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Burkitt's Lymphoma with Otolaryngological Localisation in Children: Epidemiological and Clinical Aspects as Well as Virological Diagnosis at Brazzaville

Otouana Dzon HB[1], Ngouoni GC[2], Diembi S[3], Tsierie-Tsoba A[2], Ondzotto GW[2], Itiéré-Odzili AF[2], Ondzotto G[2], Moukassa D[4]

[1]Department of ENT, Talangaï Reference Hospital, Congo

[2]Department of ENT, University Hospital Center of Brazzaville, Congo

[3]Department of ENT, Adolph SICE General Hospital, Congo

[3]Faculty of Health Sciences, Masters Department, Congo

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***Corresponding author:** Otouana Dzon HB, Department of ENT, Talangaï Reference Hospital, Congo

ABSTRACT

Introduction: Burkitt's disease is a lymphoproliferative pathology where the Epstein Barr virus (EBV) is the main risk factor. The aim of this work was to study the epidemiological and clinical aspects of Burkitt's lymphoma and establish the virological diagnosis in the otolaryngological localization in children.

Patients and methods: This was a 10-year descriptive study carried out in Brazzaville jointly by the ENT department and the pathological anatomy and cytology laboratory of the University Hospital. These were tumor biopsies from the ENT sphere with histological evidence of Burkitt's lymphoma only in children under 18 years of age. A histopathological confirmation analysis was performed before performing the immunohistochemistry technique using anti-EBNA-1 monoclonal antibodies specific for EBV.

Results: a total of 7 cases of Burkitt's lymphoma were collected representing 5.8% of all ENT cancers. The average age was 12.2 ± 4.8 years (extremes: 6 – 15 years) with a ratio of 0.4 in favor of girls and all the children were immunocompetent. The most frequent localization was maxillary (n=6) followed by the orbito-nasal localization (n=1) all unilateral. In immunostaining on paraffin sections there was an overexpression of the majority viral protein EBNA-1 (n=6) indicating co-infection with EBV in 85.7% of cases.

Conclusion: in accordance with literature data, in Brazzaville, Burkitt lymphoma in children is mainly associated with the Epstein-Barr virus. The EBNA-1 gene can be considered as a diagnostic biomarker whose overexpression is an important mechanism in carcinogenesis.

Keywords: Burkitt's lymphoma; Epstein Barr virus; EBNA-1 gene; immunohistochemistry.

INTRODUCTION

Burkitt's lymphoma is a blood disorder classified in the category of B-cell non-Hodgkin's lymphoma [1]. It is an aggressive, rapidly evolving tumor, present endemically in Africa in children as well as in immunocompromised subjects in non-endemic areas, and sporadically in temperate regions [1,2]. African Burkitt lymphoma is the most common neoplasia in children in endemic regions where the Epstein-Barr virus (EBV) as well as other environmental factors are involved in its genesis which involves complex mechanisms of cellular regulations [1-4]. In the ENT sphere, this tumor retains characteristics common to all lymphomas and specific characteristics. The common characteristics are the possibility of distant extension and the usual response to chemotherapy while the particular characteristics linked to the ENT location imply certain behaviors in the search for the initial location, in the treatment and in the overall survival estimated at 90% even at the advanced stage [5,6]. However, biological diagnosis, and even monitoring during and after treatment, require a sufficiently equipped technical platform, particularly in the immunomarking technique, which still remains an enigma in several African countries [6]. Thus, the evaluation of a viral association by EBV will make it possible to contribute to the etiological diagnosis and improve the management of this pathology in Congolese children. The aim of this work was to describe the epidemiological-clinical aspects of Burkitt lymphoma and to establish a virological diagnosis in ENT locations in children.

PATIENTS AND METHODS

This was a descriptive and transversal study lasting 10 years from January 1, 2012 to December 31, 2021. It was carried out in three (3) locations, namely: the ENT-CCF department and the laboratory. pathological anatomy and cytology at the Brazzaville University Hospital Center as well as at the Faculty of Health Sciences. All children under 18 years of age with Burkitt lymphoma with histological proof were included. Each of them had a complete medical file including all epidemiological, clinical and pathological data. Biologically, these were paraffin-embedded tumor biopsy specimens on which a histopathological confirmation analysis was carried out before carrying out the immunohistochemistry technique using anti-EBNA-1 monoclonal antibodies specific for EBV. The children excluded from this study were those for whom tissue samples did not allow immunostaining to be carried out due to lack of fixation of endogenous peroxidases or excessive dehydration. The immunostaining technique on paraffin sections was manual and the revelation was carried out following the kit manufacturer's recommendations. The positivity of the signal was retained in the face of a labeling of more than 50% of the cells and its intensity was assessed (minimal, moderate, intense). Thus the parameters studied were epidemiological (frequency, age, sex), clinical (history, functional signs, tumor site) and the results of immunostaining (expression of the viral antigen EBNA-1). Data entry and analysis were done using Microsoft Excel 2013.

