Testicular cancer: Management challenges in an African developing country

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Background. Advances in oncology have greatly improved the prognosis of testicular cancer. In developing countries, however, the outcome is still poor.

Patients and methods. Twenty-four patients managed for testicular cancer at two centres (University of Nigeria Teaching Hospital, Enugu, Nigeria, and JAMA Urological Clinic, Enugu) between April 1984 and March 2003 were prospectively studied. Histopathological data were obtained in all cases.

Results. Peak age incidence was 20 - 29 years. Testicular swelling was the principal complaint in 23 patients. The mean interval between onset of symptoms and presentation was 5.3 months. Two patients (8.3%) presented with stage 1 disease, 7 (29.2%) with stage 2, 7 (29.2%) with stage 3, and 8 (33.3%) with stage 4. Seventy-five per cent of tumours were right-sided, and 25% were left-sided. Treatment consisted of radical orchidectomy in all patients and cisplatin-based chemotherapy and radiotherapy in some patients. One patient with a tumour in an intra-abdominal testis underwent laparotomy. The most common histological types were seminoma and embryonal carcinoma. A fifth of the patients died, while half were lost to follow-up. The mean follow-up period was 9 months.

Conclusion. Morbidity and mortality of testicular cancer is high in developing countries. Late presentation, poverty, paucity of resources and the high cost of newer imaging modalities and treatment are major challenges to management. Better health funding and education regarding testicular self-examination is essential.

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Testicular cancer accounted for 1.1% of all cancers in males in the year 2000.[1] The incidence was reported to be lower in non-whites than whites,[2] while a study on a black population showed that, while there was a low incidence of germ cell tumours, non-germ cell tumours had a similar incidence to that in the white series.[3] Testicular tumours arise from germ cells in 94 - 97% of cases. The tumours are classified into seminoma (classic, anaplastic and spermatocytic variants) and non-seminomatous germ cell tumours (embryonal carcinoma, teratocarcinoma, teratoma, choriocarcinoma, and yolk sac tumours). Non-germ cell tumours include gonadal stromal tumours and miscellaneous neoplasms.

The treatment of germ cell tumours has greatly evolved from extirpative surgery only, to cisplatin-based chemotherapy, radiotherapy and retroperitoneal lymph node dissection. These methods have now made the condition being potentially curable, with documentation of excellent survival figures in the developed world.[4] However, in the developing world, treatment outcome is still poor.[5,6] Reasons for this trend include lack of well-established first-line medical treatment that leads to late diagnosis and referral, and unavailability of treatment, poverty and reluctance to accept chemotherapy and radiotherapy.

We examined the presentation, outcome and challenges in the management of testicular cancer in Enugu, Nigeria.

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Patients and methods

The University of Nigeria Teaching Hospital and JAMA Urological Clinic are major referral centres for patients with urological ailments, including tumours, in south-eastern Nigeria, which has a population of over 20 million people. Patients are referred from peripheral hospitals, and the general outpatient department and other clinical departments of the teaching hospital. Diagnosis of testicular tumours was made on clinical grounds (palpable testicular mass with or without abdominal mass), scrotal-abdominal ultrasonography, chest radiograph, intravenous urography and estimation of tumour markers (beta-human chorionic gonadotrophin (bHCG) and alpha-fetoprotein (AFP)). Computed tomography (CT) scanning was not done because it was not available during the study period. Clinical staging was according to the Royal Marsden staging system (Table I). All diagnoses were confirmed by histopathological analysis of the operative specimens. Between April 1984 and March 2003 (19 years), 24 patients were managed in the two centres. Research ethics committee approval was obtained from both institutions for our study. Data for age at presentation, clinical features, investigation and stage of disease were collected. Also assessed were histological type, treatment given, duration of follow-up, special management problems, and outcome.

Data analysis was done by means of SPSS software, version 15 (SPSS, Chicago, IL, USA).

Results

Twenty-four patients were seen in the study period; their ages ranged from 16 to 43 years (mean 28.1 years); 20 (83.3%) were <40 years old, while 4 (16.7%) were >40 years old (Fig. 1).

