ORIGINAL ARTICLE

Soft Tissue Sarcomas In The Niger Delta Region Of Nigeria (A Referral Hospital's Study)

*** D. Seleye-Fubara** MBBCh, FMCPath, FWACP, *** S. O. Nwosu** MBBS, FWACP, FMCPath, FICS, **** E. Bob-Yellowe** MSc, MD.

Departments of *Anatomical Pathology and **Surgery, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.

ABSTRACT

Background: *Soft tissue sarcomas are rare tumours in this environment. Recently, an upsurge in frequency was noticed that called for attention. The aim of this study is to study soft tissue sarcomas based on age, sex of patients, tumour sites and histologic types.*

Methodology: *A 14 year retrospective study in University of Port Harcourt Teaching Hospital (UPTH) Port Harcourt. Histological slides previously processed and stained with hematoxylin and eosin stains (H & E) were reviewed and re-evaluated. Special stains were also used for proper diagnosis of some tumours. The tumours were classified based on World Health Organization (WHO) classification of soft tissue tumours.*

Results: *Only 66 soft tissue sarcomas were used for this study which accounted for 2.8% of the total malignancies diagnosed during the period under review. The youngest was a 3 year old girl while the eldest was a 76 year old female. A total of 38 and 28 tumours were diagnosed in males and females respectively, giving a sex ratio of 1.4:1. Rhabdomyosarcoma was most frequent (39.4%) while the least was leiomyosarcoma (1.5%). These tumours are more frequent in the under 20 years (22.7%) and least in 70 years and above (7.6%). The lower limb was most affected (36.4%) while the least was the retroperitoneum (6.1%). The commonest predilection sites vary with different classes of these group malignancies.*

Conclusion: *Soft tissue malignancies are globally uncommon but they constituted an integral part of malignant tumours causing serious morbidity and mortality in this environment. The recent upsurge noticed necessitated the need for regional studies in Nigeria in order to come up with a national epidemiologic data of these malignancies.*

KEY WORDS: *Soft tissue sarcomas; Age; Sex; Tumour sites; Port Harcourt*

Paper accepted for publication 7th March 2005

INTRODUCTION

Soft tissues develop embryologically from two primitive sources (the mesoderm and the neuroectoderm of the peripheral nervous system)[1]. They are complex malignancies of non-epithelial and extra-skeletal tissues of the body, excluding the supportive tissues of various organs, hematopoietic, lymphoid and glial tissue[2]. They are therefore represented by malignancies of the adipose, fibrous, muscular, vascular, peripheral nerve sheath and those of uncertain histiogenesis corresponding with the World Health organization (WHO) classification of soft tissue tumours[3]. The aetiology is unknown but tends to be associated with urbanization with overcrowding, fumes and emission from motor vehicles and industrial machines. Others are industrial waste containing large quantities of polycyclic aromatic hydrocarbons, agricultural and agroallied chemicals, extravasated thorotrasts, irradiation, chemical and heat burns as well as trauma in addition to oncogenic viruses, genetic predisposition and immunosuppression[2,4].

Soft tissue sarcomas are distributed into the deep soft tissues of the extremities, trunk, retroperitoneum, head and neck region[5]. The malignancies occur in all ages of both sexes but with male dominance though the gender and age incidences vary among different histological types[5]. Like carcinomas, these cancers are commoner among elderly patients[2]. There is no proven ratial variation in occurrence though there are reports of black dominance[6]. Rhabdomyosarcoma is the commonest soft tissue sarcoma of childhood world wide[7], while malignant fibrous histiocytoma (MFH) is the commonest soft tissue sarcoma in adults[8].

Work on soft tissue sarcoma are very scanty in Nigeria except for a few isolated reports in Calabar, Ibadan, Lagos and Zaria[9-12]. Being

Correspondence to: **Dr. D. Seleye-Fubara**

unaware of any comprehensive study on this subject in this environment, this communication is aimed at surveying the pattern of soft tissue sarcomas and compare it with other studies elsewhere.

