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The Outcomes of Sixty-Two Patients With Burkitt Lymphoma A Single-Center Study At King Abdulaziz Medical City Jeddah, Saudi Arabia

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Abstract
Burkitt lymphoma (BL) is a highly aggressive curable mature B-cell non-Hodgkin lymphoma characterized by the deregulation of the c-MYC gene on chromosome 8. It has three clinical forms, of which the sporadic type is the most common. I conducted this study because the literature is deficient to Burkitt lymphoma in Saudi Arabia.

Method:
a retrospective study of 62 patients treated for Burkitt lymphoma in the Princess Norah Oncology Center at King Abdulaziz Medical City in Jeddah, Saudi Arabia, between 2000 and 2017. Patient characteristics, progressive-free survival rates, and overall survival rates were assessed.

Results
The majority of patients were in the high-risk group, which was defined as the disease at an advanced stage with bone marrow and CNS involvement. The survival rates with different treatment protocols were comparable to international rates. Less intense chemotherapy, such as R-EPOCH, are good alternatives for treating Burkitt lymphoma regardless of HIV status. Elderly patients have relatively low survival rates because only around one-third are cured of the disease. Thus, more studies should be conducted on high-risk elderly patient populations

Keyword - *Burkitt, lymphoma, outcome, REPOCH, RCODOX-M*

I. INTRODUCTION

Burkitt lymphoma (BL) is a highly aggressive mature B-cell non-Hodgkin lymphoma characterized by the deregulation of the c-MYC gene on chromosome 8.[3, 4]. The three clinical forms of BL are endemic (African), sporadic (non-endemic), and immunodeficiency-associated.[5, 11] Each has a different geographical distribution. The endemic variant is found in equatorial Africa and New Guinea, where it has an incidence rate that is approximately 50 times greater than in the United States.[6] The male-to-female incidence ratio is approximately 2:1. The sporadic type accounts for 1–2% of all non-Hodgkin lymphoma in adults, is the most common type globally, and has a male-to-female incidence ratio of approximately 3:1. The immunodeficiency-associated variant is primarily seen in patients with human immunodeficiency virus (HIV) infection and less commonly in patients with other causes of immunodeficiency, such as organ transplant recipients. In HIV-positive patients, BL typically affects those with a CD4 count of > 200 cells/μL. In comparison with most other HIV-associated lymphomas, the incidence of BL in the HIV-positive population has not decreased with the advent of potent antiretroviral therapies. NCI reports a CR rate of 90%[1] and a two-year event-free survival rate of 92% with intense chemo-immunotherapy treatment protocols.[2]
Different chemotherapy-intensive protocols have been used to treat BL, including HCVAD, CODOXM/IVAC,[7, 8, 9, 10], and REPOCH, which Dunlevy introduced in 2013, all of which have relatively good health outcomes, regardless of whether the patient is infected with HIV.[12]
We conducted this study because we found that the literature is deficient to Burkitt lymphoma in Saudi Arabia, to understand how its occurrence compares to international data, and determine how its outcomes differ about treatment regimen.

Patients and methods

Patient selection and clinical data collection

All patients were at least 14 years old who were diagnosed with and treated with Burkitt lymphoma in the Princess Norah Oncology Center at the King Abdulaziz Medical City in Jeddah, Saudi Arabia, between 2000 and 2017. We reviewed clinical records. We only included cases that had sufficient clinical data available for calculating event-free survival (PFS) and overall survival (OS) rates. As a result, a total of 62 patients were included in our study. We analyzed patient characteristics and calculated PFS and OS rates.
Pathology assessment

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All pathologies were reviewed in our lab. We included patients who had morphological pictures with proliferative indices > 90 and immunophenotypic characteristics of Burkitt lymphoma. Patients who were revealed to have MYC-translocation by cytogenetic testing or fluorescence in situ hybridization were considered supportive in special cases but were not required for selection.

Chemotherapy regimens

Details on the chemotherapy regimens received by the patients included in this study are summarized in Table 1. All treatment regimens included rituximab administration.

