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Epidemiological and Histopathological Profiles of Pediatric Rhabdomyosarcoma in Two Anatomy and Pathological Cytology Laboratories in Antananarivo Chu/Jra and Salfa Andohalo

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Abstract

Introduction: Rhabdomyosarcoma is rare in children under 15 years of age. In Madagascar, there are few studies concerning rhabdomyosarcoma. The aim of this study was to investigate the epidemiological and histological aspects of pediatric rhabdomyosarcomas in two Antananarivo pathological anatomy and cytology laboratories: CHU-JRA and SALFA Andohalo. **Materials and Method**: This is a retrospective, descriptive, bicentric study over a 10-year period from January 2010 to December 2019 of rhabdomyosarcoma cases diagnosed in the paediatric population. The parameters studied were age, gender, location and histological diagnosis. Results: We collected 37 cases. Patients ranged in age from 08 months to 15 years, with a mean age of 6.28 years. The sex ratio was 1.46. The most frequently encountered histological types were embryonal rhabdomyosarcoma (56.75%), followed by alveolar type (27.03%), spindle cell rhabdomyosarcoma (08.11%) and botryoid type (08.11%). Localizations in order of frequency were head and neck (24.32%), genitourinary regions (24.32%), limbs (18.92%), buttocks (18.92%), trunk (10.52%) and secondary localizations (2.70%). **Conclusion**: Pediatric rhabdomyosarcoma is rare. Localizations are mainly head and neck and genitourinary tract. The lack of immunohistochemical examination is a limitation of this study.

Keywords

Anatomy Pathology, Pediatric Cancer, Pediatric Rhabdomyosarcoma

1. Introduction

Worldwide, RMS is the third most common neoplasm among extracranial solid tumors in children after neuroblastoma and Wilms tumor [1]. The tumor is slightly more common in males [2]. In Madagascar, three cases of vulvar rhabdomyosarcoma have been published, two at the University Hospital Center (CHU) of Toamasina in 2014 by Rasoloniaina AR [3] and one at the Pediatric Surgery Care, Training and Research Unit (USFR) of the Joseph Ravoahangy Andrianavalona Hospital Center (CHU/JRA) in 2008 by Ranjevamalala AD [4]. Malignant mesenchymal tumors (MMT) in children account for 5 - 10% of all malignant tumors in children [5]. They constitute a heterogeneous group of tumors of varying differentiation according to their presumed tissues of origin. They mainly include tumors of muscular origin, and those derived from connective, vascular, nervous or adipose tissue [5]. RMS is classified into four subtypes, the most common of which is the embryonal subtype, followed by the alveolar subtype [6]. Rhabdomyosarcoma (RMS) is an aggressive pediatric soft-tissue cancer requiring urgent therapeutic management [7]. Prognosis and treatment depend on several factors, including histological type and grade… These factors intervene independently [4] [8]. Although a few case series concerning this study have been carried out in Madagascar [7] [9], no bicentric study of the peculiarity of paediatric rhabdomyosarcoma in hospitals with technical facilities and specialist physicians in the field has been carried out. The aim of this work is to evaluate, through these 37 cases, the epidemiological and anatomopathological particularities of rhabdomyosarcoma tumors at CHU/JRA and SALFA Andohalo, Antananarivo Madagascar. The specific reasons of our study in these 2 laboratories are that both of them received the must number of the specimen in the capital an from almost regions of Madagascar. Also, they are sited next to the surgical pediatric and pediatric oncology departments.

