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Epidemiological, Clinical and Anatomopathological Aspects of Cancers in Central African Republic Children

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Abstract

Objectives: To determine the epidemiological, clinical and anatomopathological aspects of childhood cancer in CAR. **Patients and Methods:** This was a retrospective study carried out from May 2015 to May 2018, at the Center Hospitalier Universitaire Pédiatrique de Bangui (CHUPB). The study population consisted of patients aged under 15 followed in the UHOPB for malignant tumors on clinical, radiological or ultrasound suspicion of malignancy and confirmed or not by histology or biology. A questionnaire was used to collect the data which was analyzed using SPSS11.0 software. **Results:** During the study period, we collected 107 cases of childhood cancer. The annual hospital incidence was 1.27% in 2016; 1.93% in 2017 and 1.50% in 2018 The average monthly frequency of patients followed is 35.66. The intensity of pain assessed in the 99 patients ranged from 02/10 to 09/10 with an average of 5.41/10. The mean duration of the disease was 3.3 months with extremes at 1.2 months and 36 months. A predominance of comorbidity with HIV is 41.66%. Histologically diagnosed malignant tumors are dominated by 30.4% Burkitt's lymphoma. **Conclusion:** Data on cancer incidence are scarce in developing countries and for the most part are hospital statistics. In CAR, it will be important to set up a national register for collecting information.

Keywords

Cancer, Child, Epidemiology, Central African Republic

1. Introduction

Childhood cancer is the second leading cause of death worldwide, followed by accidents [1]. A chronic pathology poorly understood by the population of countries with limited resources, the incidence of childhood cancer is estimated at 160,000 new cases with approximately 90,000 deaths worldwide [2]. In French-speaking sub-Saharan Africa, more than 15,000 children under the age of 15 suffer from cancer each year [3]. In the Central African Republic (CAR), there are no exhaustive data; but in a study carried out in 2002, childhood cancers represent 5% of all cancers diagnosed in the pathological anatomy department [4]. According to the WHO, the epidemiological outlook for 2030 foresees a continued progression of cancers in terms of incidence and mortality [5]. Created in 2015 with the support of the Franco-African Pediatric Oncology Group (GFAOP), the Pediatric Hematology-Oncology Unit (UHOPB) of the Pediatric University Hospital Center of Bangui (CHUPB) is the only reference unit for the management of pediatric cancers in the Central African Republic. This unit takes care of all cases of childhood cancer in the country referred to it. Case management is done within the framework of multidisciplinary meetings bringing together pediatric oncologists, radiologists, pediatric surgeons, pathologists and biologists. This is a first national experience. The present study, which marks the third of the said unit, aims to determine the epidemiological, clinical and anatomopathological characteristics of cancer cases treated in the UHOPB of the CHUPB. Therapeutic aspects will not be the subject of this study.

2. Patients and Methods

This was a retrospective study from May 1, 2015 to May 31, 2018, a three-year period. This study was carried out at the Paediatric University Hospital Center of Bangui (CHUPB) and in the pathological anatomy department of Bangui. The study of patient files and the register of the UHOPB service made it possible to recruit all patients under the age of 15 followed in the UHOPB for malignant tumors confirmed by histology or biology. All patients followed for strong suspicion of a malignant tumor on radiology and/or ultrasound for which the histological or biological diagnosis has not been made. Patients whose files were not usable were not included, as were tumors with an uncertain diagnosis of malignancy. A pre-established form made it possible to collect the data, including socio-demographic parameters (age, sex, origin of the patients, the socio-economic level of the parents), the delay of the first consultation, the clinical and paraclinical signs, the diagnosis of the tumor, the histological type of the tumor when possible, the biological diagnosis retained and the repercussions, the medical pathologies on which the cancer appeared. The socio-economic level of the parents was classified as a low level if the food expenditure per person is less than 600 FCFA (Franc of French Colony of Africa), average if the food expenditure is between 600 and 1200 FCFA per person, sufficient if the expenditure is greater than 1200 FCFA per person. The level of pain was classified according to two