Clinical presentation

Twenty-three (96%) patients presented with intra-scrotal testicular masses; one presented with an undescended intra-

Table I. Royal Marsden Hospital staging of testicular cancer

Stage	
I	No evidence of metastasis
IM	Rising concentrations of serum markers with no other evidence of metastasis
II	Abdominal node metastases
A	<2 cm in diameter
B	2 - 5 cm diameter
C	>5 cm diameter
III	Supradiaphragmatic nodal metastasis
M	Mediastinal
N	Supraclavicular, cervical or axillary
O	No abdominal node metastases
ABC	Node stage as defined in stage II
IV	
Lung	
L1	<3 metastases
L2	≥3 metastases, <2 cm diameter
L3	≥3 metastases, one or more of which is >2 cm diameter

Stage IV subgroups include H+ (liver metastases), Br+ (brain metastases), Bo+ (bone metastases).

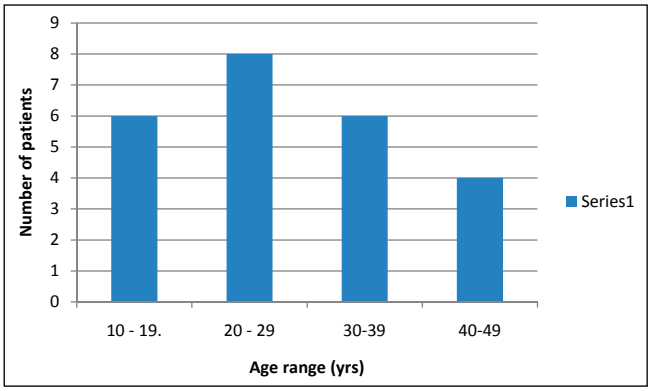

Fig. 1. Age distribution of patients.

abdominal testes mass. Most (75%) tumours were right-sided while 25% were left-sided (Fig. 2). The mean duration of symptoms before presentation was 5.3 months (range 1 - 12 months). Presentations other than testicular mass were abdominal mass (9 – 38%), primary infertility (3 – 13%), gynaecomastia (6 – 25%) and undescended testes in 1 (4%) patient.

Evaluation

Following a full history and physical examination, scrotal-abdominal ultrasonography, chest radiograph and intravenous urography were done. CT scanning was not available, which challenged our management as it limited the staging of retroperitoneal nodes. AFP was elevated in 3 patients, both AFP and BHCG were elevated in 16 patients, and both AFP and BHCG were negative in 5 patients. Most patients presented at stages 2, 3 and 4 (29%, 29% and 33% respectively (Table II). In the absence of CT imaging, we relied on abdominal ultrasonography to detect gross retroperitoneal lymph node involvement. As this is a poor substitute, many of our patients might have been understaged, which was an obvious limitation as staging accuracy of abdominal disease was suboptimal.

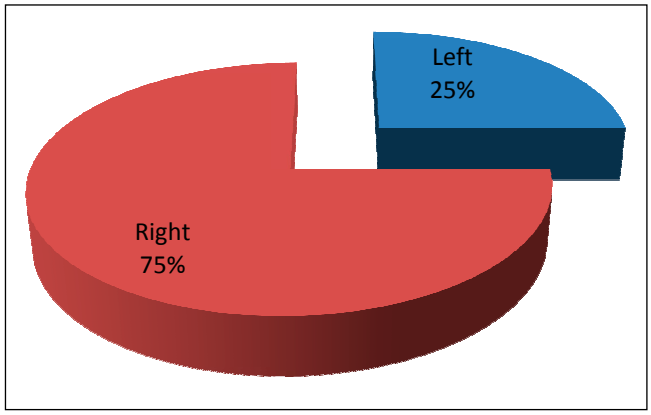

Fig. 2. Laterality of testicular cancer.

Table II. Tumour stage of 24 patients with testicular cancer

Stage 1	2 patients	8.3%
Stage 2	7 patients	29.2%
Stage 3	7 patients	29.2%
Stage 4	8 patients	33.3%
Total	24 patients	100%

Cervical non-supraclavicular lymph node involvement was seen in 3 patients, and supraclavicular lymph nodes in 4; pulmonary metastases occurred in 7, and liver metastases in 1 patient. Definitive diagnosis was based on histopathological analysis of the operative specimen in all cases. The histological types seen were seminoma (8), embryonal carcinoma (8), teratoma (5) and mixed (3) (Fig. 3).