MATERIALS AND METHODS

A 14-year retrospective review of 68 soft tissue sarcoma seen in the University of Port Harcourt Teaching Hospital (UPTH), one of the referral hospitals in the Niger Delta was carried out by the authors. Only 66 had adequate records for inclusion (97%) while the remaining 2(3%) were excluded from the study due to inadequate records.

The tissues were initially fixed in 10% formalsaline, processed and embedded in a paraffin wax. They were then sectioned, mounted on glass slide and stained with hematoxylin and eosin (H & E) stains. Missing and broken slides were recut from the tissue blocks and stained. In some cases, special stains like the periodic acid Schiff (PAS) was used in 13.6% cases for the demonstration of either intracytoplasmic crystals, mucin and glycogen in malignant fibrous histiocytoma, rhabdomyosarcoma and leiomyosarcoma. Phosphotungstic acid hematoxylin (PTAH) was used in 3% case to demonstrate skeletal muscle striation which stains blue-black with the cytoplasm staining pale pink. Variables considered for the studies included the ages of patients, sex and anatomic sites of the tumour which were retrieved from the clinical records and histology request forms. The tumours were classified based on (WHO) specification[3]. The results were collated and analyzed using multiway frequency tables.

RESULTS

A total of 2389 malignant tumours were diagnosed. A total of 66 were soft tissue sarcoma which accounted for 2.8% of cases. The youngest was a 3 year old girl while the eldest was a 76 year old female. There were 40 cases reported in this hospital in 1999; giving an upsurge of 65% in this study.

Table I shows the sex distribution and the frequency of various histological types of soft tissue sarcomas in this environment. There were 9(15.6%) liposarcomas, one leiomyosarcoma (1.5), 26 rhabdomyosarcoma (39.4%), 5 peripheral nerve sheath sarcomas (7.6%), 12 fibrous histiocytic malignancies (18.2%), 8 vascular sarcomas (12.1%) and 5 sarcomas of uncertain origin (7.6%). On the whole 38(57.6%) sarcomas were diagnosed in males and 28(24.4%) in females giving a sex ratio of 1.4:1.

Table II shows age distributions and frequencies of various histological types of soft tissue sarcomas in the UPTH. The highest frequency occurred in children of ages below 20 years (22.7%), and all were rhabdomyosarcomas. Rhabdomyosarcoma is also the only tumor diagnosed in the age group 20-29 years (9.6%) and 10.6% for the age group 30-39 years. The age group 40-49 years had 15.2% cases and liposarcoma had the highest frequency; while 18.2% cases was recorded for the age group 50-59 years with fibrous histocytic malignancies as the most frequent. Fibrous histiocytic and vascular malignancies are highest in the age group 60-69 years which recorded a total of 16.7% cases each while only 7.6% cases were recorded for the age group 70 years and above with vascular malignancy forming majority.

Table III shows the anatomical distribution of the various classes of soft tissue sarcomas in UPTH. The upper limbs had 18.2% cases of which the most frequent was fibrous histiocytic malignancies. The lower limbs had majority of the cancers 28.8% with fibrous-histiocytic malignancies as most frequent. The head and neck region had 19.6% with rhabdomyosarcoma as most frequent; while the retroperitoneum had 7.6% of which rhabdomyosarcoma is the most frequent. The trunk recorded 25.8% with rhabdomyosarcoma forming majority.