evaluation methods hetero-assessment using the FLACC scale (Face, Legs, Activity, Cry, Consolability) in children under 6 and self-assessment using the AVS (Analog Visual Scale) in children over 6 years old. All cases confirmed by histology on an operating specimen or biopsy, by cytology, or failing that by clinical arguments, were considered as cancer. In the latter case, the clinical signs suggestive of the disease must be accompanied by radiological and/or biological signs, in particular tumor markers. Data were entered and saved in Word/Excel 2010 software, then analyzed using SPSS 11.0 software. The study was conducted in compliance with ethical law and medical secrecy.

3. Results

During the study period, 107 cases of childhood cancer were hospitalized. The age of the patients varied from 42 days to 15 years, *i.e.* an average of 5.7 years and the age group most represented is that of 0 to 4 years of age (Table 1).

The sex ratio was 1.61 reflecting a male predominance. The annual hospital incidence of cancer cases respectively was 1.2% (n: 24/1880) in 2016; 1.9% (n:43/2225) in 2017 and 1.5% (n:40/2550) in 2018. The average frequency of patients followed being 35.66 (Figure 1).

Patients came from the city of Bangui in 46.73% of cases (50/107), those from the provinces 53.27% (57/107). The educational level of parents or guardians was assessed for 105 patients (see Table 2).

Table 1. Distribution of patients according to age groups.

Age group	Frequency	Percentage
0 to 4 years old	53	49.53
5 years to 9 years	29	27.10
10 years to 15 years	25	27.36
Total	**107**	**100**

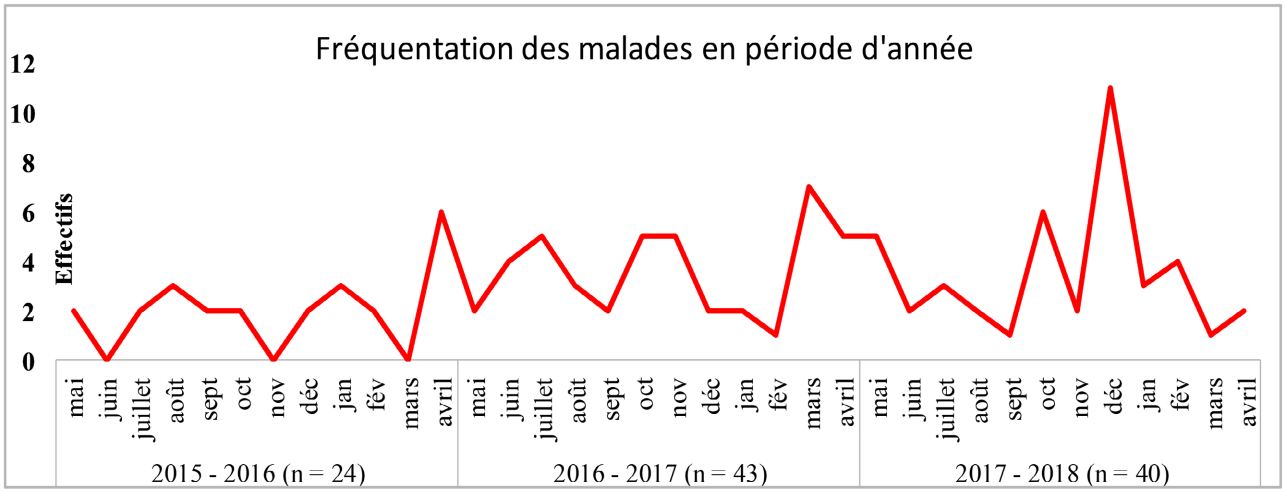

Figure 1. Curve of the monthly evolution of cancer cases in the department.

Table 2. Level of education of parents/guardians.

