

## CASE REPORTS

### Multiple malignant tumors of the orbit

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#### Abstract

The retinoblastoma is the most frequent malign tumor of the children, starting with the maximum frequency between the ages of one to three years. It is part of the categories of rare diseases, whose frequency is estimated at 1:15.000–1:20.000 newborn babies. It is a tumor of the neuroblast-type placed at the retina level. The retinoblastoma can be unifocal, when a single tumor is present, or multifocal, when it is about more tumors at the level of the same eye or with extension to both eyes. The retinoblastoma can have at the basis two mechanisms of appearance, thus distinguishing two types: the hereditary and the sporadic, non-hereditary. In approximately 40% of the cases, the children affected have the hereditary type of the illness; this includes the cases of the children with bilateral retinoblastoma and approximately 5% of those with tumor at a single eye. The hereby paper presents two clinical cases (mother and daughter) with the histopathological diagnosis of retinoblastoma, followed up on a period of four years. The first case, that of a 4-year-old child, with the histopathological diagnosis of bilateral retinoblastoma with left intra-orbital invasion, to which enucleation has been made to the right eye and left orbit exenteration (on three years interval). The second clinical case is that of a 30-year-old woman who shows up at the clinic with a left intra-orbital tumor recidivation; it is significant to reveal the fact that the first surgical intervention (left eye enucleation) took place 29 years ago and the histopathological diagnosis settled post-operation was that of retinoblastoma. The histopathological diagnosis of the tumor recidivation was of squamous carcinoma. The clinical and histopathological aspects of the two clinical cases presented are being debated, the appearance of a tumor formation in the same topographic area after a long period and the importance of the genetic advice in the families diagnosed with retinoblastoma.

**Keywords:** hereditary retinoblastoma, enucleation, exenteration, squamous carcinoma.

#### ■ Introduction

Retinoblastoma is a malignant tumor of the eye that originates from developing cells of the retina. The estimated incidence is between one in 15.000 and one in 20.000 birth children [1]. Diagnosis is based on clinical signs and symptoms and is usually made under the age of five year. Most often, the first presenting sign is a white pupillary reflex (leukocoria). Strabismus is the second most common sign, and may accompany or precede leukocoria. In adults, retinoblastoma is extremely rare and may originate from retinomas, which are benign precursor lesions. About 60% of patients have retinoblastoma in only one eye (unilateral retinoblastomas); most patients with unilateral retinoblastoma have sporadic disease, i.e., no other case of retinoblastoma has been noted in their family. About 40% of patients have retinoblastoma in both eyes (bilateral retinoblastoma). Only 10% of all patients have a positive family history of retinoblastoma (familial retinoblastoma). It is important to examine the retina of all first-degree relatives of retinoblastoma patients, as this may identify retinomas or retinal scars, which may indicate predisposition to retinoblastoma even though full malignant retinoblastoma did not

develop. Patients with familial or bilateral retinoblastoma have an increased risk of specific neoplasms outside of the eye (second tumors), including osteogenic sarcoma, soft tissue sarcoma, and malignant [2]. Retinoblastoma can be associated with developmental delay, growth retardation, and congenital malformations.

#### ■ Patients and Methods

Two clinical cases diagnosed with retinoblastoma have been taken up for study, mother and daughter hospitalized in the Ophthalmology Clinic of Emergency County Hospital, Cluj-Napoca, in the years 2003, 2004, respectively 2006.

The first patient is a female child, who, at the age of one year (2003) is hospitalized in the clinic with right eye leukocoria; from the heredo-collateral history we mention the fact that both parents have been diagnosed and treated in childhood with the retinoblastoma diagnosis (for whom, in both cases was made the enucleation of the affected eye). After the clinical ophthalmological examination, the paraclinical and laboratory examinations (that include the echographic examination, cranium and orbital NMR-examination)

the diagnosis of intra-orbital tumor formation on the right eye was settled without scleral invasion.

The enucleation of the right eye is practiced, followed by general and local antibiotic treatment, hydroelectrolytic rebalance; the histopathological examination sets the diagnosis of retinoblastoma without phenomena of scleral invasion.

Post-operation, the child followed up the oncological treatment (protocol 2<sup>nd</sup> stage) that consisted in orbit radiotherapy 40–45 Gy/week, week 6 post-operation, without chemotherapy treatment due to the age.

At the age of 2 years (2004), the child is hospitalized again in the Ophthalmology Clinic of Emergency County Hospital, Cluj-Napoca, showing at the level of the superotemporal part of the left eyesclera two brown spots, weakly delimitated, of approximately 3/5 mm. The left eye ophthalmoscopic examination has revealed a tumor formation of approximately 3.5 PD (papillary diameters), supero-temporal of optic papilla.

