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A retrospective analysis of paediatric lymphomas at Chris Hani Baragwanath Academic Hospital in Soweto, South Africa☆

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1. Introduction

Lymphomas are the third most common paediatric malignancy worldwide [1-6]. Childhood lymphomas exhibit unique characteristics when compared to adult lymphomas in terms of histopathological spectrum, site of involvement and prognosis [2,3]. Published data of paediatric lymphoma (PL) indicates approximately 60% are non-Hodgkin lymphomas and 40% are Hodgkin lymphomas (HL) [1]. Males are more commonly affected, [3,5] with an estimated male predominance of 70% [3]. NHL has a median age at diagnosis of 10 years [5]. The main NHL subtypes in the paediatric age group are Burkitt lymphoma (BL), diffuse large B-cell lymphoma (DLBL), lymphoblastic lymphoma (LL) and anaplastic large cell lymphoma (ALCL) [1-5].

Children with NHL usually present with aggressive extranodal disease, while adults commonly present with indolent, localised disease [2,3,5]. Despite the aggressive nature of paediatric NHL, the prognosis is favourable and superior to that of adults [2]. The cure rates of paediatric NHL are approximately 70–90% [1-5]. In children with immunodeficiency, there is an increased incidence of rare high-grade B-cell NHLs such as plasmablastic lymphoma (PBL) [10], primary effusion lymphoma (PEL) and primary CNS lymphoma (PCNSL) [2,11]. In the setting of HIV infection, paediatric lymphomas are inclined to manifest in uncommon extranodal sites, behave aggressively and consequently have a poor prognosis [2,10-12].

CHL comprises 80–90% of Hodgkin lymphoma (HL) in children [13]. In the developed world, children most commonly present with CHL between the ages of 12 and 15 years. In South Africa (SA), the average age of diagnosis is 8.6 years [14] and males are at higher risk for this disease. In immune competent individuals, nodal involvement is characteristic and the cervical lymph nodes are affected in 75% of patients [15]. Mixed cellularity (MC) CHL is the most common subtype in developing countries, while nodular sclerosis (NS) CHL is most common in the developed world. This discrepancy is thought to be due to the high prevalence of EBV in developing countries and its strong association with MC CHL [16]. An increased incidence of HL has not been noted among HIV seropositive children [7-9]. This finding is in contrast with the increased incidence of CHL in HIV seropositive adult patients [17,18]. HL in HIV often presents at an advanced stage, with involvement of extranodal sites. These patients have an inferior survival outcome when compared to HIV negative patients afflicted with HL [17,18].

In SA, the high prevalence of Human Immunodeficiency Virus (HIV) has been associated with an increased incidence of high grade paediatric lymphomas (PL) [7-9]. The prognosis of patients afflicted with HIV-associated lymphomas has improved following the advent of highly active antiretroviral treatment (HAART). In this scenario, improved immune status is a pivotal factor that enhances survival outcome [2].

There is limited published epidemiological data pertaining to PL in Africa. This study provides a retrospective overview of PL at Chris Hani Baragwanath Academic Hospital (CHBAH) and aims to contribute clinicopathological findings of PL in SA, in the setting of high HIV prevalence.

Ethical approval of this study was obtained from the Human Research Ethics Committee at the University of the Witwatersrand (clearance certificate number M120982).

2. Methodology

An observational retrospective cross-sectional study design was used. The target population included all cases of PL diagnosed in patients under 15 years of age from January 2007 to June 2013 (66 months), at the National Health Laboratory Service, Division of Anatomical Pathology at CHBAH, Soweto, SA. The group of patients was obtained using a Systematized Nomenclature of Medicine

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(SNOMED)-based search of the laboratory dataset. The stained slides (haematoxylin and eosin, immunohistochemistry and in situ hybridisation) were retrieved from the laboratory archives and reviewed by a pathologist (RSP) to confirm the histopathological diagnosis of all the cases included in this study. Data was subsequently extracted from the histopathology reports and the clinical files of patients. Age at diagnosis, gender, disease stage at presentation, topographic region of involvement at diagnosis (nodal or extranodal), HIV status (seropositive, negative or unknown), HAART administration and survival outcome were documented. HIV status was assessed in accordance with the national consolidated guidelines (December 2014) for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults.