Table I.Sex distribution and histological types of soft tissue Sarcomas in UPTH

Types of soft tissue sarcoma	M	F	Total	Percentage
Adipose tissue sarcomas				
*Liposarcoma	2	7	9	13.6
Smooth muscle sarcomas				
*Leiomyosarcoma	1	-	1	1.5
Skeletal muscle sarcomas				
*Rhabdomyosarcoma	17	9	26	39.4
Peripheral Nerve Sheath Sarcomas				
*Malignant schwannoma	-	1	1	1.5
*Neurofibrosarcoma	3	1	4	6.1
Fibrous-histiocytic sarcoma				
*Fibrosarcoma	2	1	3	4.6
*Malignant fibrous histiocytoma (MFH)	5	2	7	10.6
*Dermatofibrosarcoma proteuberans	1	1	2	3.0
Vascular Sarcomas				
*Lymphangio sarcoma	-	1	1	1.5
*Angiosarcoma	1	-	1	1.5
*Kaposis sarcoma	3	2	5	7.6
*Malignant hemangiopencytoma	-	1	1	1.5
Sarcomas of uncertain origin				
*Alveolar soft part sarcoma	1	1	2	3.0
*Synovial sarcoma	2	1	3	4.6
Total	38(57.5%)	28(42.4%)	66	100%

Table II.Age distribution and frequencies of histological types of soft tissue sarcomas in UPTH

	Age (years)							
Types of soft tissue sarcoma	< 20	20-29	30-39	40-49	50-59	60-69	70and>	Total
Adipose tissue sarcoma	-	-	1	3	2	2	1	9
Smooth muscle sarcoma	-	-	-	-	-	1	-	1
Skeletal muscle sarcoma	15	6	2	-	1	2	-	26
Peripheral nerve sheath sarcoma	-	-	1	1	2	1	-	5
Fibrous and histocytic sarcoma	-	-	2	2	4	3	1	12
Vascular sarcomas	-	-	-	2	1	3	2	8
Sarcomas of uncertain origin	-	-	1	2	1	-	1	5
Total %	15 (22.7%)	6 (9.1%)	7 (10.6%)	10 (15.2%)	11 (16.7%)	12 (18.2%)	5 (7.6%)	66 (100%)

Table III.Anatomical distribution of various classes of soft tissue sarcomas in UPTH

Classes of soft tissue sarcomas	Upper limb	Lower limbs	Head & Neck	Retroperi-tonium	Trunk	Total
Adipose tissue Sarcomas	2	4	1	-	2	9
Smooth muscles sarcomas	-	-	-	1	-	1
Skeletal muscle sarcomas	2	1	8	3	12	26
Peripheral nerve sheath	1	2	-	-	2	5
Fibrous and histiocytic sarcomas	4	5	1	1	1	12
Vascular sarcomas	2	4	2	-	-	8
Sarcoma of uncertain origin	1	3	1	-	-	5
Total	12	19	13	5	17	66
Percentage	(18.2%)	(28.8%)	(19.6%)	(7.6%)	(25.8%)	(100%)

DISCUSSION

Soft tissue sarcomas are known to be very rare when compared with carcinomas[2,5], confirming our findings where it accounted for only 2.8% of total malignancies in the period under review. The study also recorded an upsurge of 65% since the last publication covering 1990-1999 where only 40 cases were seen[8]. Soft tissue sarcomas are commoner in males probably because, they are more exposed to the carcinogenic agents produced by industrial machines, chemicals and fumes[2,4] since they form majority of the workforce in various industries and agriculture than females in the area of study.

Some chemicals, physical agents, hormones and viruses are carcinogenic agents that acts on genome of somatic and germ cells causing irreversible injury to DNA, resulting in gene mutation and deletion, chromosomal translocation and gene amplification on the target cell. The P53 gene is the most common target for mutation or deletion in human tumors occurring in more than 50% of all human cancers[13]. Normally, P53 is a negative regulator for cell division. Cases of germline mutation in one P53 allele have inherited predisposition to develop cancers in many organs termed Li-Fraumeni Syndrome. The Li-Fraumeni Cancer Syndrome is a rare autosomal dominant syndrome, characterized by the occurrence of diverse mesenchymal and epithelial neoplasm at multiple sites. In some individuals, there is a germline mutation of P53 tumour suppressor genes and the deletion of the remaining 'wild type' allele leading to the formation of a wide range of neoplasms including soft tissue sarcomas[13,14].