RESULTS

A total of 120 files of children followed for various otorhinolaryngological cancers were collected during the study period. Among them, seven (07) had Burkitt lymphoma, representing 5.8% of otolaryngological and head and neck cancers. There were 5 girls (71.4%) and 2 boys (28.6%) for a ratio of 0.4 as presented in Table 1. The average age was 12.2 years ± 6 (6 to 17 years) and the most representative age group was 6 to 10 years. No pathological history was reported and all children were immunocompetent. The main warning signs were left

hemifacial swelling (n = 6, or 85,7%) (Figure 1). linked to a bucco-maxillary location followed by left cervical spinal lymphadenopathy (n = 1, or 14.3%). Verification of the diagnosis of lymphoma by a pathologist revealed a diffuse proliferation of small B cells with rounded nuclei, known as a starry sky image (Figure 2). Immunostaining with anti-EBNA-1 monoclonal antibodies revealed a molecular prevalence of Epstein-Barr virus (EBV) at 85.7%, mainly in the oral-maxillary location (P = 0.001) (Table 2). The overexpression of the EBNA-1 gene by nuclear marking was intense on more than 50% of the cells as shown in Figure 3. All the children were referred to the clinical hematology department for medical treatment with multi-cancer chemotherapy.

TABLES

Table 1: Distribution of children by age and sex.

Age (year)	Sex		
	Male N (%)	Feminine N (%)	Total N (%)
06 - 10	1 (14,3)	5 (71,4)	6 (85,7)
10 - 14	0	0	0
14 - 17	1 (14,3)	0	1 (14,3)
Total	2 (28,6)	5(71,4)	7(100)

N = workforce, %: percentages

Table 2: EBV immunostaining and tumor location.

Tumor location	EBV			
	Positive N (%)	Negative N (%)	Total N (%)	p-value
Lymph node	0	1 (14,3)	1 (14,3)	
Oral-maxillary	6 (85,7)	0	6 (85,7)	0,001
Nasal	0	0	0	
Total	6 (85,7)	1 (14,3)	7 (100)	

N = workforce, %: percentages

FIGURES

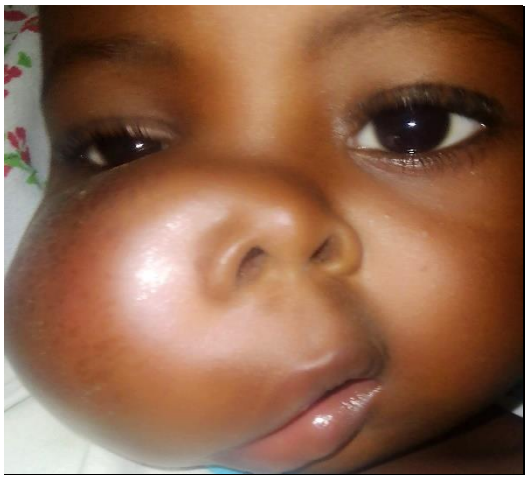

Figure 1: Right infraorbital swelling in 3-year-old girl.

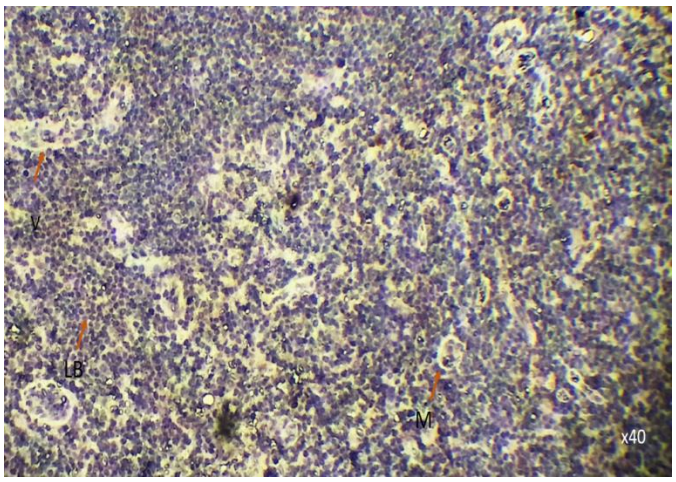

Figure 2: Starry sky image characteristic of a Burkitt lymphoma (diffuse proliferation of small B cells with rounded nuclei). Laboratory of pathological anatomy and cytology, University hospital center of Brazzaville.