Levels of education	Frequencies	Proportions
uneducated	2	1.9%
Primary	15	14.29%
Medium	53	50.48%
University	35	33.33%
Total	**105**	**100%**

Table 3. Different pathologies or blemishes on which the cancer is grafted (comorbidity with the cancer).

Associated pathologies	Frequencies	Proportion%
Juvenile diabetes	1	8.33
sickle cell disease	2	16.66
Hypersplenism	1	8.33
Viral hepatitis	1	8.33
Malnutrition	1	8.33
Tuberculosis	2	16.66
HIV	5	41.66
Total	13	100

Of the 107 patients, 8 were not assessed upon hospitalization. The pain intensity assessed in the 99 patients ranged from 02/10 to 09/10 with an average of 5.41/10. The average duration of disease progression before their hospitalization was 3.3 months with extremes at 1.2 months and 36 months. The cancer was associated with different types of comorbidities which are reported in **Table 3**.

Of the 107 cases of cancer, 35 (32.71%) were diagnosed on clinical and radiological arguments while 72 (64.29%) had an anatomopathologic and/or biological diagnosis. A total of 72 patients underwent cytological or histological sampling for diagnostic purposes, from which four histogenetic groups of cancers were identified as shown in **Figure 2**. The distribution of cancers according to histological types is also presented in detail in the **Table 4**.

Of 10 cases of nephroblastoma diagnosed, 4 were of the blastematous type, 2 of the stromal type and 2 of the mixed type. The histological diagnosis of nephroblastomas was essentially on an operating specimen after chemotherapy. Conversely, the diagnosis of lymphomas and leukemias was based in more than 50% of cases on cytopuncture.

The rhabdomyosarcomas diagnosed in our patients were embryonic in 5 cases and alveolar in 2 cases.

4. Discussion

The burden of childhood cancer is increasing worldwide, especially in developing

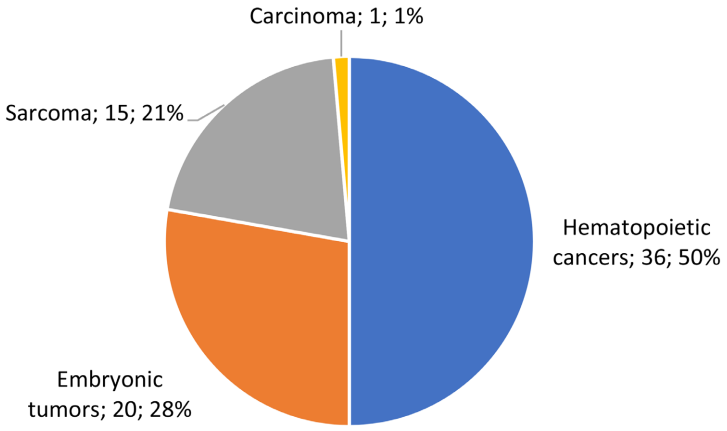

Figure 2. Distribution of cancer cases according to histogenesis.

Table 4. Distribution of cases according to histological type.

Histogenetic group	Histological type	Number	Percentage
Carcinoma	Hepatocarcinoma	1	100%
Embryonic tumors	Nephroblastoma	10	50.00
	Retinoblastoma	8	40.00
	Hepatoblastoma	1	5.00
	Neuroblastoma	1	5.00
	Total	**20**	100.00
Hematopoietic tumors	Burkitt's lymphoma	22	61.11
	Acute lymphoblastic leukemia	6	16.67
	Non-Hodgkin's large cell lymphoma	5	13.89
	Hodgkin lymphoma	2	5.56
	Unclassified lymphoma	1	2.78
	Total	**36**	100.00
Sarcoma	Rhabdomyosarcoma	7	46.67
	Ewing's sarcoma	3	20.00
	Kaposi's sarcoma	3	20.00
	Synovialosarcoma	1	6.67
	Osteosarcoma	1	6.67
	Total	**15**	100.00