Rhabdomyosarcoma, the most common childhood sarcoma[7,16] accounted for 39.4% cases in this study as against the 3% recorded elsewhere[17]. This high variation may be attributed to the sample size or may corroborate an earlier report which recorded black dominance in frequency of occurrence[6,16]. It is composed of the infantile (juvenile) rhabdomyosarcoma comprising embryonal, alveolar rhabdomyosarcomas[19] and sarcoma botyriodes which is regarded by some authors as a variant of embryonal rhabdomyosarcoma with a better prognosis[7,16,20]. The rare pleomorphic rhabdomyosarcomas are found mainly in adults[20]. The frequency is more in males in this study, corroborating another report[16] but at variance with one report where no gender variation was recorded[21]. It was also noticed that, the embryonal rhabdomyosarcoma is expectantly the commonest in this study while the alveolar variant is the most aggressive and associated with the worst prognosis[5].

The fibrous histiocytic tumour accounted for 18.2%, of which malignant fibrous histiocytoma (MFH) was the majority. It is also known to be the commonest soft tissue sarcoma in adults[8,22] and responsible for 10.6% of the total malignancies; a figure which is at variance with the 20% recorded elsewhere[23]. This variation may be attributed to the sample size and the geographical areas of study. The study also recorded no childhood MFH confirming its rarity in childhood in this environment and the world at large. Fibrosarcoma occurred in both sexes with 2:1 male dominance in this environment and accounted for 4.6% of soft tissue malignancies. The sex distribution is in keeping with other studies[24,25]. In one of our patients, fibrosarcoma was associated with persistent hypoglycaemia. This perhaps is the paraneoplastic syndrome that led to the early clinical diagnosis of the tumour. Dermatofibrosarcoma protuberans is an intermediate tumour of low grade malignancy which may be mistaken histologically for MFH or fibrosarcoma[26]. There is no sex variation in frequency of this tumour, corroborating the records of other workers[27].

The frequency of liposarcoma is higher than those reported in other studies where it constituted 10-12% of total soft tissue sarcomas[22]. This may be attributed to the sample size. Females are predominating with a sex ratio 3.5:1. This may be due to the fact that females are naturally steatopygic and hence better suited to accumulate fat; no wonder it is commoner in obese women in this study. Development of this tumour is usually *de novo*[28]. It is commoner in females aged 38-45 years contradicting other report where 40-60 years was recorded[2,29]. The fats of this tumour is not available for metabolism[2]. One of our patients presented with inguinal hernia of which the content showed liposarcoma.

Vascular tumours were responsible for 12.1% of cases with no sex variation in occurrence. Of the eight cases, Kaposi's sarcoma (KS) was the most frequent (7.6%) while lymphangiosarcoma, angiosarcoma and malignant hemangiopericytoma shared the remaining 4.5% in equal proportions. The KS as in other studies is commoner in males[30]. Currently, KS is about the commonest AIDS (especially HIV1) defining malignancy in this environment, corroborating other reports[31]. In three of our patients, KS occurred in rare anatomical sites including the conjunctiva, eyelid and the sole of the foot and these patients were HIV seropositive. Human herpes virus (HHV) serotype 8 is also associated with KS[12,32] but his was not found in our study. Clinical features of KS differ when comparing the classic and endemic forms with the immunocomprosed type but in all cases, the histological pattern is basically similar, implying that, host factor are the determinants of the clinical behaviour of the tumour; this remark is similar to other report elsewhere[33].

