TUMOURS OF THE TESTIS IN NIGERIANS: A TWENTY YEAR REVIEW OF THE LAGOS UNIVERSITY TEACHING HOSPITAL EXPERIENCE

O. E. AKAISO, O. N. EKEKE, G. IJIMAKINWA, C. P. ONYEABOR, D. N. OSEGBE

Urology Unit, Department of Surgery, Lagos University Teaching Hospital, Surulere, Lagos, Nigeria.

Correspondence to: D. N. Osegbe

Urology Unit, Dept. of Surgery, Lagos University Teaching Hospital.

Abstract

Twenty five patients seen at the Lagos University Teaching Hospital between 1979 and 1997 formed the material for this study. We sought to determine the hospital incidence, age distribution, tumour histological types and treatment outcome in these patients. The hospital incidence was 0.25/100,000/year. Germ cell tumours accounted for 74% of cases while nongerm cell tumours made up 26%. The mean age of the patients was 32.7 years. Four of the patients had undescended testes. Testis cancer was commoner on the right (ratio right: left 2:1). Most of our patients presented with advanced disease and could not benefit from Cisplatin based combination therapy. The low hospital incidence of testicular tumours noted in this study and the predominances of germ cell tumours in our patients correlates with reports from other centers in Nigeria and other centers in Nigeria and other African Countries.

Key Words: Testicular Tumours, Nigerians, Epidemiology, Pathology, Managerment.

Introduction

Testicular neoplasm account for 1-2% of all neoplasms in males[1-4]. In Caucasians aged between 20 and 35 years, these tumours are the most common malignancy, excluding leukaemia. However testicular tumours are not common in blacks[1-4]. The hospital incidence in various centers in Africa range from 0.1-0.25/100,000/year[1-4]. The mean lifetime risk of developing a testicular germ cell tumours in these Western Countries is 1/500[5]. Public awareness and campaigns for testicular self examination have an impact on the earlier detection and diagnosis. A patient seen in our outpatient Department with advanced cancer of the testis prompted us to review our experience with Testicular tumours in Lagos University Teaching Hospital over the past 20 years (1979-1997).

Case Presentation

Mr E.O., a 44 year old fisherman from South Eastern Nigeria presented a seven months history of right testicular swelling and right upper quadrant abdominal pain. There was associated nausea, vomiting, weakness and marked weight loss. He denied any history of previous trauma to the testis. Physical examination revealed an asthenic man with bilateral pitting pedal oedema, enlarged right supraclavicular lymph node and bilateral, matted, inguinal lymph nodes which were mildly tender. A hard, irregular, tender and fixed mass was palpated per abdomen, measuring 15cm x 12cm extending from the right hypochodrium down to the right iliac fossa. He also had hepatomegaly. The enlarged right testis measured 6cm x 7cm x 6cm, firm, smooth, non tender with thickened spermatic cord up to the inguinal region. The left testis was normal in size, shape and consistency. A diagnosis of right testicular tumour with retroperitoneal lymph node and hepatic metastases was made. The results of investigations done are shown in Table I.

He had the right radical inguinal orchidectomy with left Inguinal lymph node biopsy. The operative findings were, large, yellowish right testicular tumour with haemorrhagic and necrotic areas on cut surface and thickened spermatic cord with tumour infiltration of the surrounding cremasteric muscle and enlarged right and left inguinal lymph nodes.

The histological diagnosis was Non-Hodgkins lymphoma, he was treated with chemotherapy. He had a dramatic response and was discharged home after one month but relapsed and died eight months later.

Materials and Methods

The case notes of patients in Lagos University Teaching Hospital between 1979 and 1997 formed the materials for this study. The age, clinical presentation, histological types and treatment were recorded and the data analysed. The hospital incidence was calculated based on new cases seen during the 20 year

period.