Data analysis was performed using Statistica 12. The Fisher's exact test was used to compare categorical data. The Mann-Whitney test was used to determine if there was a significant age difference in the various epidemiological groups at diagnosis. Continuous data was assessed for normality using the Shapiro-Wilk test. Parametric continuous data was reported as means, while non-parametric data was reported as medians. Kaplan-Meier survival curves and log-rank tests were used for survival analysis (Medcal software, version 15.2.1). Statistical analyses that demonstrated probability (p-value) of < 0.05 (α-level 0.05) were interpreted as significant.

3. Results

A total of 59 cases of PL were confirmed during the study period of 66 months. For 7 cases, no clinical information was available and these cases were excluded from the data analysis.

Of the 52 cases analysed, there were 27 (52%) cases of NHL and 25 (48%) cases of CHL. Seventeen patients (33%) were HIV seropositive and 35 patients (67%) were HIV seronegative.

Forty two males and 10 females were diagnosed with PL during this study period (male to female ratio of 4.2:1).

3.1. Histopathological subtypes

There were 27 NHL cases (as shown in Table 1) which occurred in 20 males and 7 females (male to female ratio of 2.86:1).

Of the patients who were diagnosed with NHL, 15 (56%) were HIV seropositive and these patients comprised 88% of the total HIV positive group (n = 17) in this study.

NHL subtypes that occurred in the HIV seropositive group are shown in Table 2.

Table 1
NHL histopathological subtypes.

NHL subtype	Number of cases	% of NHL (n = 27)
Burkitt lymphoma	12	44.4%
B-cell LL	3	11.1%
PBL (Fig. 1)	3	11.1%
DLBL	2	7.4%
B-cell lymphoma, unclassifiable, with features intermediate between DLBL and BL	2	7.4%
T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL)	1	3.7%
T-cell LL	3	11.1%
ALCL	1	3.7%

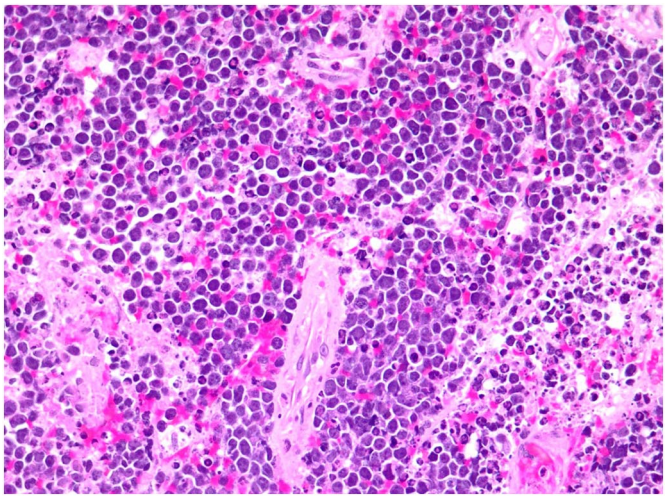

Fig. 1. Morphological features of PBL(× 400 magnification).

Table 2
NHL in the HIV seropositive group.

NHL subtype	Number of cases in the HIV seropositive group	Percentage of the total number of NHL (n = 27)	Percentage of the NHL subtype in the total group (HIV seropositive and seronegative patients)
BL	7	25.9%	58.8% (n = 12)
PBL	3	11.1%	100% (n = 3)
B-cell LL	1	3.7%	33.3% (n = 3)
THRLBCL	1	3.7%	100% (n = 1)
DLBL	1	3.7%	50% (n = 2)
ALCL	1	3.7%	100% (n = 1)
T-cell LL	1	3.7%	33.3% (n = 3)

NHL was confirmed in 12 patients (44%) (as show in Table 3) who were HIV seronegative. These patients constituted 34% of the HIV negative group (n = 35).

Table 3
NHL cases per histopathological subtype in the HIV seronegative cohort.

NHL histopathological subtypes	Number of cases in the HIV seronegative cohort	Percentage of the total number of NHL (n = 27)	Percentage of the NHL subtype in the total cohort (HIV seropositive and seronegative patients)
BL	5	18.5%	41.7% (n = 12)
B-cell LL	2	7.4%	66.7% (n = 3)
DLBL	1	3.7%	50% (n = 2)
B-cell lymphoma, unclassifiable, with features intermediate between DLBL and BL	2	7.4%	100% (n = 2)
T-cell LL	2	7.4%	66.7% (n = 3)