Brief Report

The Burden of Pediatric Malignant Solid Tumors in a Developing Country

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Summary

Objective: This study evaluates the burden of pediatric malignant solid tumors (PMST) in southeastern Nigeria.

Methods: Analysis of 174 cases of PMST managed at the University of Nigeria Teaching Hospital Enugu, from January 2002 to November 2007.

Results: PMST comprised 2.8% of pediatric admissions. Tumors encountered were lymphomas 77 (44.3%), Wilms’ tumor 35 (20.1%), sarcomas 20 (11.5%), neuroblastoma 15 (8.6%), retinoblastoma 14 (8.0%), teratomas 8 (4.6%) and hepatoma 5 (2.9%). Mean time for diagnosis was 3.3/2.4 months.

Advanced disease occurred in 135 (77.6%), while 39 (22.4%) had early disease. Only 166 (95.4%) commenced planned therapy, with 67 (40.4%) lost to follow-up. Of 99 children available for evaluation, 43 died (11 treatment related and 32 from relapse). Overall, 56 (56.6%) were alive after a mean follow-up of 20.7/10.5 months.

Conclusion: PMST are enormous challenge in our setting. Delayed presentation, poor treatment compliance and healthcare funding have to be addressed to improve outcomes.

Key words: pediatric tumors, disease burden, late presentation, developing world.

Introduction

Childhood morbidity and mortality in many developing countries are changing, with malignant solid neoplasms gradually assuming preeminence [1]. Globally, the problem of malignant solid tumors is particularly more pressing in developing countries [1–3]. In most developed countries, early diagnosis and recent advances in therapy have contributed to the significantly improved outcome of these tumors [4–6]. The outcome in most developing countries has however remained generally poor [7–12].

Recent studies estimate that about 85% of childhood cancers occur in developing countries and that the rate may exceed 90% in the coming decades [13]. However, most oncologists in developed countries might not be familiar with the burden, and the quandary of managing pediatric malignant solid tumors in a developing country. This may possibly hinder cooperation between the oncologists in the two settings.

This retrospective study aims to evaluate the burden of managing pediatric malignant solid tumors in southeastern Nigeria.

Patients and Methods

In southeastern Nigeria, most PMST are managed at the University of Nigeria Teaching Hospital Enugu (UNTH). Basic investigative studies for evaluation of solid tumors are available for these cases. On the other hand, MRI; radioisotope scan; tumor chemistry and tumor biology studies; and radiotherapy are not available (patients requiring radiotherapy are sent to Abuja, Lagos or Ibadan for this modality of treatment).

In UNTH, diagnosis of PMST is determined clinically using the available radiological evaluation. Confirmation was by histology of tissues obtained either surgically or by needle biopsy.

From January 2002 to November 2007, 174 cases of histologically confirmed PMST were managed in UNTH. These cases were analyzed. Excluded were
orthopedic and neurosurgical cases as most of these were managed outside our hospital.

Data of these children were sourced from the case notes, Cancer registry, theatre records and death registry. Data collected include: age at presentation, gender, presentation, duration of symptoms before presentation, documented reason for late presentation (for patients presenting >3 month after onset of symptoms), and treatment given before presentation. Also assessed were definitive diagnosis, treatment, outcome, duration of follow-up and documented hindrances in management.

Data Analysis

The Statistical Package for Social Sciences (SPSS 11.5 version) was used for data entry and analysis. For continuous variables, mean values and standard deviation were calculated and the mean compared using independent t-test. Proportions were compared with Chi-square.

Results

PMST comprised 2.8% of pediatric admissions (174/6156). The mean age at presentation was 6.9±4.1 years (range 1 month to 15 years) (Table 1). There were 108 (62.1%) males and 66 (37.9%) females (ratio 1.6:1).

The Malignant Solid Tumors

Lymphomas

There were 77 (44.3%) children with lymphoma. These include Burkitt’s lymphoma (n=57, 74%), other non-Hodgkin’s lymphoma (n=13, 16.9%) and Hodgkin’s lymphoma (n=7, 9.1%). The median age at presentation was 7 years for Burkitt’s, 12 years for other non-Hodgkin’s and 10 years for Hodgkin’s lymphoma respectively. Eight children (10.4%) presented with early disease and 69 (89.6%) with advanced disease.

Wilms’ tumor

The median age for the 35 children who presented with Wilms’ tumor was 4 years. Tumor involved the left kidney in 21 and right kidney in 14. Of these, six presented with stage II disease, 18 with stage III, and 11 with stage IV. There was no stage I or stage V disease.

Sarcoma

The sarcomas were rhabdomyosarcoma (n=12, 60%), fibrosarcoma (n=4, 20%), lymphosarcoma (n=2, 10%) and mesenchymoma (n=2, 10%). The median age at presentation for rhabdomyosarcoma was 5 years, and the other sarcomas 11.5 years. There were six children with stage II disease, nine with stage III and five with stage IV.

Neuroblastoma

There were 15 (8.6%) children with neuroblastoma. The median age at presentation was 5 years. Clinical staging showed: stage II (n=2, 13.3%), stage III (n=7, 46.7%), and stage IV (n=6, 40%). Stages I and IVS were not encountered. Primary sites of involvement were adrenals in 10, paraspinal in two, and unknown in three cases respectively.

Retinoblastoma

Of the 14 children with this tumor, 12 (85.7%) were unilateral and two (14.3%) were bilateral. Four (28.6%) presented with early disease while 10 (71.4%) had advanced disease. The median age at presentation was 2.6 years (range 6 months to 8 years).