The malignancies of the peripheral nerve sheath and those of uncertain histiogenesis were rare and accounted for 7.6% each in this study. Neurofibrosarcoma was the most frequent peripheral nerve sheath malignant tumour, differing from another study[34] with male dominance in sex distribution. Alveolar soft part sarcoma was the commonest in the malignancies of the uncertain origin which accounted for 3% of cases which is by far higher than the 1% recorded elsewhere[2]. Again, the disparity may be due to the sample size and the geographical areas of study. The clinical course of this tumour is indolent and asymptomatic in most of our patients but end up in death of the patient as observed in other studies[35]. The 4.6% recorded for synovial sarcoma in this series is similar to the 5-10% recorded in the United Kingdom[36]. It occurs frequently in males varying with another study which reported no gender difference in occurrence[37,38]. Leiomyosarcoma, the least frequent soft tissue sarcoma accounted for 1.5% cases, occurring in the intestine of a 64 year old man; corroborating its rarity reported by another author[39]. One would think about leiomyosarcoma of the uterus which is fairly common but this does not fit into the definition of soft tissue[2] and hence excluded. Soft tissue malignancies were situated deep into the soft tissues of the lower limbs, truck, head and neck region, upper limbs and the retroperitoneum in decreasing order of

frequency. This distribution is in keeping with an earlier report in Nigeria[8].

Finally, soft tissue malignancies are globally uncommon when compared to malignancies of epithelial tissues but they constitute an integral part of malignancies in the Niger Delta region of Nigeria causing morbidities and mortalities. An elaborate study of the individual tumours and histological classes are necessary as there is an upsurge of these tumours in this environment.