The cerebral and orbital NMR-examination points out in the posterior pole of the left eye a formation of approximately 16/8 mm, discreetly non-homogenous, with the central area with hyposignal, well limited, that does not exceed the posterior wall of the globus; the optic nerve has the structure unmodified, do not appear intra-cerebral formations that substitute space. The right eye diagnosis is set – operator anophthalmous (retinoblastoma). Left eye – intraocular tumor formation and the surgical intervention is suggested (enucleation of the left eyeball).

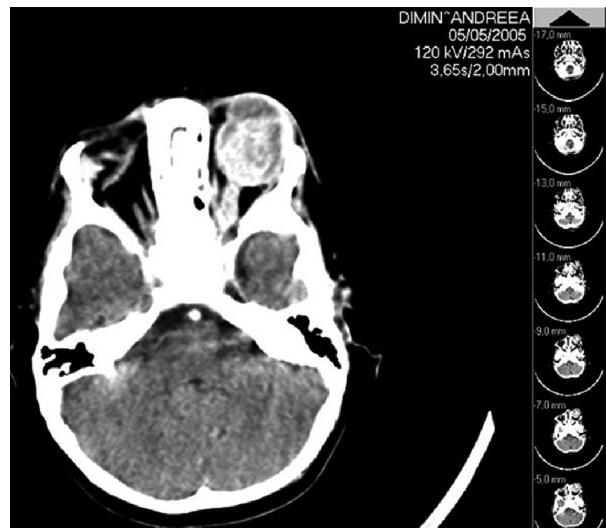
The mother refuses the surgical treatment, the child is hospitalized in the Oncology Clinic for chemotherapy (May 2004–January 2005), according to the protocol 2<sup>nd</sup> stage (Cyclophosphamid, Doxorubicin, Vincristin + Cisplatin, Etoposid). [3]. She does not show up at the periodical ophthalmological checks and in 2005 is hospitalized for the third time in the Ophthalmology Clinic with right eye – operator anophthalmous, and left eye – painful, digital hypertonic globus, exophthalmic, deformed, irritated, with perforations with leak of serous-sanguinolent liquid, without visual acuity (Figure 1). The left eye cannot be ophthalmoscopically examined.



**Figure 1 – Pre-operator aspect of the left eye in the 3-year-old child.**

The cerebral and orbital NMR-examination reveals in the left orbit a non-homogenous formation of 2.4/2.3 cm, supero-posterior developed, with multiple

hyperdense images, iodine-fixing that extends in the optic nerve up to the level of the chiasm. The optical nerve appears thickened, irregular and non-homogenous, with multiple millimetric, hyperdense images, without secondary cerebral determinations (Figure 2).



**Figure 2 – Cerebral MRI. Exam shows the extension of the tumor along the intraorbital and intracanalicular segments of the optic nerve.**

There is a surgical intervention and the exenteration is practiced, the hemostasis on the ophthalmic artery, periosteum ablation, the Dynamic Titanium Mesh. The immediate post-operation evolution was favorable, the child dies after one-year post-operation, by cardiac insufficiency (Fallot tetralogy).

The second patient is a 30-year-old woman (the mother of the child previously presented), who is examined at the Ophthalmology Clinic of Cluj-Napoca, in December 2006. A massive tumor formation is found, with vegetant aspect, exulcerated, with starting point at the level of the left orbit, rough on touching, unpainful (Figures 3 and 4).

Anamnestically, the tumor has been growing for about six months, spontaneously, without connection to the external factors (traumatism, exposure to UV-rays). It is worth mentioning the fact that the patient is monophthalmus (left eye) from the age of one year, ulterior to an intraocular tumor – affirmative – the histopathological diagnosis of retinoblastoma.



**Figure 3 – Pre-operator aspect of the 30-year-old women; the tumor of the left orbit is massive, vegetant, exulcerative.**



**Figure 4 – Pre-operator aspect of the 30-year-old women; the extension of the superior eyelid and the dilation of the superficial veins are visible.**

She followed an oncological treatment for three months (Vincristine, Cyclophosphamide, Etoposide and Carboplatin), (Figure 5), then was operated and was practiced the total exenteration with prosthesis Dynamic Titanium Mesh [4]. The histopathological result is that of squamous carcinoma. The post-operation evolution is favorable (Figure 6), the patient shows up constantly at the medical check performed by a panel of experts (oncology, radiology, ophthalmology, neurology).