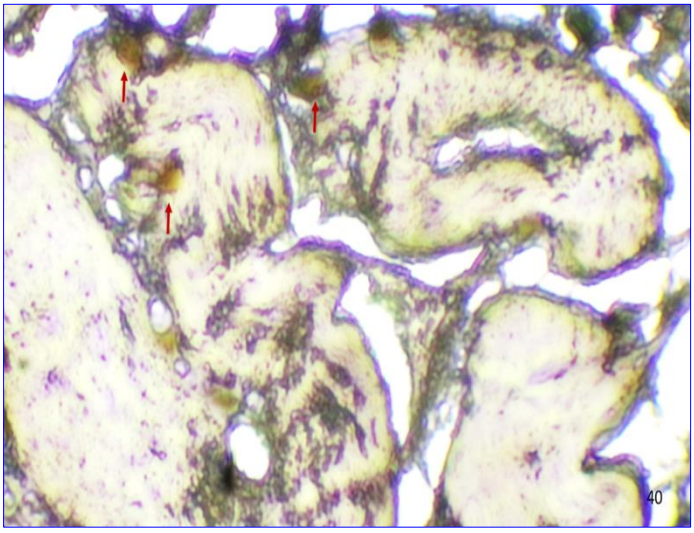

Figure 3: Anti-EBNA-1 immunohistochemistry (positive nuclear staining). Laboratory of pathological anatomy and cytology, university hospital center of Brazzaville.

DISCUSSION

African Burkitt lymphoma remains rare in otolaryngological location in Brazzaville. It represented only 5.8% of all otolaryngological cancers and girls were affected twice as often as boys, which seems completely contrary to the data reported in the literature [7-9]. This was only a small series of 7 children listed in our services, unlike other observations resulting from large meta-analytic and sometimes multicenter studies which give a real appreciation of the epidemiological situation in terms of the ratio between girls and the boys. If the present study reports an average age of 12.2 years as also presented by Bouda et al, Gopal et al [7,8], however other authors report different average ages and not close to ours. This is the case of Vans et al [10], and Berhnardt et al. [11] who respectively report 6 years and 8 years as average ages. In general, in Brazzaville, as in other African cities,

parents only bring children for specialized consultation at advanced stages of the disease, whereas in better-equipped countries consultations occur early. This explains the differences in average ages in Africa and particularly in Brazzaville compared to fairly industrialized and better equipped cities. Many authors both in Africa and in the West have described the influence of HIV infection in Burkitt's disease alongside the endemic or African form which would be specific to the Epstein-Barr virus [12]. However, all the children in this study were immunocompetent, which is an exception given the seroprevalence of HIV infection in African cities which remains increasingly high and worrying [13]. Indeed, in the case of HIV infection, if the viral load is still high and the antiviral treatment is not yet optimized, there is a susceptibility in children to develop Burkitt lymphoma [14,15]. The unilateral bucco-maxillary location observed mainly in this study (85.7%) has also been reported by numerous authors such as Boidy et al, Patte et al [16,17]. For these authors, African or tropical Burkitt's lymphoma, although classically localized in the maxilla, can also develop at the orbital and lymph node level. The main risk factor for this type of African lymphoma is the Epstein-Barr virus, the carcinogenic activity of which is a genetic mutation with translocation type t (8, 14) (q24; q32) through the oncogene C- MYC [10]. In the present study, immunostaining on paraffin sections was used as a viral diagnostic technique using EBV-specific anti-EBNA-1 monoclonal antibodies. It emerged that the overexpression of the EBNA-1 gene was indicative of the presence of EBV within tumor tissues, and therefore this virus would be the main risk factor for Burkitt lymphomas in Brazzaville with a molecular prevalence of 85.7%. Histopathologically, this is a star-sky image characterized by a diffuse proliferation of small B cells with rounded nuclei whose anti-EBNA-1 marking is positive on more than 50% of the cells as was the case in this study. This strong molecular signature of EBV in Burkitt's lymphoma with otorhinolaryngological localization allows precise diagnostic referral to the clinical hematology department with the aim of organizing medical treatment by anticancer polychemotherapy. This pathology remains a therapeutic emergency requiring combinations of anti-mitotic agents, namely: Cyclophosphamide, Vincristine, Doxorubicin or Adriamycin and high dose Methotrexate [18,19]. Recent studies complement this protocol with targeted therapy based on Rituximab. This is a pharmaceutical molecule intended to prevent the surface proteins of cancer cells from emitting mitotic signals, which will allow the destruction of a large quantity of cancer cells [20]. All the children in this study were referred to hematologists for continued treatment and none of them was reviewed by an ENT specialist for possible biopsies on residual lesions.

CONCLUSION

In accordance with literature data, in Brazzaville, Burkitt lymphoma in children is mainly associated with the Epstein-Barr virus. The majority of these were immunocompetent girls seen for hemifacial swelling in relation to a bucco-maxillary location. The EBNA-1 gene can be considered as a diagnostic biomarker whose overexpression indicates the presence of EBV.

