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Malignant childhood tumours in Calabar, Nigeria

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Summary

Children suspected with cancers seen during a 5-year period (Jan 1983 – Dec 1987) in the University of Calabar Teaching Hospital (UCTH) Calabar, Nigeria were prospectively studied. A total of 60 cases were confirmed in those aged below 15 years with a majority (38.3%) of the children under 3 years. The pattern shows a preponderance of Burkitt's lymphoma followed by nephroblastoma and soft tissue sarcoma as the commonest malignancies. A low relative frequency of leukaemias (8.3%) and no intracranial tumours were encountered. This pattern closely resembles that of other Nigerian reports but contrasts with the situation in Britain and America, with their high leukaemia and intracranial tumour frequency ratios. Generally, there appears to be a low prevalence of malignancies among children in Calabar and presumably the south-eastern part of Nigeria. Difficulties in their management are attributable to late presentation, high patient default rate, complete lack of radiotherapy, and shortage of chemotherapeutic agents.

Résumé

Les enfants soupçonnés d'avoir le cancer examinés pendant une période de 5 ans (janvier 1983 au décembre 1987) à University of Calabar Teaching Hospital (UCTH), Calabar, au Nigéria, étaient prospectivement étudiés. 60 cas au total étaient confirmés parmi ceux ayant moine de 15 ans dont la majorité (38.3%) furent les enfants de moins de 3 ans. Le type indique une prépondérance de lymphoma de Burkitt suivi du nephroblastoma, le sarcoma du tissu mou étant les malignités les plus courantes. Une fréquence relativement faible de leukaemias (8.3%) sans tumeur intracramienne étaient rencontrée. Ce modèle ressemble étroitement à ce d'autres rapports Nigérians mais fait contraste aveo la situation en Bretagne et aux Etats Unis, où la proportion de leukaemia et la fréquence de tumeur intracranienne sont très élevées. Généralement, la prédominance de malignités paraît basse parmi les enfants à Calabar et, probablement, dans la partie Sud-Est du Nigéria. On attribue les difficultés dans leur maniement à la présentation tardive, au taux défectueux de maladies, au manque complet de radiothérapie et à l'insuffisance d'agents chémothérapeutiques.

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Introduction

While infections and malnutrition remain the leading causes of morbidity and mortality in African children [1,2], cancer relatively accounts for a high proportion of deaths in the technologically advanced countries of the world [3]. With the current efforts to combat hunger and eliminate childhood infectious diseases, cancer may in the near future also emerge as one of the leading problems of children in the developing countries. Studies on the epidemiology of childhood cancer among Nigerian children are few and emanate almost exclusively from the south-western part [4-6] of the country. Previous surveys [4, 5] in Nigeria reveal, in the overall, a predominance of solid tumours such as lymphomas, retinoblastoma, nephroblastoma and neuroblastoma, in descending order of frequency. Nigerian children tend to have a low incidence of leukaemia and brain tumours. Conversely in Europe [7] and America [8], in both black and white children, the ratio frequency pattern is that of high leukaemia, high intracranial tumours and relatively low lymphoma and retinoblastoma.

Nigeria is a vast country with land mass of 3.4 million square kilometres and an estimated population of one hundred million. Racial, ethnic and geographical variations are known peculiarities of cancer, hence there is the need for collaborative and multi-centre surveys to reflect the experience in various regions and sub-regions.

To the best of our knowledge there has been no previous surveillance of childhood cancers in the south-eastern part of Nigeria. This survey was there-

Table 2: Relative ratio frequencies (RRF%) of the various histologic types of malignancies and their sex distribution $n = 60$