Results

A total of twenty five (25) cases of testicular tumours were seen over 20 years. This gives a rate of 1-2 cases per year. During this period about 1 million new male hospital attendance was recorded, giving a hospital incidence of 0.25/100,000 per year. The mean age of the patients was 32.7 years; while the mean ages for teratoma and seminoma were 27 and 35 years respectively. In children (1.5 – 3 years) two cases of embryonal carcinoma and two cases of Interstitial cell tumours were seen. The mean age for lymphoma was 45 years. Testicular tumours were more common on the Right (ratio Right: Left 2:1)

Table II shows the pattern of histologic types seen in our series. Germ Cell Tumours (GCT) accounted for the majority of cases (72%) while Non Germ Cell Tumours (NGCT) made up of 28%. Teratomas were the most frequent histological type(26%) of testis cancer (i.e. 52% of Germ Cell Tumours) whilst Seminomas constituted 32% of testis cancer (i.e. 44% of Germ Cell tumours). One case of mixed histology (i.e. 4%) Seminoma Plus Teratoma was diagnosed. NonGerm Cell Tumours were made up of paratesticular tumours (Rhabdomyosarcomas – 12%), Interstitial i.e. Leydig cell and Sertoli cell tumours (8%), and Lymphomas (8%).

Table I: Results of Investigations in Case Presented

A
HBC:PCV = 26% (anaemia)
ESR = 114mm/hour

B
SGPT = 112 Su/L(0-34)
SGOT = 54u/l (0-45)
Alkaline phosphate 161 iu/l (42-121)

C
LDH = 671u/L(91-180)

D

E
IVU - External mass compressing the right Kidney

F
CT Scan Large retroperitoneal mass
(enlarged lymph nodes) with hepatic metastasis

G
HIV Screening. Negative for I and II

H
Histology. Diffuse mixed (large and small cell)
Non Hodgkin's lymphoma

Table II: Histologic Testicular Tumours in LUTH - Frequency and Age Incidence

No	Neoplasm	Number	%	Age Range (Years)	Mean Age
1	Seminoma	8	32	20-45	35
2	Embryonal CA	3	12	1 1/2 - 35	80
3	Yolk Sac Tumour	3	12	3 1/2 - 42	26
4	Malignant Teratoma Undifferentiated	2	8	25 - 30	27
5	Seminoma-Teratoma	1	4	25	25
6	Seminoma and Malignant Teratoma (Undifferentiated)	1		27	27
7	Rhabdomyosarcoma	3	12	12 - 20	18
8	Sertoli Cell Tumour	1	4	2	2
9	Leydig Cell Tumour	1	4	3	3
10	Lymphoma	2	8	41 - 47	45

Table III: Histologic Type of Testicular Tumours in LUTH

Tumours Type	Lagos (%)	United Kingdom (%)
Teratoma	30	32
Seminoma	42	40
Seminoma + Teratoma	4	14
Interstitial Cell Tumours	8	1.5
Lymphomas	8	7
Paratesticular Tumours	12	5.5

Table IV: Staging Classification: ROYAL MARSDEN HOSPITAL STAGING[6,12]

Stage 1:	Tumour confined to Testis: not bridging Tunica Albuginea. No evidence of metastasis IM. Rising Post orchidectomy Marker only (HCG, AFP)
Stage 2:	Abdominal lymphadenopathy below diaphragm (Paraortic Nodes) A:<2CM B: 2-5CM C:>5CM
Stage 3:	Supradiaphragmatic lymphadenopathy (mediastinal lymph Node) Or No abdominal disease A. <2CM B: 2-5CM C:> 5CM
Stage 4:	Extralymphatic Metastases H: -Liver metastasis L1 <3 lung metastasis L2 <3 lung metastasis (2CM) L3:>lung metastasis (>2CM)

Table V: Management Strategy for Testicular Cancer

Stage	Seminoma	Teratoma
1	3000 cGY to para-aortic and Ipsilateral pelvic nodes	Surveillance
2a	3000 cGY to para-aortic and bilateral pelvic nodes	BEP chemotherapy consider more aggressive regimens for poor prognostic groups
2b	500 cGy boost to main disease	+Surgical Resection Residual Masses
2c	BEP chemotherapy	
3	3000cGy to site of Residual	As above
4	Tumour bulk if CR is not achieved rapidly	

Discussion

The hospital incidence of Testicular tumour in our Centre is low (0.25/100,000 per year). Magoha in an earlier study reported a lower incidence in this center. (0.1/100,000 per year)[4]. Similar observations have been made by Odunjo and Elesha in reports from Lagos, Enugu, Ibadan and from other African countries[5,6,7]. American Blacks have also been reported to have lower incidence rates compared to Caucasians.