Table 1. Types of chemotherapy received

Chemotherapy protocol	No. of patients	Percentage of patients
RCODOX-M/RHCVAD (intensive)	36	58.1%
DA-R-EPOCH (less intensive)	17	27.4%
RCHOP/RCVP (palliative)	*9*	*14.5%*

Results

Patient characteristics and chemotherapy regimens

A total of 90 patients were initially identified for inclusion in this study, of which 28 were excluded because they had incomplete records or different diagnoses, resulting in 62 patients being included in this study. Slightly over half of them were over 45 years old, and approximately 60% were male. Approximately 92% were in the high-risk group according to the NCI risk classification. The performance status was 1–2 for 58% of the patients. The majority of the patients had no comorbidities. Approximately 5% of the patients had multiple comorbidities, such as diabetes mellitus, renal impairment, and liver disease. Table 2 contains patient characteristic summary information.

Table 2. Patient characteristics

Patient characteristic	**No. of patients**	**% of patients**
Age		
< 45 years old	32	51.6
> 45 years old	30	48.4
Gender		
Male	25	40.3
Female	37	59.7
B symptoms		
Yes	39	62.9
No	19	30.6
N/A	4	6.5
ECOG		
1-2	36	58.1
3-4	8	12.9
N/A	18	29
Comorbidities		
None	42	67.7
DM	12	19.4
Single comorbidities other than DM	5	8.1
Multiple comorbidities	3	4.8
HIV+VE	9	14.5
HIV-VE	53	85.5
CNS+VE	13	21
CNS-VE	47	75.8
N/A	2	3.2
BM+VE	23	37.1
BM-VE	39	62.9
PLT		
< 100	11	17.7
> 100	51	82.3
LDH		
Normal	6	9.7
High	56	90.3
Low Risk	5	8.1
High Risk	57	91.9

The records analysis revealed that 14.5% of the patients were HIV-positive, 75.8% were CNS-negative, and 21% were CNS-positive. More than one-third of the patients had bone marrow involvement upon diagnosis. Just over half of the patients had platelet counts less than or equal to 100 upon diagnosis. A significant majority of the sample was categorized as high-risk and had high LDH readings. Most of the patients suffered from febrile neutropenia toxicity. Less than two-thirds of the sample received intensive chemotherapy. The CR/PR rate was 90.3%, and 8.1% of patients suffered treatment-related death.

The two-year OS rate was 77.6 ± 5.6% (Table 3) and the two-year PFS rate was 59.8 ± 6.4% (table 4). CNS-positivity was correlated with poor OS and PFS durations (P-value $\leq$ 0.05). Similarly, patients with multiple comorbidities and bone marrow involvement had the relatively short OS and PFS durations. HIV status and chemotherapy protocol did not affect OS and PFS durations.

Table 3. Two-year OS rates.

	No. of patients	Two-year OS rates	P-value
OS	62	77.5 ± 5.6%	
Age			0.249
< 45	32	87.1 ± 6%	
> 45	30	66 ± 9.3%	
Gender			
Female	25	74.2 ± 9.1%	0.827
Male	37	80 ± 6.8%	
Comorbidities			
None	42	81.5 ± 6.4%	0.001
DM	12	82.5 ± 5.5%	
Single comorbidities other than DM	5	84.3 ± 13.1%	
Multiple comorbidities	3	0%	
HIV+VE	9	49.4 ± 22.8%	0.43
HIV -VE	53	78 ± 5.9%	
CNS+VE	13	68.4 ± 13.1%	0.096
CNS-VE	47	84.3 ± 5.5%	
N/A	2	0%	
BM+VE	23	63.8 ± 10.4%	0.014
BM-VE	39	85.6 ± 6%	
Chemotherapy			0.548
Protocol	36	77.2 ± 7.1%	
Intensive	17	75.7 ± 12.4%	
R-EPOCH	9	64.8 ± 16.5%	
Palliative			

Table 4. Two-year PFS rates.

	No. of patients	Two-year OS rates	P-value
PFS	62	59.8 ± 6.4%	
Age			0.424
< 45	32	65.6 ± 8.4%	
> 45	30	53.4 ± 9.6%	
Gender			0.494
Female	25	63.7 ± 9.7%	
Male	37	56.8 ± 8.5%	
Comorbidities			0.001
None	42	59.5 ± 7.6%	
DM	12	72.2 ±13.8%	
Single comorbidities other than DM	5	75 ± 21.7%	
Multiple comorbidities	3	0%	
HIV+VE	9	50.8 ± 17.7%	0.365
HIV-VE	53	61.5 ± 6.8%	
CNS+VE	13	40.4 ±14.9%	0.017
CNS-VE	47	67.6 ± 6.9%	
N/A	2	0%	
BM+VE	23	45.5 ± 10.8%	0.365
BM-VE	39	61.5 ± 6.8%	
Chemotherapy			0.209
Protocol	36	60.1 ± 8.3%	
Intensive	17	73.3 ± 11.4%	
R-EPOCH	9	33.3 ± 15.7%	
Palliative			

Discussion

Burkitt lymphoma is curable, but there is a lack of data about its behavior and response to Saudi Arabia's treatment. We conducted this retrospective single-center study about Burkitt lymphoma to help overcome this lack of data.