Histologic Type	Male	Female	Total	RRF%
LYMPHOMA				
Burkitt's	6	5	—	—
Hodgkin's	3	—	—	—
Total	9	5	14	23.3
NEPHROBLASTOMA				
Total	3	7	10	16.7
CONNECTIVE TISSUE SARCOMA				
Embryonal Rhabdomyosarcoma	1	3	—	—
Malignant fibrous histiocytoma	—	1	—	—
Malignant haemangioendothelioma	1	—	—	—
Unclassified soft tissue sarcoma	1	—	—	—
Total	3	4	7	11.6
LEUKAEMIA				
Acute lymphoblastic	1	1	—	—
Acute myelomonocytic	1	—	—	—
Juvenile chronic myeloid	1	—	—	—
Unclassified	1	—	—	—
Total	4	1	5	8.3
NEUROBLASTOMA				
Total	3	1	4	6.7
RETINOBLASTOMA				
Total	1	3	4	6.7
BONE AND TUMOUR				
Osteosarcoma	1	2	—	—
Amelobastoma	1	—	—	—
Total	2	2	4	6.7
GENITAL, GONADAL AND GERM CELL				
(i) Ovary				
Solid teratoma, malignant	—	1	—	—
(ii) Vagina				
Embryonal Rhabdomyosarcoma	—	1	—	—
(iii) Testis				
Embryonal carcinoma	3	—	—	—
Total	3	2	5	8.3
NON GONADAL TERATOMA				
Sacroccoccygeal				
Embryonal ca	1	—	—	—
Occipital immature teratoma	—	1	—	—
Total	1	1	2	3.3
EPITHELIAL TUMOURS				
Thyroid ca	—	1	—	—
Nasopharyngeal ca	1	—	—	—
Renal cell ca	—	1	—	—
Hepatocellular ca	—	1	—	—
Total	1	3	4	6.7
MISCELLANEOUS				
Carcinoid tumour (caecum)	—	1	1	1.7
GRAND TOTAL	31	29	60	100

ca = carcinoma

Table 3: Age distribution of Calabar children with the relatively more common tumour in the series

Histological Types	Age Groups (Years) 0-3	4-6	7-9	10-12	13-15	Total
1. Lymphoma						14
Burkitt's	—	—	6	3	2	
Hodgkin's	—	—	—	1	2	
2. Nephroblastoma	9	1	—	—	—	10
3. Connective tissue sarcomata	2	2	3	—	—	7
4. Leukaemias	2	—	2	1	—	5
5. Embryonal Rhabdomyosarcoma	2	1	2	—	—	5
6. Retinoblastoma	3	1	—	—	—	4
7. Neuroblastoma	2	—	1	1	—	4
8. Embryonal carcinoma (EST)	2	1	1	—	—	4

(EST) Endodermal Sinus Tumour

The commonest site of Burkitt's lymphoma was the jaw bone especially the maxilla and it affected the mandible in only one case (Fig. 1). Three of the five females with Burkitt's tumour presented with palpable ovarian masses of which cytological examination of the ascitic fluid was diagnostic in all the three. Peripheral lymph node involvement in Burkitt's occurred in only one child, aged 7 years, with enlarged lymph nodes in the neck. Strikingly all the children with Burkitt's lymphoma appeared well-fed.

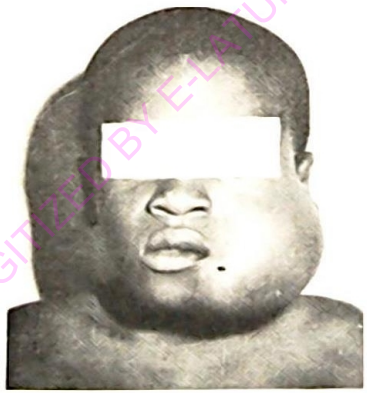

Fig.1: African Burkitt – Facial swelling of mandible.

Nephroblastoma (Wilm's Tumour)

Nephroblastoma was the second most common childhood tumour, occurring in 10 of the 60 children and giving a relative ratio frequency (RRF) of 16.7%. The tumour was on the right in 6 cases, on the left in 3, and bilateral in 1 case (stage 5). The mean age incidence was 2.45 years ± 1.56 (range 5 months to 6 years). The peak age incidence was 3-3.5 years, this group accounting for 50% of all the Wilm's tumour victims. Of the 10 cases, the sex ratio was 1:2.3 in favour of females. All the patients presented late with large tumours crossing the midline in 7 of the 10 cases. The stage 4 disease was the most (50%) frequent, with 1 case each in stages 2, 3 and 5. The case with stage 5 tumour was a 3-year-old female who presented with bilateral renal masses — the diagnosis was confirmed by exfoliative cytology of the ascitic fluid and a needle biopsy since the tumour was considered inoperable. Only 2 patients, both males, presented with stage 1 tumour, one of whom had right hemihypertrophy (trunk and limbs) ipsilateral to the involved kidney.

He remained alive and well 18 months following nephrectomy and chemotherapy. The other patient with stage 1 disease was lost to follow-up after nephrectomy. The one child with stage 2 disease had his tumour probably at birth, as it was reportedly palpable at six weeks of age, but medical opinion was not sought until he was five months old. He had

right nephrectomy and adjuvant chemotherapy with vincristine and cyclophosphamide, this being our treatment of choice for all operable renal tumours. This particular patient was prone to drastic drops of his haemoglobin following therapy, which necessitated transfusion after each course. He responded well to treatment for nearly six months, but died suddenly from fulminating hepatitis as the age of 11 months. The child with the stage 5 disease was taken away from hospital to die at home. Generally our survival rate from Wilm's tumour is poor due to late presentation and drug shortage. Only one patient is known to survive to date, that is, 3 years after nephrectomy and chemotherapy.