REFERENCES

1. Rafaramino F, Maminirina A, Razafindrabe L, Rabarijaona A, Randriamampandry P, Rakotobe L. Epidemiological aspects of Burkitt's lymphoma in children of Madagascar. Bull Soc Pathol Exot. 2021;94(5):385-8.

2. Doumbé P, Mbakop A, Essomba Mboumi MT, Obama MT, Kago I, Gonsu J, et al. Burkitt lymphoma in Cameroon children: descriptive and clinico-anatomical aspects. Bull Cancer. 2017;84(4):379-83.
3. Charmot G, Rodhain F, Roze JM. Epidemiology of Burkitt's lymphoma in tropical areas -its relationship with malaria. Nouv Presse Med. 2021;7(4):277-9.
4. Geser A, Brubaker G. A preliminary report of epidemiological studies of Burkitt's lymphoma, Epstein-Barr virus infection and malaria in North Mara, Tanzania. IARC Sci Publ. 2021;32(60):205-15.
5. Togo B, Keita MA, Diallo M, Traoré F, Traoré CB, Mohamed AG et al. Lymphome de burkitt pédiatrique à révélation orl: quelle prise en charge en milieu sub sahélien? Réflexion sur trois cas. J. TUN ORL. 2008;20:62-6.
6. de-Thé G. Epstein-Barr virus and Burkitt's lymphoma worldwide: the causal relationship revisited. IARC Sci Publ. 2018;60:165-76.
7. Bouda GC, Traoré F, Couitchere L, Raquin MA, Guedenon KM, Pondy C, et al. Advanced Burkitt Lymphoma in Sub-Saharan Africa Pediatric Units: Results of the Third Prospective Multicenter Study. J Glob Oncol. 2019;5:1-9.
8. Gopal S, Gross TG. How I treat Burkitt lymphoma in children, adolescents, and young adults in sub-Saharan Africa. Blood. 2018;132(3):254-263.
9. Patte C, Auperin A, Michon J, Behrendt H, Leverger G, Frappaz D et al. The Société Française d'Oncologie Pédiatrique LMB89 protocol: highly effective multiagent chemotherapy tailored to the tumor burden and initial response in 561 unselected children with B-cell lymphomas and L3 leukemia. Blood. 2001;97(11):3370-9.
10. Vance GH, Lotodo T, Kigen N, Stohler R, Choi H, Njuguna F, et al. Improvement of diagnosis in children with Burkitt lymphoma in Kenya: feasibility study for the implementation of fluorescence in situ hybridisation testing for MYC and the MYC/IGH translocation. Ecancermedicalscience. 2023;17:1505-9.
11. Bernhardt MB, Brown AL, Grim AT, Scheurer ME, El-Mallawany NK, Ozuah NW. Safety analysis of high-dose methotrexate in pediatric non-Hodgkin lymphomas. Pediatr Blood Cancer. 2022;69(11): e29940-5.
12. Fousseyni Traoré, Carole Coze, Jean-Jacques Atteby, Nicolas André, Claude Moreira, Pierre Doumbe, et al. Cyclophosphamide monotherapy in children with Burkitt lymphoma: A study from the French-African Pediatric Oncology Group (GFAOP) Pediatr Blood Cancer. 2011;56(1):70-76.
13. James L, Singh S, Mampunza S, Baer F, Michael G. Increased HIV in Greater Kinshasa Urban Health Zones: Democratic Republic of Congo (2017–2018). AIDS Res Ther. 2020;17(1):67.
14. American cancer society. Non-Hodgkin lymphoma. 2014.
15. American society of clinical oncology. Lymphoma non-hodgkin Overview. 2014.
16. Boidy K, Kamara I, Dohoma Silue A, Meite N, Botti RP, Tolo-Diebkile A. Etude retrospective rapportant 20 cas de lymphoma de Burkitt au CHU de Yopougon. Bull. Cancer. 2019;103(3):275-8.
17. Patte C, Brugières L, Terrier-Lacombe MJ. Lymphomes malins non-Hodgkinien de l'enfant. Paris, France, Flammarion Médecine-Science. 2008;157-168.

18. Mhamed Harif, Sihem Barsaoui, Said Benchekroun, Rachid Bouhas, Pierre Doumbé, Mohammed Khattab, et al. Treatment of B-cell lymphoma with LMB modified protocols in Africa-Report of the French-African Pediatric Oncology Group (GFAOP). Pediatr Blood Cancer. 2008;50(6):1138-1142.
19. Burkitt D. Determining the climatic limitations of a children's cancer common in Africa. BMJ. 1962;2(5311):1019-1023.
20. Véronique Minard-Colin, Laurence Brugières, Alfred Reiter, Mitchell S Cairo, Thomas G Gross, Wilhelm Woessmann, et al. Non-Hodgkin lymphoma in children and adolescents: Progress through effective collaboration, current knowledge, and challenges ahead. J Clin Oncol. 2015; 33(27):2963-2974.