Most of our patients were in the high-risk group and had similar age and gender distributions found in international data.

Most of the HIV-positive patients discovered that they were HIV-positive upon presentation. There was no correlation between CD4 count and disease response or behavior.

Burkitt lymphoma is typically aggressively treated with intense chemotherapy using the Magrath or HCVAD protocol. The survival rates of patients in this study are comparable to those treated in other centers.

The median patient age in this study was 45 years old, whereas the median age of patients in another study was 69 years old.[19] Age has a multifactorial effect on health outcomes and is correlated with increased

treatment toxicity.[9] Most of the patients presented with B symptoms, which is similar to the results of another study.[11] The performance status results in this study were similar to those in two other studies.[8, 19] Most of the patients in this study who received intensive chemotherapy received either Hyper-CVAD or R CODOX-M/IVAC, which is similar to the results of several other studies.[9, 13, 14]

In this study, 21% of patients were CNS-positive, which is different from another study that found only a single patient with CNS involvement.[19] CNS involvement is expected in 15% of Burkitt lymphoma cases.[9] A retrospective multicenter study with similar patient demographic characteristics as the patients in this study found that 42% presented with bone marrow involvement. Additionally, they found that 54% of patients had high LDH, while in this study, over 90% did.[8] A significant number of patients in this study were characterized as high-risk, unlike another study in which only 10% were.[12]

In this study, CNS-positivity was positively correlated with health outcomes. This result was similar to that found in another study which found that CNS-positivity in childhood and adolescence was negatively correlated with health outcomes.[15] It was also the strongest predictor for relapse.

In this study, bone marrow involvement was negatively correlated with health outcomes. This result was similar to those in other studies, which found that bone marrow involvement was negatively correlated with predicted health outcomes.15, 16 In this study, there was a strong correlation between having multiple comorbidities and predicted health outcomes unique to the Saudi Arabian population. A recent study on the complications and comorbidities among Saudi Arabian diabetic patients in northern Saudi Arabia reported that peripheral neuropathy, retinopathy, diabetic septic foot, and amputation occurred in 40%, 38%, 14% 4% of patients respectively. Out of the 50 patients included in that study, 12 (24%), 18 (36%), and 8 (16%) had thyroid disease, dyslipidemia, and renal complications, respectively.18 In this study, all HIV-positive patients received REPOCH therapy with HAART medications to control viral activity. This study showed that HIV status did not influence OS or PFS durations, which was similar to another study in which HIV-positive and -negative patients received REPOCH chemotherapy which revealed that the groups had similar four-year PFS and OS durations.10–12 The fact that the survival rate in our study was 75.7 ± 12.4 might have been a product of the fact that this protocol was used to treat CNS-positive HIV-positive patients.

The older patients in our study had positive health outcomes despite receiving less intensive palliative chemotherapy, especially those without significant comorbidities. Thus, more studies should be conducted on elderly patients receiving less intensive palliative chemotherapy.

Limitations

The study had strengths and limitations. Much of the literature does not address Burkitt lymphoma in elderly patients, so this study makes a significant contribution in showing that age is not a cause of X. However, this study was limited in that it was retrospective. However, its results can serve as an epidemical baseline for Burkitt lymphoma in PNOC.

Conclusion

Burkitt lymphoma is a highly aggressive disease. The initial evaluation of patients plays a major role in developing a therapeutic plan. This study's results showed that CNS status, bone marrow involvement, and the presence of multiple comorbidities affect OS and PFS durations. Future studies should be prospective, include cytogenetic information, and be conducted with patients from multiple centers on the national level. Future studies should also be conducted solely focused on elderly patients to determine the optimal treatment option for them.