REFERENCES

1. William PL, Wendel-Smith CP. Basic human embryology. 2nd Ed. Kent, England: Pitman Med Pub, 1978: 40-45.
2. Enzinger FM, Weiss SW. Soft tissue tumours. 2nd Ed. St Louis CV: Mosby, 1988:1-964.
3. Enzinger FM, Lattes R, Torloni R. Histological typing of soft tissue tumors. International Histological Classification of soft tumors (3) Geneva: WHO, 1969.
4. Wingren G, Fredrickson M, Noorlind-Brage H, Wordenskjold B, Axelson O. Soft tissue Sarcoma and occupational exposure. Cancer 1990; 66:806-811.
5. Rosai J (ed). Soft tissues. In: Ackerman's Surgical pathology. 9th Ed. Vol II. Philadelphia: Mosby, 2004: 2237-2371.
6. Curtter SJ, Young IL. Third National cancer survey incidence data. National Cancer Institute (NCI) Monograph 1975;41:1-3.
7. Hicks BA, Hensle TW, Burbige KA, Oeter Almer R, Bladder management in children with genital sarcoma. J Paediat Surg 1993; 28:1019-1022.
8. Seleye-Fubara D. Histological study of soft tissue tumours in University of Port Harcourt Teaching Hospital, Port Harcourt (a ten year retrospective study). National Postgraduate Medical College of Nigeria dissertation. November 2001.
9. Otu AA. Kaposi's Sarcoma. Niger Med Pract 1990;19:87-92.
10. Ani AN, Attah EB, Ajayi OO. Dermatofibrosarcoma protubrans. An analysis of 8 cases in an African population. Am Surg 1976;934-940.
11. Banjo AAF, Elesha SO, Abudu OO. Hemangiopericytoma of the uterus. Niger Med Pract 1997; 33:65-67.
12. Rafindadi AH, Malami GA. Vascular tumours in Zaria A ten year pathological review. Niger Postg Med J 1999; 6:157-160.
13. Harris AL. Mutant P53 the commonest genetic abnormality in human Cancer? J Pathol 1990; 162: 5-6.
14. King P, Craft AW, Malcolm AJ. P53 expression in three separate tumors from patient with Li-Fraumeni's Syndrome. J Clin Pathol 1993; 46:676-677.
15. Birch JM, Harthley Al, Valblair BA, Kelsy AAF. Cancer in the families of children with soft tissue sarcoma. Cancer 1990; 66:2339-2248.
16. Malone M. Soft tissue Sarcoma in childhood. Histopathol 1993; 22:203-216.
17. Bourviey DP, Charles DO, Fox W, Frishberg DP. Solitary testicular relapse of rhabdomyosarcoma in adult. Cancer 1990; 65:2611-2614.
18. Horn RC, Enterline HT. Rhabdomyosarcoma. A clinicopathological study and classification of 39 cases. Cancer 1958;11:181-199.
19. Nakhleh RE, Swanson PE, Dehner LP. Juvenile (embryonal and Alveolar) rhabdomyosarcoma of the head neck in adults. Cancer 1991; 15:1019-1024.
20. Young TL, Miller RW. Incidence of malignant tumors in children. J Paediat 1975;86:254-258.
21. Jaffe BF, Fox JE, Batsaki JG. Rhabdomyosarcoma of middle ear and the mastoid. Cancer 1971; 21:29-37.
22. Kawashiwa H, Sunao I, Takahashi Y. Primary malignant fibroushistiocytoma of descending colon. Surgery today (Jap J Surg) 1997;27:851-854.
23. Weiss SW, Enzinger FM. Malignant fibrous histiocytomma. An analysis of 200 cases. Cancer 1978; 41:2250-2266.
24. Huvous AG, Higinbotham NL. Primary fibrosarcoma of bone. A clinicopathologic study of 130 cases. Cancer 1975; 23:837-847.
25. Chin W, Fay R, Ortega P. Malignant fibrous histiocytoma of prostate. Urology 1986; 27:363-365.
26. Connelly JH, Evans HL. Dermatofibrosarcoma protuberans. A clinicopathologic review with emphasis on fibrosarcomatous area. Am J Surg Pathol 1992; 16:921-925.
27. Taylor HB, Helwig EB. Dermatofibrosarcoma protuberans. A study of 115 cases. Cancer 1962; 15:717-720.
28. Kauffman SL, Stout AP. Lipoblastic tumor in children. Cancer 1959; 12:912-925.
29. Binder SC, Katz B, Sheridan B. Retroperitoneal liposarcoma. Ann Surg 1978; 187:257-261.
30. Hjalgrm H, Melbye M, Leker S, Fris Ch M. Epidemiology of classic Kaposi's Sarcoma in Denmark (1970-1992). Cancer 1996;77:1373-1378.
31. Beral V, Peterman TA, Berkelmann RL, Jaffe HW. Kaposi's Sarcoma among persons with AIDS. A sexually transmitted infection. Lancet 1990;335:123-128.
32. Cheng Y, Caeser E, Pessin MS. Identification of Herpes virus like DNA sequence in AIDs associated Kaposi's sarcoma. Science 1994; 266:1865-1867.
33. Ziegler JL, Templeton AC, Vogel CL. Kaposi's Sarcoma. A comparism of classical, epidemic and endemic forms. Seminar in Oncology 1984; 11:47-52.
34. Sordillo PP, Hajdu S. Malignant Schwannoma. Clinical Characteristics, Survey and response to therapy. Cancer 1981; 47:2503-2506.
35. Grey GF, Click AD, Kurtin PJ, Jones HW. Alveolar soft part sarcoma of uterus. Human Pathol 1986; 17:297-300.

36. Stout AP. Sarcoma of the soft tissue. Cancer 1961; 11:210-231.
37. Schmidt D, Thum P, Med C, Harms D, Treuner J. Synovial sarcoma in children and adolescent. A report from Kiel Pediatric tumor registry. Cancer 1991; 67:1667-1672.
38. Coffin CM, Dehner LP. Soft tissue neoplasm in childhood and adolescence. A clinicopathologic review of 944 cases. Lab Invest 1986; 54:12A.
39. Kohno H, Nagasue N, Arakis S, Kato T. Ten year Survival after Synchroneous resection of Liver Metastasis from intestinal Leiomyosarcoma. Cancer 1981; 47:1421-1423.