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Neuroblastoma in Senegal: Epidemiological, Morphological and Pronostic Study of 35 Cases Diagnosed from 2017 To 2023

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ABSTRACT

Objective: *This study aims to describe the epidemiological, morphological and histo-prognostic particularities of neuroblastoma in Senegal.*

Methodology: *This was a cross-sectional and retrospective study conducted from January 2017 to December 2023. This analysis focused on all cases of neuroblastoma confirmed histologically and having benefited from an immunohistochemistry study in the PCR laboratories of HOGIP and UCAD in Dakar.*

Results: *During the study period of 07 years we collected 35 cases representing 5.27% of pediatric tumor cases (n = 664). The mean age was 5.42 years with a standard deviation of 4.33. The sex ratio was 0.94. The location of the neuroblastoma was unique in 88.57% of cases and of adrenal topography in 22.86%. The tumor was diagnosed at the metastatic stage at the time in 25.71% of cases. The most common macroscopic appearance was a well-limited multinodular tumor of firm consistency presenting necrotic-hemorrhagic changes on section. The diagnosis of neuroblastoma was suggested on the morphology in 32 cases (91.42%). All cases were confirmed by immunohistochemistry. Histological analysis highlighted the poorly differentiated histological subtype predominating in (57.14%) of cases. Using the INSS classification, 74.29% of patients were in Stage 2B and 25.71% in Stage 4.*

Conclusion: *the low incidence of neuroblastoma in Senegalese children raises questions about the non-exhaustiveness of cases that benefited from diagnostic biopsies and the possibility that a certain number of cases may have regressed spontaneously. The prognosis was poor because the majority of cases were diagnosed at advanced stages.*

Keywords

Neuroblastoma, Nervous system, Immunohistochemical, Tumor, Pediatric tumor.

Introduction

Neuroblastoma is a malignant embryonal tumor that affects the normal development of the sympathetic nervous system. It is the third leading cause of cancer in children under 15 years of age (after high-risk leukemia and central nervous system tumors) and is responsible for 15% of cancer deaths [1,2].

Its high frequency in developed countries (7 to 10%) is due to overdiagnosis of cancers detected by non-invasive imaging and screening tests [3]. On the other hand, in African and Asian populations the frequencies are lower.

This can be explained by a high prevalence of other childhood cancers in these populations [4,5].

A morphological study is often sufficient because neuroblastoma is the prototypical example of the "small round blue cell" tumor, dissociated by a neurofibrillary matrix. However, the use of a panel of immunohistochemical markers is recommended in certain cases. Neuroblastoma is a very complex and heterogeneous disease. This heterogeneity is associated with many factors such as age at diagnosis, stage of the disease, biological and histological characteristics of the tumor and many genetic alterations such as MYC-N amplification and ploidy [6]. All of these factors influence the prognosis and treatment options. The objectives of this work were to determine the epidemiological profile, to describe the histopathological and prognostic aspects of neuroblastoma in the laboratories of Anatomy and Pathological Cytology (ACP) of Dakar.

Materials and Methods

We conducted a cross-sectional and retrospective study with multicenter recruitment conducted in two (2) Pathological Anatomy and Cytology (ACP) laboratories in the Dakar region (Senegal): Idrissa POUYE General Hospital (HOGIP) and Cheikh Anta Diop University (UCAD). All anatomopathological examination reports concluding with neuroblastoma, confirmed by immunohistochemical study and followed up in these sites from January 2017 to December 2023 (7 years) were included. Immunohistochemical confirmation was carried out in Morocco for samples from the first 5 years (2017-2021) and in Dakar for the year 2022 and 2023. Epidemiological data: Frequency, age, sex and anatomopathological data: topography, immunohistochemical profile and histoprognostic stage, obtained for each patient, were archived in a computerized database using Excel software. A descriptive analysis was carried out for each variable.

Results

Epidemiological and clinical data

During the study period, 35 cases of neuroblastoma were collected, representing 5.27% of cases of childhood tumors (n=664). Of the 35 cases, 02 patients were admitted in 2017, (03) patients in 2018, (02) patients in 2019, (03) patients in 2020, (04) patients in 2021, (10) patients in 2022 and (11) patients in 2023.