REFERENCES

[1] Costa LJ, Xavier AC, Wahlquist AE, Hill EG., Trends in survival of patients with Burkitt lymphoma/leukemia in the USA: An analysis of 3,691 cases. Blood. 121:4861,(2013).

[2] Magrath, I, Adde M, Shad A, et al., Adults and children with small non-cleaved-cell lymphoma have similar excellent outcomes when treated with the same chemotherapy regimen. J Clin Oncol, (1996) 14:925.

[3] Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood, 127(20) (2016) 2375.

[4] Hummel M, Bentinck S, Berger H, et al., A biological definition of Burkitt's lymphoma from transcriptional and genomic profiling, In Molecular Mechanisms in Malignant Lymphomas Network Project of the Deutsche Krebshilfe, N Engl J Med., 354(23) (2006) 2419.

[5] Magrath I., Epidemiology: clues to the pathogenesis of Burkitt lymphoma, Br J Haematol, 156(6) (2012) 744-756.

[6] van Imhoff GW, Appel IM, Veeger NJ, Kluin PM, Kluin-Nelemans JC., Gender- and age-related differences in Burkitt lymphoma epidemiological and clinical data from the Netherlands, Eur J Cancer, 40(18) (2004) 2781-2787.

[7] Mead GM, Sydes MR, Walewski J, et al., An international evaluation of CODOX-M and CODOX-M alternating with IVAC in adult Burkitt's lymphoma: Results of United Kingdom Lymphoma Group LY06 study, Ann Oncol, 13(8) (2002) 1264.

[8] Hoelzer D, et al., Improved outcomes of adult Burkitt lymphoma/leukemia with rituximab and chemotherapy: A report of a large prospective multicenter trial. Blood, The Journal of the American Society of Hematology, 124(26)(2014) 3870-3879.

[9] Jacobson C, LaCasce A., How I treat Burkitt lymphoma in adults. Blood, The Journal of the American Society of Hematology, 124(19)(2014) 2913-2920.

[10] Ribera JM, Garcia O, Grande C, et al., Dose-intensive chemotherapy including rituximab in Burkitt's leukemia or

lymphoma regardless of human immunodeficiency virus infection status: Final results of a phase 2 study (Burkimab). Cancer, 119(9) (2013) 1660-1668.

[11] Casulo C, Friedberg J., Treating Burkitt lymphoma in adults. Current Hematologic Malignancy Reports, 10(3)(2015) 266-271. doi:10.1007/s11899-015-0263-4.

[12] Dunleavy K, Pittaluga S, Shovlin M, et al., Low-intensity therapy in adults with Burkitt's lymphoma. N Engl J Med., 369(203) 1915-25.

[13] Magrath, I, Adde M, Shad A, et al., Adults and children with small non-cleaved-cell lymphoma have similar excellent outcomes when treated with the same chemotherapy regimen, J Clin Oncol Offic J Am Soc Clin Oncol. 14 (1996) 925-34.

[14] Thomas DA, Faderl S, O'Brien S, et al., Chemoimmunotherapy with hyper-CVAD plus rituximab to treat adult Burkitt and Burkitt-type lymphoma or acute lymphoblastic leukemia. Cancer. 106 (2006) 1569-80.

[15] Salzburg J, et al., Prevalence, clinical patterns, and CNS involvement outcomes in childhood and adolescent non-Hodgkin's lymphoma differ by non-Hodgkin's lymphoma subtype: A Berlin-Frankfurt-Munster Group Report, Journal of Clinical Oncology, 25(25) (2007) 3915-3922.

[16] Cairo MS, Gerrard M, Sposto R, et al., Results of a randomized international study of high-risk central nervous system B non-Hodgkin lymphoma and B acute lymphoblastic leukemia in children and adolescents, Blood, 109(2007) 2736-2743.

[17] Song JY, Venkataraman G, Fedoriw Y, et al. Burkitt leukemia limited to the bone marrow has a better prognosis than Burkitt lymphoma with bone marrow involvement in adults. Leukemia & Lymphoma, 57(4) (2016) 866-871. doi:10.3109/10428194.2015.1085529.

[18] Alshaya, Abdulrahman K, et al., The common complications and comorbidities among Saudi diabetic patients in northern Saudi Arabia, Open Journal of Endocrine and Metabolic Diseases, 7(7) (2017) 151.

[19] Perry, Anamarija M, et al., B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma: A study of 39 cases, British Journal of Haematology, 162(1)(2013) 40-49.