countries [1]. As part of the development of the health system, a pediatric oncology unit was created within the CHUPB with the support of GFAOP. This capacity building has facilitated the diagnosis and treatment of certain cancers. This problem-solving method for pediatric cancers has been commented on by Hessissen *et al.* [6]. For many reasons, childhood cancer is a rare pathology in the sub-region and especially in the Central African Republic [7] compared to

endemo-epidemic pathologies (malaria, gastroenteritis, bronchopneumopathy), which justifies the choice of the retrospective study to recruit a maximum of cases. This study carried out in Bangui does not claim to provide exhaustive data on the cancerous pathology of children throughout the country, given its extent, the weakness of the means of diagnosis and management of these pathologies and the communication difficulties which make it impossible to identify all cases. However, it makes it possible to report the result of a first experiment and to provide some partial data which would make it possible to draw attention to these pathologies still misunderstood or neglected in the country. Whereas in 2008, Koffi *et al.* published 51 cases of childhood cancers in 8 years [7], our study made it possible to collect 107 cases of cancers suspected clinically or with a histological or biological diagnosis of cancers during the three years of activity, *i.e.* an average frequency of 36 cases per year. This result indeed shows a trend towards an increase in the number of cases, probably due to the existence of a care service. The improvement of the technical support platform in the provinces and in Bangui, characterized by an increase in the number of doctors, could also justify this trend. These data are comparable to those of the sub-region, particularly in Togo and Côte d'Ivoire where [8] [9] through work carried out in hospitals, the authors respectively noted this low annual hospital incidence of around 14 cases in 2014. Delgado *et al.* [10] in the USA in an international multicenter study, had shown that out of 100% of child cancer treatment units, 60% of these units admitted less than 100 new patients per year. However, the trend of increasing patients per year has been proven by Aristizabal *et al.* [11] in Baja California, Mexico, where the number of leukemia patients increased from 21 to 70 per year in six years. In Guatemala, Raul *et al.* [12] also found this trend for all pediatric cancers in general from 1990 to 2014. Our study also showed that there is no seasonal influence on the development of cancer in places where our patients live (**Figure 1**).

The predominance of boys in our sample (66/41) confirms the observations already made in 2008 (33 boys for 18 girls), thus showing that in CAR cancer concerns more male subjects. The average age is 5.7 years with extremes of 42 days to 15 years. Other studies [8] [9] have also shown this male predominance with a sex ratio of 1.2, but their average ages varying between 8 and 8.6 years. In our cohort, the most represented age group is that of 0 to 4 years (53%) followed by that of 5 to 9 years (27%). This same order of frequency was reported by Zinsu *et al.* [13] in Cotonou (Benin), out of 34 patients hospitalized in three years, they had found 15 patients from 0 to 4 years old, *i.e.* 44.12%. This frequency is also reported by Roberto *et al.* [14]. This predominance of the age group from 0 to 4 years would be explained by the high frequency of early childhood tumors in Sub-Saharan Africa (Nephroblastoma and Retinoblastoma) because it is at this age that these two types of cancer present clinically.

Pain is one of the most sought-after symptoms in oncology; in our study, patients had stage 2 pain in 52.98% of cases, followed by stage 3 pain in 32.3% of

cases. The late consultation in our sample could explain this high proportion. This frequency of pain is probably underestimated because of the difficulties of use of the different scales by the nurses of the unit, especially since the assessment of pain is subjective. One of the reasons for the long evolution of the disease would be explained by the long distance to reach the UHOPB and also a problem of late diagnosis by the personnel of the periphery. However, there is no significant link between the distance between their city of residence and the duration of disease progression before their hospitalization in the UHOPB (chi^2 being 2.4817 (p-value = 0.28 > 0.05))。