The mean age of the patients was 5.42 years [3 months-17 years] with a sex ratio of 0.94. The majority of patients (51.42%) had been diagnosed before the age of 5 years (Table 1).

Locations

In our series, 33 patients (94.29%) presented a single primary location of neuroblastoma. While 2 patients (5.71%) presented a double primary location at two different sites. The location was not specified for one patient, i.e. 2.86%, and 09 patients were metastatic at diagnosis, i.e. 25.71% of cases.

Table 1: Epidemiological characteristics of patients with neuroblastoma.

Epidemiological characteristics	Number	Percentage
Years of diagnosis		
2017	02	5,71%
2018	03	8,57%
2019	02	5,71%
2020	03	8,57%
2021	04	11,43%
2022	10	28,57%
2023	11	31,43%
Age groups in years		
0-4	18	51,42%
5-9	07	20 %
10-14	09	25,71%
15-19	01	2,86 %
Sex		
Girl	18	51,43%
Boy	17	48,57%

Table 2: Distribution of neuroblastoma according to topography.

	Location	Number	Percentage
Single primary location	Adrenal	8	22,86%
	Head and neck	12	34,29%
	Abdomino-pelvic	9	25,71%
	Others	2	5,71%
Double primary location	Abdominal+ thoracic	1	2,86%
	Maxillary+ ocular	1	2,86%
Secondary location	Lymph node metastases	06	17,14%
	Medullary metastases	01	2,86 %
	Bone metastases	02	5,71 %

Anatomopathological data

We received (19) biopsy samples (54.28%) and (16) surgical specimens (45.71%). The most frequently found macroscopic appearance was that of a firm tumor with a multinodular surface, with tissue section slices associated with necrotic-hemorrhagic changes (Figure 1).

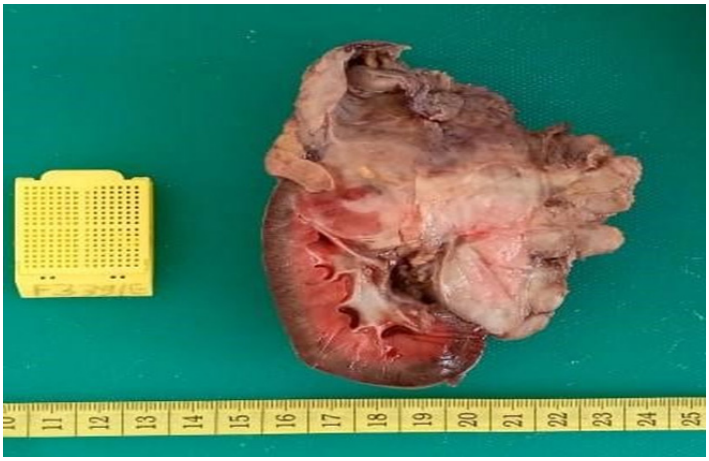

Figure 1: Macroscopy: White-grayish multinodular tumor pushing back the kidney ACP HOGIP/UCAD Lab. Dakar

A histopathological appearance of differentiated neuroblastoma (small round cells sometimes elongated with finely dispersed chromatin in 'salt and pepper' and a small amount of cytoplasm with vague cytoplasmic edges) was found in 30 cases or 85.71%. Concerning the remaining 05 cases (14.29%), a small round cell tumor was suggested (Figures 2, 3 and 4).

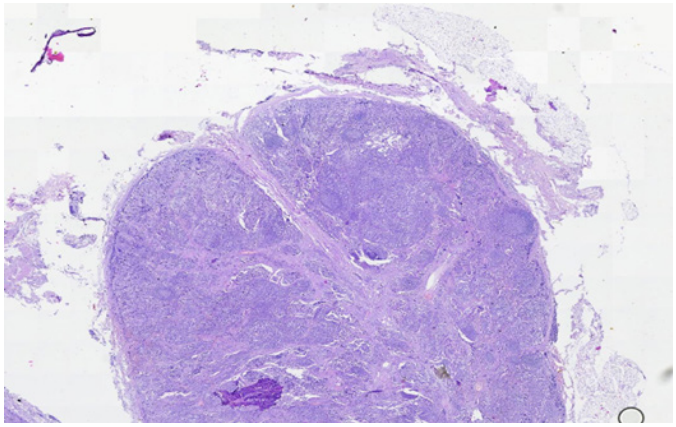

Figure 2: Microscopy: lymph node infiltrated by a neuroblastoma. Hematoxylin eosin x 100. ACP HOGIP/UCAD Lab. Dakar