However, Hispanics, Japanese and Chinese immigrants to the USA have rates intermediate between their Countries of origin and Countries of adoption, implying a causative role for environmental factors to which blacks are not equally exposed[7]. The lack of effect of migration on incidence rates in blacks suggests genetic factors may play a role in the susceptibility to testicular cancer, arguing for possible genetic resistance in blacks[7].

All age groups are affected; however, the histological types vary with age. Embryonal Carcinomas, Paratesticular and Interstitial cell tumours are commoner in children less than 10 years of age (peak at 2 years). The peak age group for Teratomas and Seminomas are 20-25 years and 35-45 years respectively.

Most tumours seen after 50 years are lymphomas[11]. The aetiology of Germ cell tumour is unknown, but available evidence supports the importance of congenital factors. Cryptorchidism, Atrophy and Trauma are the most commonly associated predisposing factors. In our series four cases of testicular tumours (16%) developed in patients with undescended testis. Two of them had previous orchidopexy, while the remaining two were cryptorchids with abdominal tumours developing in intra-abdominal testes.

In Caucasians 7-10% of patients with testicular cancer give a history of Cryptorchidism, the estimated risk of a tumour developing in patients with maldescent is thought to be 3-14 times the normal risk[3].

No history of trauma was given by our patients. However, 8-25% of all patients with testis cancer give a history of trauma[3,4]. Most authors feel that trauma is a red herring providing the mechanism for discovery of the testicular mass[3]. About 1.5% of testis tumours develop in atrophic testis. A history of mumps orchitis was present in 0.3% of these patients.

There were more tumours in the right testis (right: L. = 2:1) possibly because maldescent is commoner

in the right. Germ cell tumours (GCT) were commoner (72%) whilst Non Germ cell tumours accounted for 28%. This correlates with previous reports from our center by Odunjo and Ifeshia (GCT = 70%), Ibadan GCT = 73%, Kenya 64.5% and Uganda 75%. Conversely, 97% of cases in USA and 93.1% in UK are germ cell tumours (see Table3).

The classification of Germ Cell Tumours had developed along two different lines (American and British). The World Health Organisation modified the Mostoffi & Price classification while the British Testicular Panel formalized the British version[1,4]. The tumour spreads via three routes, viz: Lymphatic spread to periaortic, mediastinal and supraclavicular lymph nodes. Haematogenous spread goes to the Lungs & Liver while it can spread directly to the Epididymis, spermatic cord and scrotal wall. The Royal Marsden Hospital staging classification is presented in table 4. Eighty percent of our patients presented with metastatic disease.

The most common symptom was an enlarged painless testicular lump in 80% of cases. Others had a sensation of fullness, heaviness or pain (15-30%). A secondary bloody hydrocele was present in 10% of patients. Acute pain simulating epididymoorchitis may be the presenting symptom. However, testicular sensation was lost early in most patients. The epididymis was normal at first, but became difficult to feel as it was flattened or incorporated in the growth. Thickening of the spermatic cord occurred later due to cremasteric hypertrophy and enlargement of testicular vessels. Metastatic manifestation including retroperitoneal masses, hepatomegaly, ascites, lower limb lymphoedema, anorexia and weight loss, dyspnoea and haemoptysis due to pulmonary metastasis were noted. Supraclavicular lymph node enlargement was noted in the patient presented.