Among the 83 patients who performed an anatomopathological examination, 35 (*i.e.* 42%) performed cytopuncture including biology, 29 (34.9%) performed fine needle biopsy and 19 (22.8%) excision biopsies (operating specimen). T. Darré *et al.* [15] found 93% biopsy and only 7% surgical specimen. The difference can be seen here with cytopuncture which comes to the fore in our cohort. This is explained by the rarity of the biopsy needle in the city of Bangui, which has led practitioners to often limit themselves to aspirations of cells from tumor masses or by taking samples of accessible liquids or even by surgical intervention to analyze the operating room. In Togo, fluid samples are all sent to the biology department. Of the 107 patients followed in the UHOPB, 72 (67.29%) patients have their histopathological diagnosis and 35 (32.71%) have a clinical and/or radiological diagnosis. Jeremy S. *et al.* [8] in Togo had found only 51.6% of the cohort who had a diagnosis of cancer confirmed by histopathology, the rest being diagnosed according to clinical criteria. This difference can also be explained by the free care in the UHOPB during this study period, which made it easier for patients with a low socio-economic level to access these assessments (anatomopathology) whereas in Togo, it is the patients themselves who pay for their care.

Among the 72 patients having their anatomo-pathological diagnosis, the order of appearance of the origins of the cancers (histogenesis) in our cohort (hematopoietic cancer 50%; embryonic tumor 28%, Sarcoma 20% and Carcinoma 1%) was the same as that of Mukiibi *et al.* [16] in Malawi who first found haematopoietic tumors, then embryonic tumors followed by sarcomas. This trend is also found by Yao *et al.* [9] in Ivory Coast in 2012. This particularity is almost the same in sub-Sahelian Africa. Some tumors are not on our list such as brain tumor and germ cell tumor. The absence of brain tumors in our cohort is justified by lack of computed tomography (CT) and magnetic resonance imaging (MRI) in the country during this study period, given that the inclusion criteria and based on at least one radiological or biological examination. As for germ cell tumors, it would be mixed in the suspected 32.71% because the assay of Alpha-feto-protein (AFP) and Betha HCG in two patients was negative. This distribution of histogenesis is different in Western countries demonstrated by Hadley L.G, *et al.* [17]. This difference can be explained by the presence of sufficient technical facilities in the West to make early diagnosis of certain tumors that are difficult to detect.

Regarding the histological types of our malignant tumors, Burkitt's lymphoma predominates with 22 cases (30.5%), followed by nephroblastoma 10 (13.8%), retinoblastoma 8 (11.11%), rhabdomyosarcoma 7 (9.7%) and acute leukemia 6 (8.33%). This trend could be explained by the clinical manifestations which are the most visible and accessible to sampling compared to other types of cancers (brain tumours, neuroblastoma) which depend on a complete technical platform (Scanner, tumor markers). In addition to this, it should be noted that Burkitt's Lymphoma would be related to malaria-endemic areas in the presence of Epstein-barr virus.

According to PEKO in Brazzaville, lymphomas rank first at 52.3%, followed by nephroblastomas at 20% for a study on solid tumors [18]. These figures are close to our results: lymphoid tissues 30 (41.6%), embryonic tissues 16 (22%), sarcomatous tissues 15 (20.8%), except the last two groups, leukemia 6 (8.3%) and carcinoma 1 (1.38%). The distribution of malignant tumors that we have identified in our unit is consistent with reports from other middle-income countries and especially in sub-Saharan Africa as is the case of Sinfield RL, *et al.* [19]. Burkitt's lymphoma, non-Hodgkin's lymphoma, retinoblastoma, Wilms tumor and rhabdomyosarcoma are the most common childhood cancers in Africa, compared to those in Asian countries such as India and Pakistan, where the leukemia is the most common cancer according to Badar F., *et al.* [20].

5. Conclusion

Cancer incidence data are scarce in developing countries and most of them are hospital statistics. In the Central African Republic, its prevalence remains to be determined. The opening of a UHOPB with the support of the GFAOP at the CHUPB has revealed that childhood cancers remain a concern and are more frequent in the age group from 0 to 9 years with a predominance of retinoblastoma and nephroblastoma. There is a need to strengthen the national cancer control program in CAR and establish a register for collecting information.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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