration of symptom and disease stage. Although there was no significant difference in duration of symptoms between patients with stages I and II disease, those who presented with stage III disease had significantly longer duration of symptoms than those with stage I or stage II disease. This suggests that public education on the significance of symptoms related to testicular carcinoma may help with earlier stage presentation.

Physicians and patients both contribute to the delay in treatment. Patient related factors include late presentation,[8,9] embarrassment,[17] low educational status,[8,30] denial, ignorance[15-17] and poor access to health care facilities.[8,9,31,32] Physician factors include misdiagnosis[15] and treating metastasis instead of the primary disease.[17] The rarity of testicular cancer also serves as a reason for presentation, diagnostic and treatment delays.[25,27] Testicular self-examination,[33] awareness programs,[25] proper scrotal examination[33] and a high index of suspicion are ways of reducing delays in diagnosis and treatment.[17]

Most of our patients presented with painless scrotal swelling as observed in other studies.[6,17,18] Testicular cancers can present in a variety of ways and mimic other diseases.[34] Other forms of presentation include scrotal pain, trauma to the scrotum, gynecomastia, loin pain and back pain.[19,35]Gastrointestinal symptoms and lower limb edema may occur with compression of abdominal organs by retroperitoneal nodes.[17]Some researchers have noted that when there is associated pain, patients tend to present earlier.[9]

There were more right sided tumors than left sided. This is similar to the observation in other studies carried out in both Africa and Europe.[6-9,25,36] The later descent of the right testes relative to the left may account for this difference.[17]

Most patients in this study had no identifiable risk factor. Hanna *et al.*[11] reported that 90% of patients with testicular cancer had no identifiable risk factor. The identifiable risk factor in this study was undescended testes. Similar risk factor has been noted by other researchers.[16,17] Hormonal changes at puberty are important in development of testicular cancer in patients with undescended testes.[11] Orchidopexy does not remove the risk of developing testicular cancer but allows better surveillance of the relocated testes.[16]

Seminoma was the commonest histological type in our study. This is similar to other studies conducted in Africa[8,9] and in

the western countries. However, this is at variance with the finding in Ilorin, Nigeria, which reported yolk sac tumor as the most common tumor. In that report, however, most of the patients were in the first decade of life.[37] Yolk sac tumors are believed to be the most common prepubertal testicular tumor worldwide.[38] Only one of our patients, a 17-year-old, had yolk sac tumor.

Most of the patients presented with stage II disease, similar to findings in other African studies.[8,9] Later presentation necessitates more cycles of chemotherapy, increased need for second line agents and increased cost of care.[27] The patients may present with poor performance status and be unfit for chemotherapy, hence only supportive treatment can be offered in such situations. As indicated in Tables 6 and 7, four patients died within 5 years. Three of the four patients who died and did not get chemotherapy, did not because they could not afford the chemotherapy treatment. They had spent their resources on treatments with numerous "chemists" and alternative medical practitioners before presentation.[39] Death with early presentation is uncommon.[25] In this study, all the patients with stage I disease survived. The high cure rate in the developed countries has not been repeated in resource poor countries; this could be due to low level of education, lack of awareness and poverty. Two patients had neoadjuvant chemotherapy because the tumor was too large to excise via an inguinal approach. One of the two patients who had neoadjuvant treatment rejected orchidectomy and became worse eight months later. He then had repeat neoadjuvant chemotherapy and later accepted orchidectomy. This patient later succumbed to his disease after 24 months of diagnosis. Convincing patients to accept orchidectomy in Africa is largely a herculean task.[8]

Seminomas are believed to be exquisitely radiosensitive and chemosensitive. In this study, no patient received radiotherapy because it is not available in our region. In our study, at 5 years, survivors had had significantly higher mean number of chemotherapy cycles than those who had died. As indicated in Table 7, seven patients were alive at 5 years and of these, four of them completed their course of chemotherapy.

The 5-year survival rate of testicular cancer in the developed world is over 95%.[4] The 5-year survival in this study is 63.6%. The five-year survival in Tanzania is 22.2%.[9] Ugwumba *et al*.[8] also noticed poor outcomes in their study. In the Tanzania study only 2 patients (3.6%) received cisplatin-based chemotherapy and this may account for their poor 5-year survival.

Even though described as a model for curable cancer since the advent of cisplatin-based chemotherapy, in Africa however, as observed in our study and corroborated by other African research, the treatment outcome is still relatively poor compared to that obtainable in the western countries. This is as a result of the interplay between economic and sociocultural factors working against effective treatment of testicular cancers.[4,6-8]

Health awareness about testicular cancers, especially testicular self-examination would aid early presentation to the hospital if a testicular mass is noticed, and this will lead to early diagnosis and treatment. Adherence to scheduled chemotherapy regimen, provision of radiotherapy centers, and subsidizing the cost of treatment for patients would hopefully lead to an improvement in the overall outcome for patients with testicular cancers.

Conclusion

Testicular cancer was an uncommon condition in the catchment area of the UPTH, affecting relatively young men. The commonest presenting complaint was painless scrotal swelling. Most patients presented with Stage II disease, with seminoma being the commonest histopathology. All had surgical treatment; adjuvant chemotherapy improved 5-year survival. Public education is necessary to surmount sociocultural barriers to effective management of testicular tumors in our environment.

Limitations

This study is limited by the low number of patients with the disease and incomplete information obtained from records.

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Conflicts of interest

There are no conflicts of interest.

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