Endocrine manifestations including feminization with gynaecomastia, precocious puberty, loss of libido and aspermia were noted in patients with Choriocarcinoma and Sertoli cell tumour. Leydig cell tumours in prepubertal boys may cause sexual precocity and Herculean muscle development. The differential diagnoses should include Epididymorchitis Tuberculosis Testis, Torsion Testis, Varicocele, Hydrocele, Clotted haematocele, Syphilitic Orchitis and Inguinoscrotal Hernia. Alphafetoprotein (AFP); Human Chorionic Gonadotrophin (HCG) and Lactic Dehydrogenase (LDH) radioimmunoassay are useful markers in the diagnosis, staging, monitoring of response to treatment and detection of relapse of these tumours. Other staging investigations include Testicular and Abdominal Ultrasonography, Chest X-ray, Abdominal CT Scan, IVU, lymphangiogram and MRI[1,2,3]. Radical Inguinal Orchidectomy is both diagnostic and therapeutic[1,2,4]. Early groin exploration is advocated. If the tumour is grossly malignant, orchidectomy is done, if in doubt, a frozen section is taken. A scrotal approach would convert stage I tumour to stage IV[25]. Primary bilateral Retroperitoneal lymph Node Dissection (RPLND) is a standard way of staging patients with Teratoma in USA[1,2,4,5]. RPLND leads to ejaculatory impotence. True nerve sparing procedures have been developed to spare postganglionic nerve fibres[26].

Treatment depends on the stage and histologic type. In all clinical stage one disease, 30% are understated, cognizance is taken of this during treatment i.e. stage one is treated as stage two; stage two as three.

Seminoma stage I is remarkably radiosensitive and extralymphatic spread is uncommon. Treatment involves radical orchidectomy and adjuvant radiotherapy to abdominal and ipsilateral pelvic lymph Nodes. This approach is associated with 95% - 100% cure rate[1,2,4].

Stages 2a and 2b Seminoma are treated with orchidectomy and radiotherapy to Abdomen and whole pelvis in view of occasional involvement of contralateral Iliac nodes by retrograde spread. Full dose chemotherapy may be used in cases of relapse. Carboplatin (Jm8) is an alternative. For stages 2(c), 3 and 4, chemotherapy with or without radiotherapy is superior to radiotherapy alone. Bleomycin + Etoposide +Platinum (BEP) and adjuvant radiotherapy to any bulk disease is followed by a repeat of two courses of BEP[1,2,4]. Masses remaining after treatment may be removed by surgery[1,2].

Stage I disease is less radiosensitive, with a high metastatic potential while extralymphatic spread is common.

The treatment options include:

(i) Adjuvant Abdominal and Pelvic Radiotherapy
(ii) Retroperitoneal lymph Node Dissection (RPLND)
(iii) Adjuvant Chemotherapy
(iv) Surveillance

Most Oncologists follow a policy of Orchidectomy plus Surveillance with meticulous follow up by Chest x-rays, CT Scans of chest and abdomen and routine

assays of AFP, HCG [4,11,20].

The standard treatment for these patients (Stage A or I Teratoma) in North America is true RPLND [1,11,15].

Stages II-IV Teratoma: Primary Chemotherapy followed by Surgical resection of any residual masses [3,11,17,22].

The BEP regimen of 3 cycles is preferred. Attempts to reduce toxicity by avoiding Bleomycin led to introduction of Vinblastine (PEV). Toxicity problems include nephrotoxicity (Cisplatin); interstitial pneumonitis, pulmonary fibrosis (Bleomycin); Myelosuppresion, Gram Negative Sepsis, Thrombocytopenia, Anaemia (BEP), Hypotension (Etoposide), Nausea and vomiting; Peripheral Neuropathy, Allopecia, Induction of secondary Malignancies e.g. leukaemia and Infertility. Most of our patients presented late and could not benefit from Cisplatin based chemotherapy. The prognostic factors include age of the patients; tumour volume, serum AFP/ HCG, histology of tumour and small vessel invasion. The 5 year survival rate in advanced Countries is 95% for seminoma (stage 1) and 100% for nonseminomas; and >70% for advanced disease treated as outlined above.

Conclusion

This study shows that Testicular tumours are uncommon in Lagos. Most of our patients presented with advanced disease. Increased public awareness and health education with emphasis on testicular self examination would help in early detection of cases.