2. Materials and Method

This is a retrospective, descriptive, bicentric study of pediatric rhabdomyosarcoma tumor cases at the CHUJRA and SALFA Andohalo pathological anatomy laboratories over a 10-year period from January 2010 to December 2019. Histopathological diagnosis was made on biopsy specimens or operative excision specimens from children aged 0 to 15 years. These specimens were examined after fixation with 10% formalin, kerosene embedding, cut to 2 - 3 µ and stained with standard hematoxylin-eosin (HE) stain. There is no specifics of sampling and staning procedures avalaible in these laboratories concerning rhabdomyosarcoma. Readings

were taken under a light microscope at various magnifications. Children aged 0 - 15 diagnosed histologically as rhabdomyosarcoma during the period of the study was recruted. Incompletely filled in liaison forms, *i.e.* forms without age and/or gender, clinical information, patient and prescriber contacts, etc., were excluded. The sampling was exsaustive. Histological types were determined according to the latest World Health Organization (WHO) 2013 classifications. This analysis focused on the epidemiological and anatomopathological characteristics of children with Rhabdomyosarcoma at the CHU/JRA and SALFA Andohalo anathomopathology laboratories.

3. Results

Thirty-seven cases of primary brain tumors were diagnosed, with an average of 3.7 cases per year. The median age was 6.28 years (0 - 15 years) (**Figure 1**). The majority of rhabdomyosarcomas in our setting predominated in the 0 - 5 age group (56.75%) of cases (**Figure 1**). A slight male predominance was observed, with 59.46% (n = 22) males versus 40.54% (n = 15) females, with a sex ratio (M/F) of 1.47 (**Table 1**). Topographically, the sites were mainly head and neck and genitourinary, with a rate of 24.32% each (**Figure 2**). Four histological types were diagnosed, two of which predominated: embryonal rhabdomyosarcoma (56.75%) followed by alveolar rhabdomyosarcoma (27.03%), accounting for more than half of all cases (83.78%). Botryoid and spindle cell rhabdomyosarcomas each accounted for 8.11% of cases. (**Figure 3**). It was constituted by the embryonal type. The remainder were in the 6-10 and 11 - 15 age groups with the other histological types (**Figure 4**).

Table 1. Patient distribution by gender.

Genre	Number (n = 37)	Percentage (%)	Sex-ratio
Male	22	59.46	1.47
Female	15	40.54	

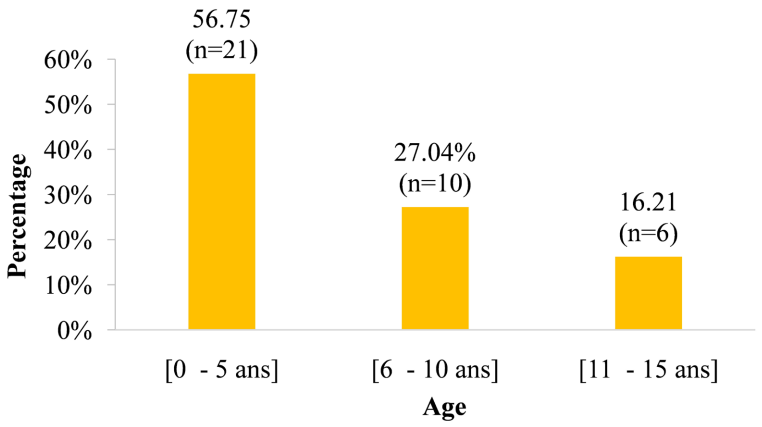


Figure 1. Age distribution of patients.

Figure 2. Distribution according to rhabdomyosarcoma location.