Malignant teratomas

The teratomas encountered were ovarian (n=5), and sacrococcygeal (n=3). For the ovarian tumors, the median age at presentation was 9 years (range 8–10 years), and for sacrococcygeal tumors 5 months (range 3–11 months). Overall, four children presented with early disease and four with advanced disease.

Hepatoma

The five children with this tumor presented at a median age of 14 years (range 12–15 years). They all had advanced disease.

Delay in Presentation

Table 2 summarizes the time from onset of symptoms to presentation. Overall, the average duration of

<table>
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<tr>
<th>Age</th>
<th>Lymphoma</th>
<th>Wilms’ tumor</th>
<th>Sarcoma</th>
<th>Neuroblastoma</th>
<th>Retinoblastoma</th>
<th>Teratoma</th>
<th>Hepatoma</th>
<th>Total</th>
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<td>10–15 years</td>
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<td>174</td>
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symptoms before presentation was $3.3 \pm 2.4$ months. Neuroblastoma had the most delay in presentation (mean duration of symptoms $= 4.5 \pm 5.5$ months). One hundred and nine (62.6%) presented $\geq 3$ months from onset of symptoms. Presentation $\geq 3$ months was related to delayed referral from peripheral hospitals ($n = 69$, 63.3%), ignorance ($n = 15$, 13.8%), poverty ($n = 7$, 6.4%), or unspecified ($n = 18$, 16.5%). A significant proportion of children with $\geq 3$ months of symptoms at presentation had advanced disease (93.6 vs. 50.8%; $p < 0.001$) compared to cases presenting earlier.

**Treatment**

Eight (4.6%) children were taken away by the parents before planned therapy. The remaining 166 (95.4%) cases were commenced on planned therapy. Therapy involved surgery alone ($n = 15$), chemotherapy alone ($n = 76$), surgery and chemotherapy ($n = 64$), and combination of surgery, chemotherapy and radiotherapy ($n = 11$). Of the 166 children, 67 (40.4%) abandoned therapy following commencement and were lost to follow-up. The remaining 99 (59.6%) continued their therapy, out of which only 56 (56.6%) followed the prescribed regimen. Forty-three cases (43.4%) for financial reasons, or unavailability of the chemotherapeutic drugs, were irregular with the treatment regimen.

**Outcome**

Overall, only 99 children were available for evaluation. Thirty-two (32.3%) relapsed with fatal outcome, 11 (11.1%) succumbed to treatment related complications (five cases of uncontrollable hemorrhage; four cases of overwhelming septicemia; two cases of cardiogenic shock), and 56 (56.6%) survived (Table 3). The overall morality rate in the cases evaluated was 43.4%. Cases with late stage of disease at presentation had higher mortality (52.1 vs. 19.2%; $p = 0.003$) than cases with early disease. Poor compliance with therapy was also associated with increased mortality (72.1 vs. 21.4%; $p < 0.001$). The 56 surviving children have been followed up for a mean duration of $20.7 \pm 10.5$ months. Thirty-three have been followed up for $\geq 2$ years.

**Discussion**

We found that the number of cases of PMST in our setting might be on the increase. A comparison with earlier studies from sub-Saharan Africa [14–16] and some other developing countries [8, 17] indicate an increase in PMST cases attending tertiary care. Again, the number of cases reported from these referral centers might not reflect the true incidence of these tumors as unspecified number of these cases [18], may not be seeking care in mainstream health facilities.

The spectrum of PMST in our study is similar to what is reported in many developing countries: high proportion of lymphomas predominantly the Burkitt’s type [8, 9, 14, 15, 19, 20]. This is contrary to what is found in Europe and North America where central nervous system (CNS) tumors are the commonest solid tumors [4–6, 21]. Though this study did not include CNS tumors, there is evidence that hospital incidence of CNS tumors might be increasing in some developing countries [20–23].

Delayed presentation was a hindrance in the management of our patients. Although the retrospective study precluded a systematic recording of the explanations for late presentation, we found records in which reasons were listed. These included delayed referral from the peripheral hospital, ignorance of the problem by the parents and poverty.

It is also evident from this study that a substantial number of children did not comply with the treatment protocol. This mainly affected chemotherapy. Common reasons adduced for non-compliance were inability to afford the chemotherapeutic drugs, and irregular availability of these drugs. Some previous reports from other developing countries have also indicated high rate of non-compliance.
While the reasons for the poor compliance may be established, it is difficult to decipher the factors responsible for the high rate of abandonment of treatment in developing countries. Although poverty may be responsible, an appreciation of the socio-cultural dynamics of the people might be invaluable in unraveling other likely factors.

Multidisciplinary collaboration is another factor reported to contribute to improved outcome in oncology [24]. Significantly, this was lacking in the management of most of our patients. While this is consistent with what has been previously reported in some developing countries [25], the reason for the lack of multidisciplinary collaboration is unknown.

Our mortality rates are rather high when compared with mortality from developed countries [4–6]. Several studies [10, 13, 26] have decried the dismal outcome of these tumors in developing countries, but feasible initiatives aimed at improving these have been lacking. It may be beyond the scope of this study to concretely explain the mortality rates so as to make scientific suggestions for definite improvements. However, a number of our findings suggest areas where improvements are needed. The perennial problem of delayed presentation, and inadequate treatment are areas for possible intervention.

Solving these problems may require intervention on many levels: social; public health (education of the public to recognize early features the disease, including need and benefits of early treatment; developing outreach programs); local government (e.g. increasing health care funding, subsidizing treatment, improving facilities); and international (improving local health care infrastructure, training, collaboration, overall poverty reduction). Formation of local collaborative oncology groups and development of effective, safe and feasible treatment protocols based on the available and affordable drugs may be invaluable in the long term.

References