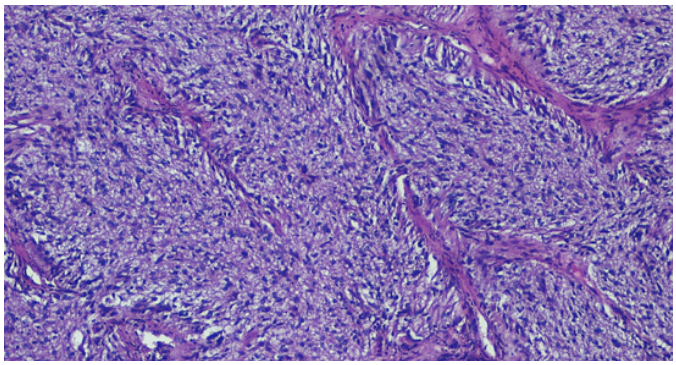

Figure 3: Neuroblasts grouped in clumps and discohesive trabeculae with loose fibrillar foci of neuropil Hematoxylin eosin x 100 Labo ACP HOGIP/UCAD.

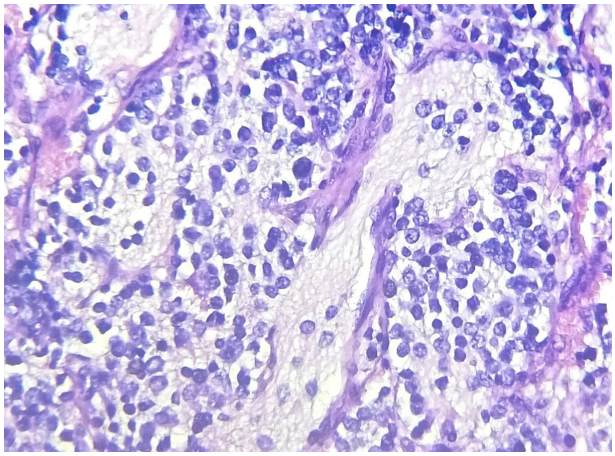

Figure 4: Small, round, sometimes elongated cells with finely dispersed 'salt and pepper' chromatin and a small amount of cytoplasm with vague cytoplasmic borderswith a moderate neuropil. (HEx40) Labo ACP HOGIP/UCAD.

An immunohistochemical study was carried out for all patients in the series. Neuroblastomas characteristically showed positive staining for synaptophysin, chromogranin, CD56, and neuron-specific enolase. S-100 protein staining was used to identify cytodifferentiated cells such as Schwann cells (Figures 5, 6, 7, and 8).

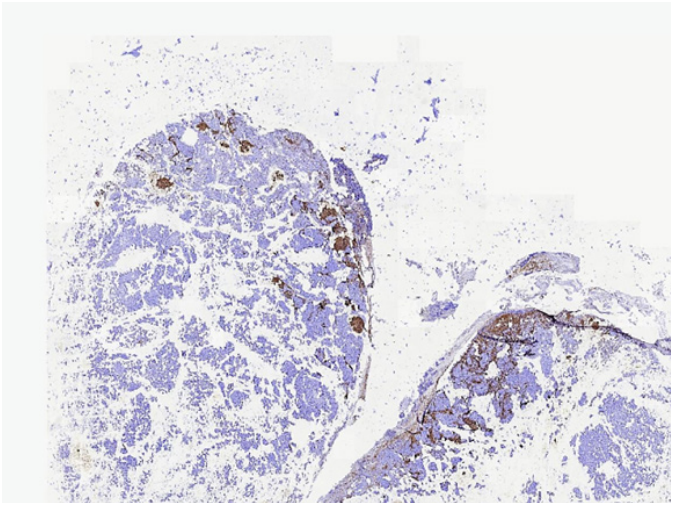

Figure 5: CD45 positive on residual lymphoid tissue. ACP HOGIP/ UCAD Lab. Dakar.