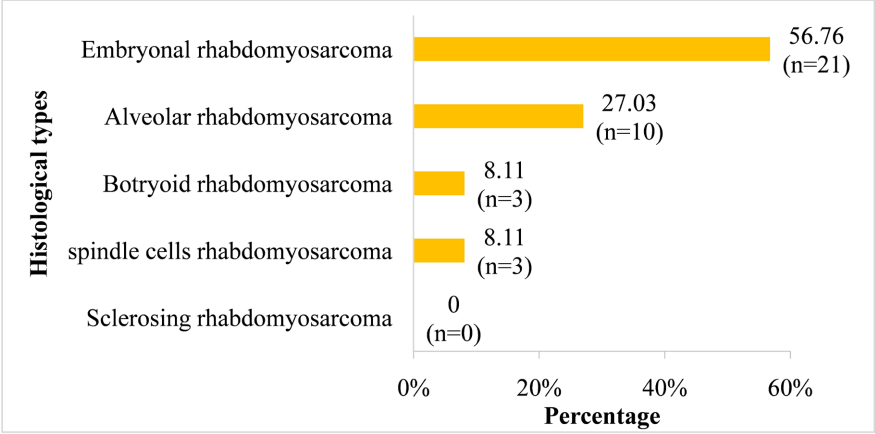


Figure 3. Distribution by histological type.

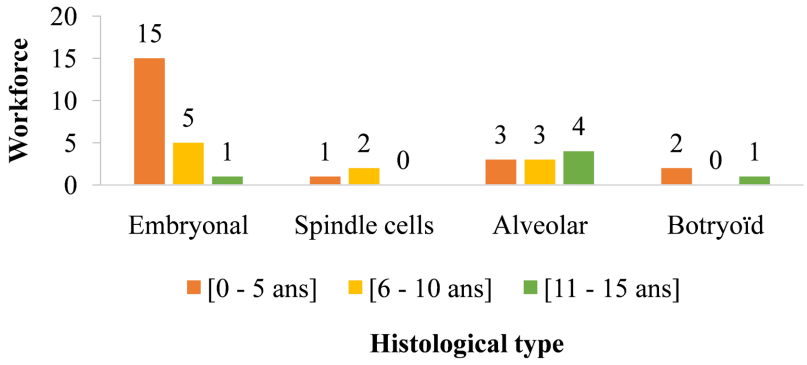


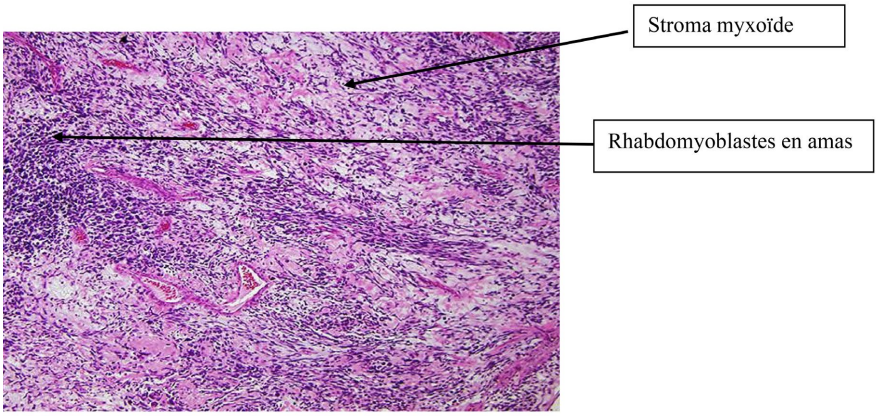
Figure 4. Correlations between age groups and diagnostic entities.

4. Disussion

Rhabdomyosarcoma is rare. It accounted for around 4 cases per year in our study. Nevertheless, it is the most common soft tissue sarcoma (STS) tumor in children, accounting for over 50% of all cases, and most often occurs before the age of 14

