Presentation and Clinical Response to Treatment of Burkitt Lymphoma in Uganda

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Background

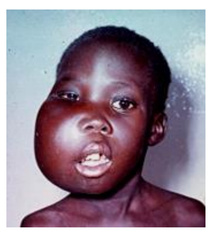
Hematologic malignancies in sub-Saharan Africa have emerged as a major cause of morbidity and mortality[1,3]. The management of these conditions in sub-Saharan Africa remains inadequate. Services are concentrated in major population centers in the more economically advanced areas, despite the fact that the majority of the population lives in rural areas[7]. In Uganda there is only one cancer institute located in the capital and there are no histopathology laboratories in the north part of the country.

St Mary's Hospital Lacor is located in Gulu, North Uganda, offering services to people living within 100 mile radius and sometimes beyond[5,6]. Lymphoma treatment is given at no cost to pediatric patients since 2003. Recently the hospital experienced a significant drop of communicable diseases and malaria related morbidity and mortality in the pediatric population, while the impact of pediatric cancers increased. In 2008 the hospital equipped and upgraded the pathology services and in 2010 began to participate in international clinical and research studies on Burkitt's Lymphoma to improve diagnostic capacity and quality of care. Lacor Hospital is a site for a Burkitt Lymphoma NCI study called EMBLEM and trough this collaboration in 2013 an hospital based cancer registry specifically designed to meet the needs of a rural hospital has been established, to improve care and follow up of patients, and to identify challenges.

Between 2009 and 2012, 554 new cases of pediatric malignancies were made and 308 (55%) were Burkitt's Lymphoma.

We are in the process of reviewing all these cases, and we have completed the analysis over 118 subjects.

Fig 1: St Mary's Hospital Lacor. The 3° largest hospital in Uganda



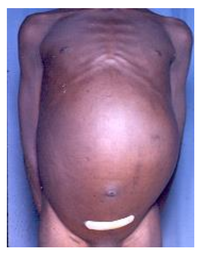


Fig 2: Endemic Burkitt Lymphoma Patients

Methods

Demographic, clinical, laboratory and treatment information was abstracted from charts of pediatric (<15 years) BL cases from November/2010 to October/2011 and keyed into a clinical database. Analysis was performed using frequency tables and survival methods

Results

118 new cases of pediatric malignancies were diagnosed. 82% were hematological malignancies. Burkitt's Lymphoma(BL) cases were 83. 70% of BL cases came from the north-western region of the country, from within the EMBLEM study region. M:F ratio was 2.39 and median age 7.8 years. Common symptoms of presentation were: Fever 35 (42.17%), weight loss 32 (38.55%), limb paralysis 12 (14.46%), body part swelling 51(61%). ECOG performance status was evaluated in 48 cases (57%) and had the following distribution: ECOG 4 in 11 cases (23%), ECOG 3 in 29 cases (60%), ECOG 2 in 4 cases (8%), ECOG 1 in 4 cases (8%). Common Sites of involvement were abdomen in 67 cases (80%), and Jaw in 27 cases (32%), Lymphnodal, Pleural/mediastinal and bone marrow involvement were rare and occurred in 4, 2, and 1 cases respectively. Central nervous system (CNS) involvement was assessed clinically by the presence of one or more of the following symptoms: cranial nerve palsy, paraplegia and paraparesis, or by the presence of CSF cytology positivity for malignant cells. CNS resulted involved in 34 cases (40%).

At the baseline laboratory investigations Hb was <7 g/dL in 15 cases and creatinine > 1.5 mg/dL or Urea > 50 mg/dL occurred in 14 cases of the 83 tested. HIV serology was positive in 1 case out of the 62 evaluable. LDH was not routinely available.

74 (89%) patients were treated and were evaluable for response. 94.6% of patients treated received a combination of intravenous (iv) cyclophosphamide, vincristine, low dose methotrexate plus intrathecal prophylaxis (drug cost $430 per patient fully treated and per capita health expenditure $3). 21 patients (63.6%) were enrolled in a clinical research study.

