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Retrospective Comparative Histopathological Study According to UICC's New pTNM Pathological Classification, Retinoblastoma in African-Rwandan Child Versus the Caucasian-Belgian Child

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Abstract

Retinoblastoma (RB) is a highly malignant tumor, rare, primarily of infants and young children. We made a retrospective comparison of histopathological sections of 15 African-Rwandan children and 13 Caucasian-Belgian children. This study was carried out with the aim of highlighting a possible difference between the two groups, according to the UICC's new pTNM pathological classification.

We found that at the time when the diagnosis of RB was made, African-Rwandan children had a mean age of 32.69 months compared to 15.46 months in Caucasian-Belgian children. This has had the detrimental effect in the large majority of the first group (84.60%), advanced stages, the tumor (pT3b, pT3c and pT4) having a poor visual prognosis and even vital in some cases. In contrast, in the second group, no children (0%) presented them.

It is therefore essential that an early diagnosis of RB be made, in order to avoid the heavy visual handicap and the infant mortality, due to the spread of this disease.

Keywords: *RB; UICC pTNM Classification; Africans-Rwandans; Caucasians-Belgians; Heavy Visual Impairment; Mortality*

Introduction

RB is a highly malignant tumor of the retina, neuroectodermal origin, affecting mainly the infant and young child. Its frequency is 1 child out of 20,000, without predilection of race or sex. The RB is rare but is the most common malignant tumor (14%) in children around the world [1-4].

The retinoblastoma gene sits on chromosome 13 (13q14) [1]. It is called RB, having 200 kb, 27 exons, mRNA 4.7 kb, and encodes a protein (P105 RB) of 928 amino acids. This protein acts as an anti-oncogene in a normal cell [2,3].

For the tumor to develop, both gene alleles must be mutated. In bilateral retinoblastoma, there is a first germline mutation present in all cells of the body. The second mutation is always somatic and affects the retinal cells already carrying the first mutation. This is why the RB gene functions as a recessive gene, but the disease is transmitted in a dominant autosomal mode. In the unilateral, unifocal and non-hereditary RB, like most cases, both mutations occur in the retinal cell [1,3].

Ten years after onset of hereditary RB, about 15% of survivors develop secondary cancer. After age 50, the risk is 51% while it is only 5% in sporadic forms. The early signs of BR, such as leukocoria and strabismus, may sometimes allow the diagnosis of small tumors in the macular region. Other late signs are buphthalmia, iridian heterochromia, pseudohypopion, and in the most advanced

forms, tumor endophthalmitis. In pathology, 5 types of retinoblastoma have been described, depending on the location of the tumor: the exophytic, endophytic, mixed, diffuse and necrotic infiltrant types. The differential diagnosis is with Coats disease, uveitis, inflammatory pseudotumor, retinal detachment, hyalite, toxocara canis, cat scratch disease, myelin fibers, morning glory syndrome, dysplasia retino-vitreous, colobomas, and benign astrocytomas [1,3,5].

Current therapeutic management requires the collaboration of a multidisciplinary team, namely ophthalmology, radiology, pediatric oncology, histopathology and psychology [1,6].

We present in this work the results of the examination of histopathological sections, African-Rwandan and Caucasian-Belgian children.

Materials and Methods

Equipment

From August 1980 to March 1990, 16 cases of RB were diagnosed in 15 Rwandan children at the Kigali Hospital Center by the co-author from Belgium. We have neither the age nor the sex of two of them. So, we recruited in Belgium in the Ophthalmology Department of UZ Ghent, the first 13 children who presented the RB, from the same period almost, going from January 1981 to June1992; with 15 cases of RB. All histopathological sections of these two samples were examined.

This study was conducted during my training in ophthalmology in this department.