Treatment

Radical orchidectomy and cisplatin-based chemotherapy was the most common treatment combination, and was done in 11 (46%) patients; radical orchidectomy only and radical orchidectomy with radiotherapy in 6 (25%) patients each; and laparotomy, excision of intra-abdominal testicular tumour and chemotherapy was done in 1 (4%) patient. Surgical complications included surgical site infection in 4 patients and adhesive small-bowel obstruction in the patient with intra-abdominal testes.

Retroperitoneal lymph node dissection (RPLND) was not done on any of our patients as they refused consent after being informed of the ejaculatory difficulty that might follow. The reason behind these refusals was fear of infertility, which has strong cultural and social consequences in Africa.

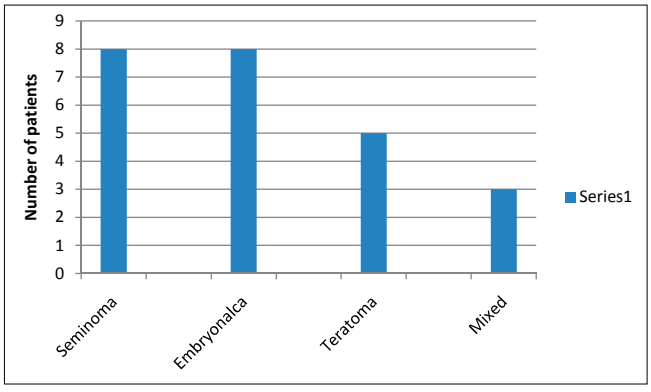

Fig. 3. Histology of testicular cancer.

Cisplatin-based combination chemotherapy using the BEP regimen (bleomycin, etoposide, cisplatin) was commenced 7 - 14 days postoperatively in 10 patients, while 2 patients with scrotal skin involvement received neo-adjuvant BEP to achieve tumour mobility and resectability.

The detailed dosage regimen used was: bleomycin 15 mg as a 24-hour infusion on days 2 and 3; etoposide 100 mg/m^2 intravenously on days 1 - 5; and cisplatin 120 mg/m^2 as a 2-hour infusion with diuresis and hydration on day 4. Four cycles were given at 3-weekly intervals. These intervals were sometimes extended to allow correction of anaemia, leucopenia and thrombocytopenia. Chemotherapy-induced nausea and vomiting were managed by methylprednisolone, metoclopramide and, in the later years of the study (from 1999 to 2003 specifically), 5-HT3 antagonists. Four cycles were chosen as the recommended minimum for all patients to compensate for probable under-staging of our patients, owing to the unavailability of CT scanning.

In all, 12 patients received chemotherapy for a minimum of 3 courses, though these were often irregular as the patients had to buy the drugs, which they usually could ill afford, and no health insurance scheme existed at the time. Chemotherapy complications frequently encountered were stomatitis and haematological. We noted a single case of bleomycin-induced pneumonitis which resolved with conservative management. When a national health insurance scheme started, its coverage was only for contributors' primary health problems, excluding cancer care.

The 6 patients who received radiotherapy were referred to centres in other cities where the facility was available, each at least 600 km away. Another 4 patients failed to receive the recommended radiotherapy because of the prohibitive distance to the radiotherapy centres and the costs involved.

Outcomes

Five patients died within 19 months of presentation and initial treatment response; all had stage 3 disease. Three failed to receive the recommended radiotherapy and re-presented in a moribund condition, while 2 had received 1 cycle of BEP only. The causes of death were superior vena cava obstruction (1), massive bilateral pleural effusion (2) and pulmonary embolism (2).

We defined loss to follow-up as any patient not seen for up to 3 years after presentation and treatment. Twelve patients were lost to follow-up, some as early as 3 months after our primary intervention. Seven patients were alive and well at 3 years and beyond. The mean duration of follow-up was 9 months. Only 3 patients were available for follow-up and well after 5 years.