52 patients (70%) achieved complete remission (CR) (median time from diagnosis 26.4 days). The median follow up was 248.8 days. 25 cases were lost to follow up. Overall survival was 83% and death observed in 15 cases (20%), mean time from diagnosis 91 days. It was related to renal failure (creatine>1.5 mg/dL) (p=0.002), to limb paralysis (p=0.002), to clinical response (p<0.0001) but not to fever, site of disease, sex and age (P>0.5).

Common symptoms at presentation

n.	83	
Fever	35	42%
Weight Loss	32	39%
Body part swelling	51	61%
Limb paralysis	12	14%
Median duration of symptoms (months)		2.0

ECOG Performance Status at presentation

n.	48	
4	11	23%
3	29	60%
2	4	8%
1	4	8%
0	0	

Anatomical Sites

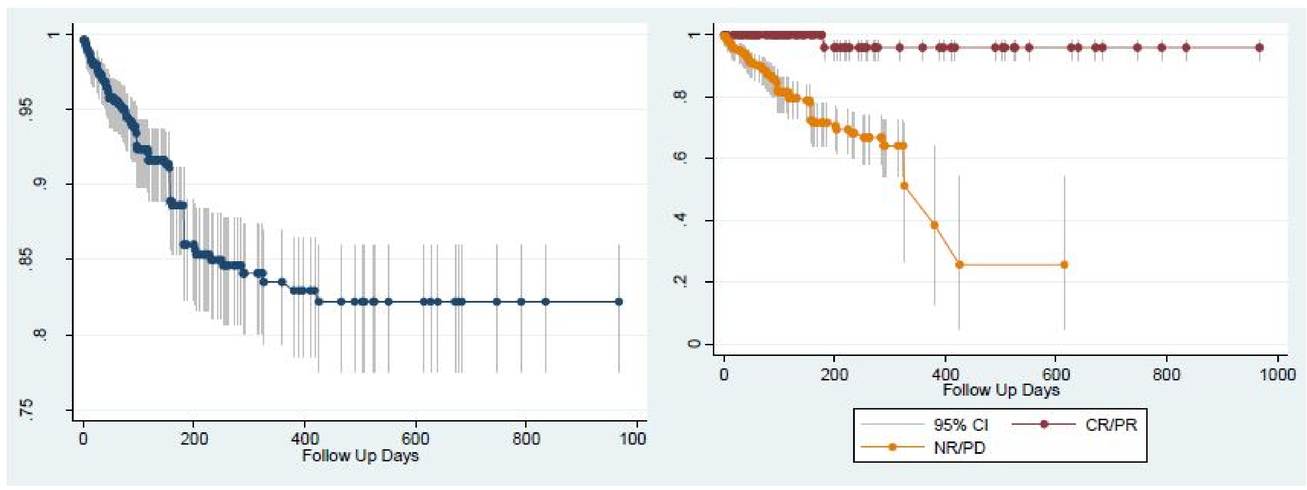
n.	83	
Abdomen	67	81%
Jaw	27	33%
CNS	34	41%
Lymphnodal	4	5%
Pleural	2	2%
Bone Marrow	1	1%

Laboratory Findings

n.	83	
Hb<7g/dL	15	18%
BUN > 50 mg/dL or Crea >1.5 mg/dL	14	17%
HIV (tested/pos)	62/1	1.6%

Response

BL cases	83	
Treated patients	74	
Complete Response	52	70%
Median time from diagnosis to remission (days)	26.4	
Median Follow up (days)	248	



Conclusions

Childhood lymphoid tumors are a big proportion of the curable non communicable diseases. The large majority of the patients come from very low income families and reach the hospital in advanced stages (40% with central nervous system involvement) poor performance status (83% in ECOG PS 3 and 4) and after a long duration of symptoms (2 months). A significant proportion of patients has already metabolic complications (18% with features of renal failure). The polichemotherapy with a low toxicity profile drugs is feasible and effective (70% of CR). However the poor follow up and the lack of compliance to the treatment affects the outcome and the accurate estimation of relapse rate.

Our study shows concerted efforts to spot cases early may improve outcomes and the potential for research using data from hospital databases. Analysis is continuing to estimate clinical benefit and to identify the social context of poor response.

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