Methods

We used the new pathological classification pTNM of the International Union Against Cancer (UICC), to compare the histopathological slides of the children of the two countries. The slides of the Rwandan children, whose age and sex are unknown, were examined but excluded from the results and discussion, which gives us denominator of 13 for each group. And each child is considered once even if he has presented a bilateral BR. Both of these measures have been applied for convenience.

pTNM Pathological Classification de l'UICC [7]:

- pT: Primary Tumour.
- pTX: Primary tumour cannot be assessed.
- pTO: No evidence of primary tumour.
- pT1: Tumour confined to retina, vitreous, or subretinal space. No optic nerve or choroidal invasion.
- pT2: Minimal invasion of optic nerve or optic coats or focal invasion of choroid.
- pT2a: Tumour invades optic nerve up to, but not through, the level of lamina cribrosa.
- pT2b: Tumour invades choroid focally.
- pT2c: Tumour invades optic nerve up to, but not through, the level of lamina cribrosa and invades choroid focally.
- pT3: Significant invasion of optic nerve or optic coats or massive invasion of choroid.
- pT3a: Tumour invades optic nerve through the level of lamina cribrosa but not to line of resection.
- pT3b: Tumour massively invades choroids.
- pT3c: Tumour invades optic nerve through the level of lamina cribrosa but not to the line of resection and massively invades choroid.
- pT4: Extraocular extension which includes any of the following:
- Invasion of optic nerve to the line of resection.

- Invasion of orbit through sclera.
- Extension both anteriorly or posteriorly into orbit.
- Extension into brain.
- Extension into subarachnoid space of optic nerve.
- Extension to apex of orbit.
- Extension to, but not through, chiasm.
- Extension into brain beyond chiasm.
- pN: Regional Lymph Nodes.

The pN categories correspond to the N categories

- pM: Distant Metastasis
- pMX: Distant metastasis cannot be assessed
- pMO: No distant metastasis
- pM1: Distant metastasis
- pM1a: Bone marrow
- pM1b: Other sites.

Results

Epidemiological aspects

Age

The age extremes in Rwanda were 11 months and 60 months, compared to 2 months and 50 months in Belgium. The average age for Rwandan children was 32.69 months versus 15.46 months for Belgian children.

Sex

We recorded six girls (46.15%) and 7 boys (53.85%) among Rwandan children, versus eight girls (61.54%) and five boys among Belgian children.

Histopathological aspects: pathological classification pTNM of UIC

pTNM classification and type of RB per individual of each sample

Number	Age (months)	Sex	pTNM	Type of RB
1	24	F	pT4	Mixed
2	30	M	pT3c	Mixed
3	11	F	pT3c	Mixed
4	60	M	pT4	Mixed (bilateral)
5	36	M	pT4	Mixed
6	14	F	pT1	Mixed (necrotic)
7	48	F	pT4	Mixed
8	36	F	pT4	Mixed
9	24	M	pT3a	Mixed
10	44	M	pT3b	Mixed
11	48	M	pT4	Mixed
12	14	F	pT4	Mixed
13	36	M	pT4	Mixed

Table 1: *African-Rwandan sample.*

Number	Age (months)	Sex	pTNM	Type of RB
1	10	F	pT2a	Mixed
2	6	F	pT2a	Mixed
3	4	F	pT1	Exophytique bilateral
4	50	F	pT3a	Mixed
5	29	F	pT2a	Mixed
6	30	M	pT2a	Mixed
7	7	M	pT1	Exophytique bilateral
8	2	M	pT1	Exophytique
9	17	F	PT2a	Exophytique
10	10	M	pT2b	Mixed
11	2	M	pT2a	Mixed
12	16	F	PT1	Mixed
13	18	F	pT1	Mixed

Table 2: *Caucasian-Belgian sample.*

M: Male; F: Female.

pTNM classification by country

All slides were identified, therefore the pTX and pTO stages were discarded. The pT1 stage was present in one Rwandan child (7.69%) against five Belgian children (38.46%). The pT2a stage identified in six Belgian children (46.15%). The pT3a stage was recorded in one child from both countries (7.69%). The pT4 stage was identified in eight Rwandan children (61.53%), against no Belgian child (0%).

Types of RB by country

All slides of Rwandan children presented the mixed type (100%), including a spontaneously necrotic case, while four Belgian children (30.76%) presented the exophytic type and the nine others (69.23%) the type. mixed.

The pTNM classification according to age

The pT1 stage was recorded in a Rwandan child (7.69%) of 14 months, versus five Belgian children (38.46%) aged from 2 months to 18 months. The pT2a stage has been found in six Belgian children (46.15%) aged from 6 months to 30 months.

The pT3b, pT3c and late stage pT4 stages were identified in 11 Rwandan children (84.60%) aged from 11 months to 60 months, however, no Belgian children (0%) presented with a tumor stage pT4.