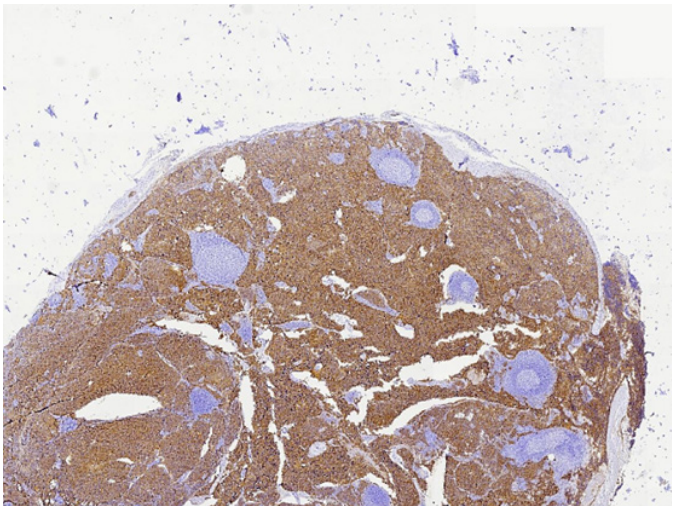

Figure 6: Diffuse positive synaptophysin on a lymph node metastasis of neuroblastoma ACP HOGIP/ UCAD lab. Dakar.

Histo-prognostic data

Age > 1 year and abdominal location are associated with poor prognosis. In our study, among the 35 cases of neuroblastoma, 33 were over 1 year old, or 92.85% of cases. Abdominal location was described in (08) patients, or 22.86% of cases. Cervical and pelvic localization were associated with a good prognosis and represented 8.57% and 11.43% respectively.

According to the INSS classification (International Neuroblastoma Staging System) 74.29% of patients were in Stage 2B and 25.71% in Stage 4. According to the INPC classification (International

Classification of Neuroblastoma Pathologies Shimada System), 30 patients had an unfavorable histology, or 85.71% and 05 a favorable histology, or 14.29% (Table 2).

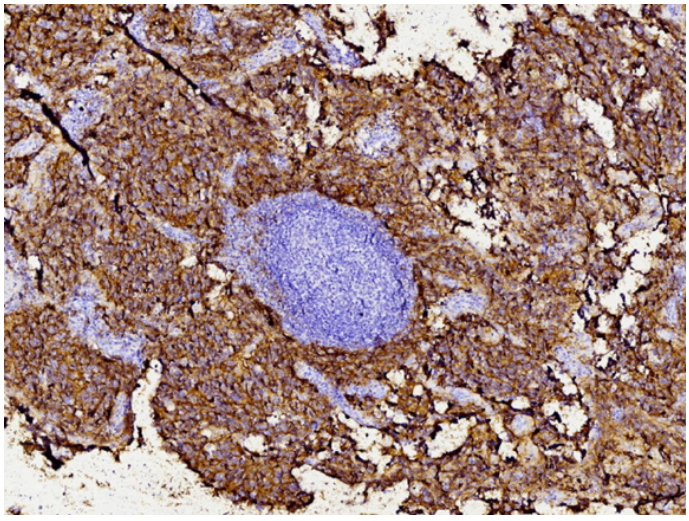

Figure 7: Diffuse and homogeneous membrane labeling by CD56 (X40) on a lymph node metastasis of neuroblastoma with residual lymphoid follicle. ACP HOGIP/UCAD Lab. Dakar

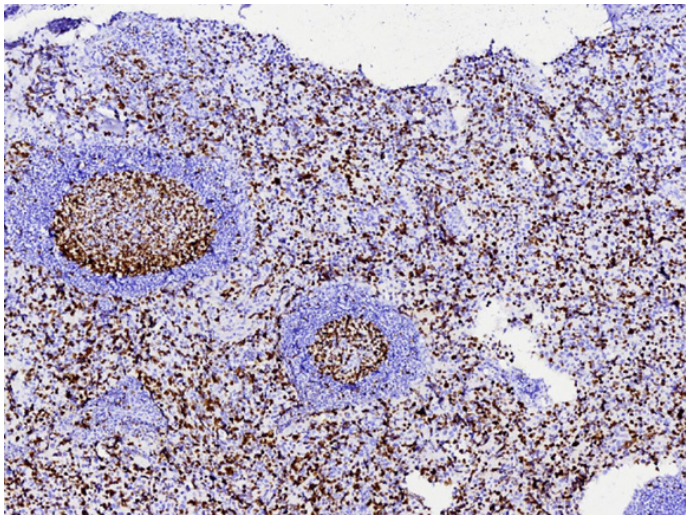

Figure 8: Nuclear labeling KI67 60% on neuroblastic proliferation outside of residual lymphoid follicles Labo ACP HOGIP/ UCAD. Dakar.