References

1. Rowland G, Donohue JP. Scrotum and Testis in Gillenwater J.Y., Grayback JT, Howards SS, Duckett J.W. (Eds) - Adult and Pediatric Urology 2nd ed, 1991; 1565 – 1598.
2. Magoha GA. Testicular Cancer in Nigerians. East African Med. J., 1995; 72: 554 - 556.
3. Senturia YD. Review: The Epidemiology of Testicular Cancer Brit. J. Urol. 1987 ; 60: 285 290.
4. Richie JP. Neoplasms of the Testis. In walsh PC, Retik AB Vaughan ED, Wein AJ eds, Campbells Urology 7th ed. Philadelphia: WB Saunders 1998; 2411-52.
5. Odunjo EO, Elesha SO, Obafunu IO. Tumours of the Testes in Lagos Nigeria Nig. Med. Pract 1990; 19: 50-52.
6. Junaid IA. Tumours of the Testis in Ibadan Nigeria Br. J. Urol. 1982; 84: 411-414.
7. Omigbo WI. Relevance of race in management of Testicular tumours. Br. Med. J. 1997 ; 1: 22-23.
8. Zimmermen R.R, Kung U. Testicular and paratesticular Tumours in Kenya. East Afr. Med. J. 1978; 55: 205-210.
9. Templeton AG. Testicular Neplasms in Ugandan African Afr. J. Med. Sc. 1972; 3: 157-161.
10. Chou P.M., Barguin N., Guman P., Sanz C.R. and Gonzonlez Cnasis F. differential expression of P53, C-Kit, and CD 34 in prepubertal and postpubertal testicular germ cell tumours Cancer 1997; 79: 2430-2434.
11. Ellis M., Sikora K. Review: The current management of Testicular Cancer. Br. J. Urol. 1987; 59: 2-9.
12. Peckham M.J. Investigation and staging: general aspects and staging classification. In Peckham M.J. ed. The management of Testicular tumours London: Arnold 1981; 89-101
13. Kohn J., Raghaven D. Tumour markers in malignant germ cell tumours. In Peckham M.J. Ed. The management of Testicular Tumours. London: Arnold 1981; 50-69.
14. Donohue J.P. and Rowland R.G. Complications of Retroperitoneal Lymph Node Dissection. J. Urol 1981; 125:348.
15. Donohue J.P., foster R et al. Nerve sparing RPLND with preservation of ejaculation. J. Urol 1998; 139:206.
16. William S.D., Birch R. and Lawrence A., Einhorn et al. Treatment of Disseminated germ Cell Tumours with Cisplatin, Bleomycin and either Vinblastine or Etoposide New Eng. J. Med. 1987; 316. 145-1440.
17. Jewett MAS. Advances in the therapy if Germ Cell Tumours of Testes. Current opinion in Urology 1994; 4: 287-290.
18. Donohue J.P., Thornhill J.A., Foster R.S., Rowland R.G. and Bihle R. Primary Retroperitoneal Lymph Node Dissection in stage A Non'seminomatous Germ cell Testis Cancer. Review of the Indiana University Experience 1965 - 1989: Br. J. Urol 1993; 71: 326-335.
19. Hendry W.F., Moman A., Nicholls O., Dearnaley D.P. Peckham M.J, Horwich A. Abdominal relapse in stage I non seminomatous germ cell tumours of the testis managed by surveillance, or

with Adjuvant Chemotherapy Br. J. Urol Int. 2000; 86: 89-93.

20. Deanaley D.P., Horwich A'Hern Retal. Combination Chemotherapy with BEP for metastatic testicular teratoma long term follow up. Eur. J. Cancer 1991; 27: 684-91.
21. Horn HW, Sheinfeld J., P.U.V.H.S., Heelan R, Bajorin D. Fetal Surgery for a post Chemotherapy residual mass in Seminoma J. Urol 1997 ;158(3): 860-862.
22. Hendry W.F., a Hern R.P. hertherongton J.W., Peckham M.J., Dearnaley D.P., Horwich. A. Paraaortic Lymphadectomy after Chemotherapy for metastatic non-Seminomatous germ cell tumours: Prognostic value and therapeutic benefit Br. J. Urol. 1993; 71: 208-13.
23. Gottesman J.E. Radical Inguinal Orchidectomy. In Crawford ED (ed): Genitourinary Cancer Surgery 1982; 262-272.
24. Bolicou M.A., Steer W.D: Testis Tumours: The Clinical significance of Tumour Contaminated Scrotum J. Urol 1984; 134: 57.