The pTNM classification according to the type of RB

All the different stages encountered in Rwandan children were mixed, whereas in Belgian children the pT1 stage was present in three children (23.07%) under the exophytic type and in two children (15.38%) under the mixed type. The pT2a stage was identified in a Belgian child (7.69%) under the exophytic type, and in five Belgian children (36.48%) under the mixed type.

The type of RB according to age

In Rwandan children, the age ranged from 11 months to 60 months, and all presented mixed type. On the other hand, in Belgian children, in four (30.76%) aged from 2 months to 17 months, the exophytic type was recorded, and in the other nine (69.23%) aged from 2 months to 50 months, the mixed type was found.

Discussion

The aim of this work was to compare and highlight a possible difference between African-Rwandan children and Caucasian-Belgian children, according to the UICC's new pTNM pathological classification.

The mean age of the African-Rwandan sample (32.69 months) (32.3 months, Akan EE., *et al.* Ibadan, Nigeria) [8] was higher than that of the Caucasian-Belgian sample (15, 46 months) (17.53 months, Martinez Y Arroya MM., *et al.* in Madrid, Spain) [9]. The evolutionary stage pT1 corresponds to an RB confined in the retina, the vitreous, or the subretinal space, without invasion of the optic nerve or the choroid. This stage was present only in one Rwandan child (7.69%) aged 14 months, under the spontaneously necrotic type, against five Belgian children (38.46%) with a mean age of 9.4 months.

The intermediate stage pT2 corresponding to a minimal invasion of the optic nerve or optic layers, or a focal choroidal invasion, was only found in one Rwandan child (7.69%) versus six Belgian children (46.15%).

The sub stages pT3b and pT3c correspond to a significant invasion of the optic nerve, or optic layers, or a massive invasion of the choroid. And the late stage pT4 corresponds to an extraocular extension of the RB. All these advanced stages of the tumor, with limited prognosis, were recorded only among African-Rwandan children (84.60%) in our sample, with an average age of 35.18 months; whereas no Caucasian-Belgian child presented them. The exophytic type was recorded only in Caucasian-Belgian children (30.76%) with a mean age of 7.5 months.

Conclusion

In African-Rwandan children, RB was diagnosed most often, late. This has had the negative consequence, a poor visual prognosis, and even vital in some cases, among them. It is therefore important that the diagnosis of RB be made as soon as possible. To this end, in the same way as congenital cataract and congenital glaucoma, the World Health Organization (WHO) could integrate early detection of RB in its project to prevent childhood blindness. This could be done through the maternal and child protection centers (PMI), the matrons and the parents of the children. They should be taught to diagnose the early signs of RB such as strabismus and leukocoria; and to consult an Ophthalmologist immediately.

Thus, heavy visual impairment and infant mortality due to metastatic spread of RB could be reduced, especially in developing countries [10].

Bibliography

1. Desjardins L. (Institut Curie Paris-France) - Le Rétinoblastome. Rev (2004).
2. Huret JL. "(chu Poitiers) - Cancers Héréditaires. II Rétinoblastome". Atlas of Genetics and Cytogenetics in Oncology and Hematology.
3. Oswald P., *et al*. "La génétique du cancer de l'enfant et ses implications cliniques. 1. L'exemple du rétinoblastome". *Louvain Médical* 118 (1999): 293-298.
4. Rossant L. "Le Rétinoblastome. Diagnostics n° 187". Asculpe éd. Paris.
5. Spencer W. "Ophthalmic pathology". Ed. Saunders Company, 4th edition, volume 2 (1996): 1332-1438.
6. Billerot C. "Le Rétinoblastome: quel impact psychologique". Le Rétino n° 35 (2000).
7. UICC (International Union Against Cancer) - TNM Classification of malignant tumours. Sixth edition.

8. Akan EE., *et al*. "Rétinoblastoma in Ubadan Nigeria: II Clinicopathologic features". *West African Journal of Medicine* 19.1 (2000): 6-11.

9. Martinez Y., *et al*. "Retinoblastoma: review of 19 cases". *Anales Españoles de Pediatría* 34.2 (1991): 107-109.

10. Handicapzero. "L'OMS lance un projet de prévention de la cécité chez l'enfant". Source: News Press (2002).

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