Leukaemia

Leukaemia constitutes about 8% of all the malignant childhood tumours in this series. Of the 5 cases diagnosed, 3 were acute, 1 was chronic while 1 unclassified case presented with infiltration of the salivary gland at the age of $4^{1}/2$ years. The youngest patient was a $10^{1}/2$ month-old male with acute myelomonocytic leukaemia.

Embryonal rhabdomyosarcoma

Five cases were diagnosed, all aged below 10 years. Four were females, and one a male, aged 7, who presented with a pharyngeal ulcer. The two youngest patients were aged 2 and 3 years respectively. The 2-year-old presented with a massive protuberant vaginal tumour while the 3-year-old presented with a right mandibular swelling. Both patients died few months after the diagnosis was made as the tumour was uniformly fatal. The remaining 2 patients aged 6 and 8 presented each with a tumour in the post-auricular area.

Embryonal carcinoma (Endodermal Sinus Tumour) EST

Four patients with embryonal carcinoma (endodermal sinus tumour) aged between 6 weeks and 9 years were encountered in our series. They were all males, one with sacroccocygeal tumour and the other 3 with testicular tumours. One of the latter had bilateral tumour of the testicles with secondaries in the small intestine. Both testicles were removed and the affected gut resected. Unfortunately the patient reportedly died in his sleep unexpectedly five weeks after discharge from hospital – no autopsy was done.

Retinoblastoma

A total of 4 cases of retinoblastoma were diagnosed in 3 females and 1 male whose ages ranged from 2-4 years. They all presented with orbital masses which was bilateral in the male patient. Retinoblastoma is the commonest primary orbitoccular tumour in Nigeria [4].

Neuroblastoma

Four patients, 3 males and 1 female, with neuroblastoma were encountered. Two of these presented, each with adrenal tumour with metastatis to the liver and skull respectively. The skull involvement occurred in the only female patient, aged 3 years. One of the males, a 3-year-old presented with a right nasal neuroblastoma. Another of the three males presented with a huge retroperitoneal neuroblastoma but had a normal intravenous urogram with none of the kidneys displaced.

Osteosarcoma

This tumour was seen in 3 patients – two females aged 12 and 14 years respectively, and a male aged 15 years. The tibia was the primary site in each of the 3 cases.

Metastatic carcinoma

Four patients presented with metastatic carcinoma from 4 primary sites namely: The thyroid, nasopharynx, kidney and the liver respectively. The patients were aged 2-13 years with equal sex representation. The sites of metastasis were the lymph nodes of the neck, mesentery and the liver. The tumours with cervical lymph node involvement were a nasopharyngeal and a thyroid carcinoma.

Mesenteric lymph nodes were involved in a female aged 8 years with hepatocellular carcinoma in a cirrhotic liver. Hepatic metastasis was seen in a 2-year-old male with renal cell carcinoma.

Other rare tumours

Four uncommon connective tissue tumours were: ameloblastoma in a male aged 15 years, malignant fibrous histiocytoma, malignant haemangioendothelioma derived from the gluteal region, and soft tissue sarcoma (unclassified) in the neck region. One case of carcinoid tumour of the caecum was diagnosed in a 12-year-old female.

Outcome

Of the 60 cancer patients, 1 is still alive, 4 died in hospital, 2 were known to have died at home while the fate of the remaining 53 could not be determined because they either left the hospital against medical advice or were lost to outpatient follow-up.

Discussion

The UCTH admits over three thousand children every year and to have encountered only 60 cases of childhood cancer in 5 years strongly suggests that malignant childhood neoplasm is a rarity in our environment. This differs from the experience in Ibadan[4] where an average of about 100 cases of childhood cancers were diagnosed annually over a 13-year period. The experience in Calabar could be attributed to underdiagnosis but this assumption is rather untenable since, as a training ground for medical doctors at both undergraduate and postgraduate levels, there is always a conscious effort to determine the exact cause of every ailment. Also since most malignancies in our childhood population are solid tumours, it would have been rather unlikely for these to escape detection. Nevertheless, it is possible that cases could have been missed since it has long been observed that a significant proportion of Nigerians patronise the hospital only as a last resort, most preferring traditional medicine and divine healing. A majority of illiterate Nigerians who constitute the bulk of our population regard a considerable number of ailments as "non-hospital disease" and therefore prefer to approach the non-orthodox means.