[9]. The number of cases per year in our study (3.7) was well below that observed in Western countries such as the USA (350 annual cases) and France (100 cases) [10] [11]. Africa lacks epidemiological data on this pathology [12]. Indeed, the limited access to anatomopathological examinations, essential for diagnosis, and their high cost in the Malagasy context could explain this great difference. In addition, a significant proportion of the population prefer to consult traditional practitioners, thereby delaying medical diagnosis and treatment. In this study, there was a male predominance, with 22 male cases (59.46%) and 15 female cases (40.54%), *i.e.* a sex ratio of 1.47. These results are consistent with those reported in other studies, notably in Marrakech by Habibi L and in the United States by the IRS IV study, where the sex ratios were 1.5 and 1.6 respectively [12] [13]. Studies in Egypt and Nigeria also found similar ratios, with values of 1.15 and 1.5 [14]. Although no precise explanation has been put forward for this male predominance, it is likely to be linked to a higher incidence of rhabdomyosarcomas in paratesticular and prostatic localizations in boys, anatomical areas with no frequent equivalent in girls [15]. In this case, the median age was 6.8 years, and two peaks in incidence were observed: the first between 0 and 5 years of age, and a second smaller peak between 6 and 10 years of age. These data are similar to those of studies carried out in Morocco and another in the USA, which found median ages of 5 and 6 years respectively, and that the majority of patients were also diagnosed before the age of 10, with two peaks in incidence, in the under-5s and adolescents respectively [5] [13]. Two other studies in Egypt at the oncology and haematology units of the paediatric department, and in Nigeria at the University of Ibadan, also found that the majority of children are diagnosed before the age of 10. They reported a median age of 6 and 6.2 years respectively [14]. This predominance could be explained by the fact that the embryonal type, which is the predominant histological type of RMS, appears at early ages (**Figure 5**). In this study, head and neck and genitourinary localizations were the most frequent, with a rate of 24.32% each. This distribution is in line with those observed in the USA by Eduardo A, in Morocco by Hessissen L *et al.*, and in Marrakech by Habibi L, who reported that the majority of RMS were found in the head and neck region, followed by genitourinary localization, with respective rates for head and neck localization of 37%, 36.4% and 44.11% [1] [9] [12]. This distribution may be explained by the predominance of the embryonal histological type of rhabdomyosarcoma, which localizes preferentially in these two anatomical regions. The characteristic cells of rhabdomyosarcoma are rhabdomyoblasts. In this study, they were rounded or fusiform cells with granular, eosinophilic cytoplasm, filaments and eccentric nuclei. In a study carried out in Europe, the cells were slightly elongated, with intracellular cross streaks and eosinophilic cytoplasm [16]. These specific striae and the elongated or fusiform appearance of the cell with several nuclei are signs of myofibroblast maturity. Immunohistochemistry even not avalaible in our laboratories could help to distinguish rhabdomyosarcoma subtype. RMS express Vimentin, indicating the connective origin of cell proliferation, desmin (intermediate filament between smooth and skeletal muscles) with cytoplasmic expression most often diffuse

regardless of the histological subtype and myogenin (nuclear expression) [17]. The expression of myogenin differs between the subtypes and constitutes a good element of histological classification: the labeling is diffuse in alveolar RMS (between 80 and 100% of tumor cells) and is much more heterogeneous in embryonic RMS, generally involving less than 2/3 of the cells [18].



Source: UPFR d'Anatomie et Cytologie Pathologiques CHU/JRA;
Coloration: Hématéine Eosine;
Grossissement: ×100.

Figure 5. Vessie: Rhabdomyosarcome embryonnaire.

This study is limited by the absence of immunohistochemistry and the fact that only people who are financially stable could pay the fees of the anatomy pathological analysis were included. And sometimes some cultures in some regions of Madagascar consider the manipulation of the sampling as a taboo. They prefer to bury samples. Anyway, this study could help researchers and clinicians bringing better care to this rhabdomyosarcoma.

5. Conclusion

Pediatric rhabdomyosarcoma is rare. It predominates in small boys. Head and neck and genitourinary localizations predominated, with embryonal RMS as the histological subtype. The sclerosing rhabdomyosarcoma subtype was not observed in this study. The epidemiological and histopathological profile of rhabdomyosarcoma in children is quite similar to that reported in the literature. However, further multicentre studies in the laboratory remains of Antananarivo and in all the coastal regions of Madagascar where there are anatomical pathology laboratories are needed to better support and confirm these data. This will enable the results to be compared with those of other existing laboratories, so as to establish a national Malagasy rhabdomyosarcoma register that can be used for other epidemiological studies on a continental scale.

Conflicts of Interest

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

paper.

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