Discussion

The peak age incidence of 20 - 29 (mean 28.1) years is consistent with other findings.[7-10] However, the distribution of the stages in our series differed markedly from that in the developed world. In developed countries, stage 1 disease is the most common and also shows a consistent rise,[7,11,12] whereas in our study stages 3 and 4 were the most common. The mean interval between onset of symptoms and presentation to a health care facility was unduly long (5.2 months, range 1 - 12 months). Late presentation is thought to be due to ignorance, fear of consequences,[13] long distances to hospitals, and strong beliefs in traditional medicine and religious charlatans.[14] The most common presenting symptom was testicular swelling, which is in agreement with another African study.[10]

An undescended testis and abdominal mass was found in one (4%) patient, which is similar to a 35-year review at Ibadan, Nigeria, where 4% of tumours arose from undescended testes.[15] Our histological distributions of tumours are in agreement with studies from Lagos,[9] where the most common tumours were embryonal carcinoma and seminoma, and from Nairobi, Kenya,[10] where the most common type was seminoma. These findings suggest a similarity in histological patterns between Nigeria (West Africa) and Kenya (East Africa), but the small number of cases does not allow firm conclusions.

Given the small number of testicular cancer, inter-institutional collaborative studies among countries will help to gain data for larger numbers of patients and so determine racial, inter-regional and temporal trends. However, this has not been the case in Nigeria; to our knowledge, only single-centre studies have been published.

The treatment of testicular cancer consists of radical orchidectomy, cisplatin-based chemotherapy radiotherapy, and retroperitoneal lymph node dissection (RPLND). RPLND was not performed on any of our patients owing to their refusal of consent after information regarding ejaculatory difficulty was given. This is a setback to effective treatment, which can be remedied by better patient education. Consent for radical orchidectomy was often given reluctantly as patients perceived the procedure as emasculating, and a threat to manhood, sexuality and fertility.

In our series, radical orchidectomy was performed on all patients. Laparotomy (for excision of a malignant intra-abdominal testis) was done on 1 patient. Surgical complications were limited to surgical site infection and an adhesive small-bowel obstruction that resolved with conservative management in the patient who underwent laparotomy.

Twelve patients received chemotherapy, although this was irregular in most instances because of difficulties in sourcing the drugs, especially cisplatin, from abroad. Other difficulties included the high cost of the drugs, which patients had to bear as there was no health insurance scheme in the country at the time. When a health insurance scheme was initiated, it had a contributory basis, i.e. only salary earners in the public and private sector (comprising less than 10% of the population) were entitled to care, which does not include treatment of malignancies. This invariably means that patients have to fund treatment from meagre personal savings and the goodwill of relatives and friends. Another problem is the formal admission each time a patient requires chemotherapy owing to the lack of a dedicated chemotherapy unit that could offer chemotherapy on a day-care basis and provide home follow-up care.

Our mean duration of follow-up was 9 months. After 24 months, 12 (50%) of our patients were lost to follow-up. A high incidence of loss to follow-up is common in the developing

world.[16] Poverty, ignorance and, possibly, poor doctor-patient communication may be factors. Radiotherapy facilities were not available in our centre (or anywhere in south-eastern Nigeria) during the study period, and patients had to travel to other centres, each at least 600 km from our centre. This usually separated patients from their support base of family and friends and affected their psyche negatively, and often led to delays in commencing radiotherapy. The long distances also resulted in non-completion of radiotherapy in many cases, as patients often had to return home to acquire more funds from relatives and friends.

Testicular cancer has excellent survival figures in the developed world, approaching 97% for low-stage disease.[17] In our series, however, the outcome was poor, with 5 patients dead within 19 months of presentation and 12 (half) of our patients lost to follow-up within 24 months. Only 3 patients were followed up for 5 years. Possible reasons for this poor outcome and, more importantly, the dismal follow-up periods, include late presentation, ignorance, and inadequate patient education regarding the value of follow-up in malignancy even when symptoms are absent. Paucity of resources for tracing patients and home visits is common in our public hospitals.

Conclusion

The management of testicular cancer in our environment includes challenges such as late presentation, high-stage disease at presentation, absence of radiotherapy facilities in south-eastern Nigeria, high cost of drugs, and virtually zero patient awareness of testicular self-examination. A holistic approach is advocated, including a significant increase in health care funding, expansion of the health insurance scheme to cover cancer treatment, improved patient education, and an emphasis on home visits to follow up such patients. The inclusion of teaching testicular self-examination into the primary and secondary school curriculum is also proposed as a preventive strategy.

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