However, in spite of all the possible shortcomings and the small number of cases available for study, a pattern appears to have emerged from the present survey. That childhood cancer constitutes 12% of all neoplasms seen in our institution is in consonance with the experience in Ibadan[4] where the overall relative ratio frequency was 12.5% in over a 13-year period of study (1960-1972). Also the relative frequency pattern of the histological types is very similar with the experience in other African reports[9, 10].

There is a preponderance of solid tumours, eminently the lymphomas. Burkitt's lymphoma, the most common childhood neoplasm in the East[10] and West African sub-regions[4], is the predominant cancer in our series. Geographically, Ibadan, Calabar both in Nigeria, and Uganda[10] occupy about the same latitude in the tropics where there is heavy rainfall, high ambient temperature and high humidity. Climatic factors, viruses, particularly Epstein-Barr[11], parasitosis such as malaria[12], helminthiasis, schistosomiasis and chronic malnutrition have all been incriminated as being co-operatively "carcinogenic" of Burkitt's tumour. However, though all our Burkitt's lymphoma patients were of the low socio-economic strata they were in a fairly good state of nutrition. It will be of considerable interest to study the specific antibody levels of common viruses and parasites among the Burkitt's tumour patients in our environment.

Nephroblastoma is the second most common malignancy in our childhood population. This differs from the Ibadan[4] experience where retinoblastoma occupies a second position to lymphoma. Also the female preponderance (M/F – 1:2.3) in this tumour contrasts with that in Kenya[13] and Ibadan[4] (sex ratio 1:1) but agrees with the European and American reports in which there is a higher female incidence. Late reporting and therefore advanced stage of tumour in this malignancy is our experience and that of other Nigerian investigators [5,14]. The frequencies of associated congenital anomalies such as aniridia, hemihypertrophy and genito-urinary defects which have been reported in Western countries[15] appear to be comparatively low in African children[4,5]. The single case associated with hemihypertrophy in our series appears to be the first to be reported in Nigeria.

As a group, connective tissue sarcoma also appears relatively common or comes next to Wilm's, although, considering single tumours, leukaemias, retionoblastoma and neuroblastoma come next (Tables), but each as a poor third to Burkitt's lymphoma and renal cancer. The three single conditions occur at almost equal frequency with leukaemia having an edge over the other two (Table 2). While leukaemia is the most common neoplasm in Caucasian children [7, 8], its relative rarity among Nigerian children has for long been observed[4, 14]. It is not likely that this relative lack is due to poor harvesting since complete blood count is a very routing investigation done on every patient admitted into our paediatric service.

There is striking absence of intracranial tumour in this report. We are speculating that this condition is deficient in our childhood population in similarity with reports on both adults and children from other African investigators[9, 16]. This is in great contrast with what obtains among children in Western countries where brain tumours such as gliomas and medulloblastoma are highly prevalent, commanding a second place to leukaemia. Since intracranial tumours usually present with considerable clinical manifestation and disability, it is unlikely that these patients could have been missed if they presented in any of our hospitals.

The high rate at which cancer patients leave the hospital against medical advice and default in outpatient follow-up, make it difficult to define the outcome of cancer patients in our environment.

Generally the prognosis of patients were poten-

tially poor as a result of late presentation and difficulties in instituting appropriate anti-neoplastic therapy. Non-availability of radio- therapy, irregular supply and high cost of cytochemotherapeutic agents in our centre militated against rewarding treatment measures. This is the experience in most tertiary care centres in Nigeria and perhaps in a majority of the Third World countries. Exciting advances are being made in developed countries in new combination chemotherapy protocols so that neoplasms such as acute non-lymphocytic leukaemia, germ cell tumours and non-Hodgkin's lymphoma have been added to the ever- growing list of the potentially curable childhood malignancies. Conversely, due to limited health resources, even conditions like leukaemia, Wilm's tumour and Burkitt's lymphoma which have long been recognised as curable cancers still remain fatal in the African population.

Although infectious and nutritional diseases unquestionably have a high prevalence in developing countries, it is high time major support was provided, perhaps with the assistance of the financially favoured countries, for cancer research and treatment. In African communities, we cannot ignore education of parents in terms of hospital-consciousness and early recognition of danger signs, which could play a major role in increasing both the diagnostic yield and salvage rate.

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