Table 3: Distribution of patients according to the primary sites, the INSS classification and the Shimada histological classification.

		Age in years	
Primary location	Adrenal	0	8 (22.86%)
	Abdomen	2 (5.71%)	6 (17.14%)
	Pelvis	1 (2.86%)	2 (5.71%)
	Head and neck	0	12 (34.29%)
INSS classification	Stage 2B	3 (8.57%)	23(65.71%)
	Stage 4	0	9 (25.71%)
Shimada classification	Favorable	2 (5.71%)	3(8.57%)
	Unfavorable	0	30(85.71%)

Discussion

The incidence of neuroblastoma in Senegalese children is low compared to that reported in developed countries. In Senegal, neuroblastoma comes in fifth place after nephroblastomas, retinoblastomas, lymphomas and sarcomas. It represents nearly 4% of the activity of the Pediatric Hemato-Oncology Unit of Dakar. In our study this incidence was 5.27% cases per 1,000,000 children/year. A previous study conducted by the Franco-African Pediatric Oncology Group obtained an incidence of 4 cases per 1,000,000 children/year [7]. The incidence reported here is similar to that of several Asian, African and Latin American countries.

It is likely that the incidence of neuroblastoma in developing countries is actually lower than that reported in developed countries. However, this variation must be interpreted with caution, because the data in developing countries are mainly hospital-based and rely on time-limited surveys, which do not allow valid epidemiological conclusions to be drawn [8-10].

Senegal does not have screening programs, such as those used in several developed countries, by which it has been shown that patients can have spontaneous regression in more than 50% of cases [11].

In our study, the average age of patients at diagnosis is 5.42 years. It is 24 months in the United States, 19 months in the United Kingdom, 32 months in Morocco, 27 months in Mexico and Denmark, 30 months in Egypt, 36 months in Algeria and 43 months in Turkey [8-14]. The age of the majority of patients at diagnosis is between 1 and 5 years. This may be attributed to the spontaneous regression of neuroblastoma in the younger age group (<1 year), the lack of diagnosis in primary health care centers, and the non-specificity of symptoms, which may lead to delayed diagnosis.

Different studies have reported a male predominance of neuroblastoma (sex ratio ranging from 1.1 to 1.5) [3], while in Morocco, a marginal female predominance has been identified (Sex ratio: 0.8) [15]. In our study, we noted a female predominance with a sex ratio of 0.94.

Only histology confirms the diagnosis of neuroblastoma and it is often done after a surgical specimen. The anatomopathological examination found in all our patients a proliferation arranged in diffuse clusters formed by small round cells sometimes elongated, with chromatin dispersed in salt and pepper, with little cytoplasm, with vague cytoplasmic edges

Regarding the diagnostic stage and the histological differentiation of Shimada, as for the literature, we did not find an association between a favorable histology and the localized stages (I and II), or between an unfavorable histological report and advanced stages (III and IV) [16,17]. Nevertheless, it will be necessary to perform a histological evaluation in all the cases that we will study in the future in order to evaluate this correlation more precisely.

For the genetic aspects, our results were consistent with those reported in the literature. It has been emphasized that neuroblastoma occurs sporadically and that only for 2% or less of patients there is a family history of Neuroblastoma; however, there are a large number of cases of distinct cancers in family members of patients with NB [18]. In our study, no cases of familial neuroblastoma were observed. From these data, we believe that there may be a nonspecific genetic susceptibility for neuroblastoma.

Conclusion

Neuroblastoma is the most common extracranial solid tumor in children. Its incidence in Senegal remains low and diagnosis is often late. Management is multidisciplinary.

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