**Figure 5 – The aspect of the tumor after three months of chemotherapy treatment.**



**Figure 6 – Post-operative aspect of the patient with left total exenteration under Titanium Mesh.**

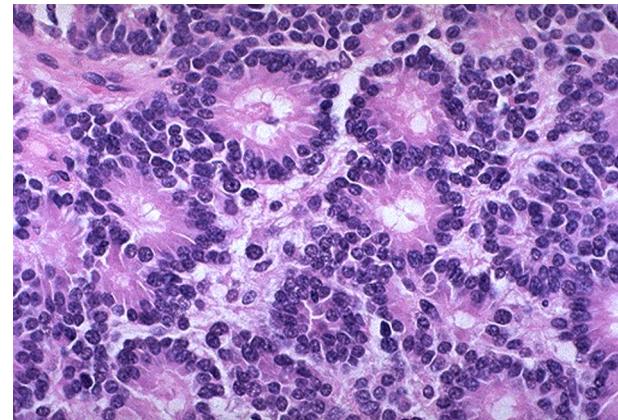
## □ Results

### Case no. 1

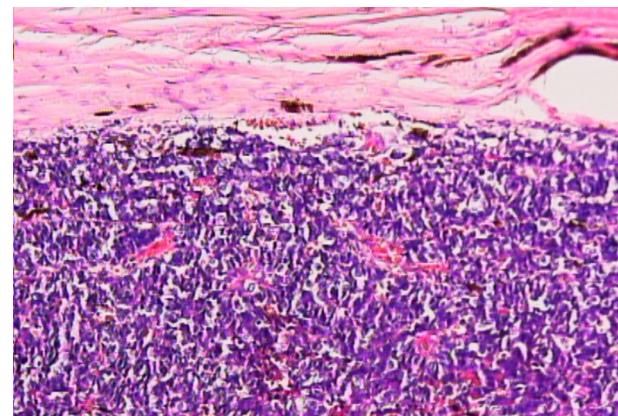
At the RE histopathological diagnosis settled post-operation was that of retinoblastoma stage 2 (tumor limited to the globus with extension to the vitreous, according to the "St. Jude" Children's Research Hospital classification).

The microscopic aspect of the tumor revealed round cells, with little cytoplasm, with big nucleuses, intensely

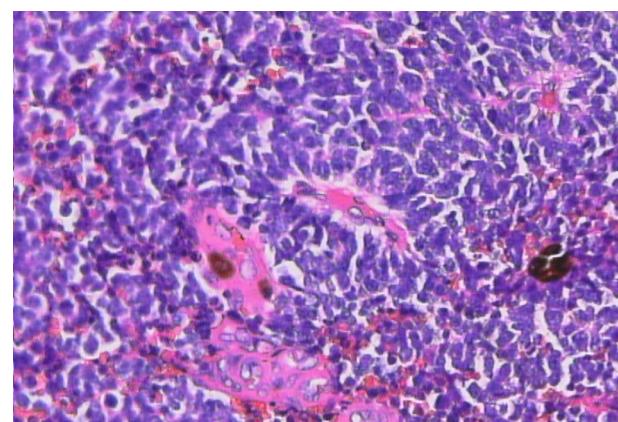
basophilic, with mitosis. Flexner Wintersteiner rosettes: group of cylindrical cells with basophilic nucleuses, placed around cavities, blood vessels or areas of necrosis, necroses, calcifications (Figures 7–9).



**Figure 7 – Flexner Wintersteiner rosettes: clusters of cuboidal or short columnar cells arranged around a central lumen. The nuclei are displaced away from lumen (HE stain, ob. 20×).**



**Figure 8 – The aspect of the retinoblastoma and unaffected sclera (HE stain, ob. 10×).**



**Figure 9 – Pseudo Flexner Wintersteiner rosettes around the vessels (HE stain, ob. 40×).**

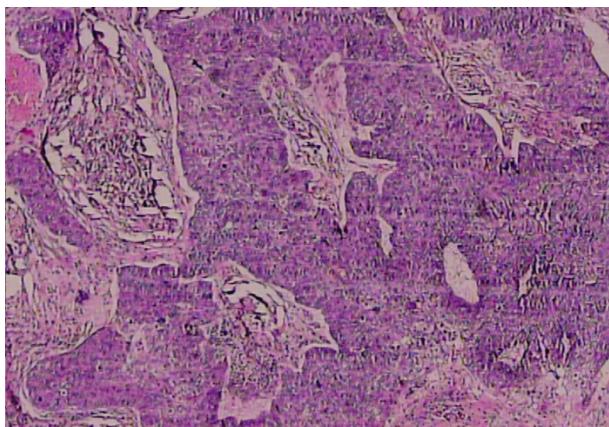
The histopathological examination of the left eye macroscopically points out a piece of 4/4/3 cm with vegetant aspect (Figure 10); the whole cavity of the eye is taken by a violet mass with the diameter of 3 cm. Microscopically is found a retinoblastoma with aspect of scleral invasion and tumor emboli in the vessels from the striated muscular layer.



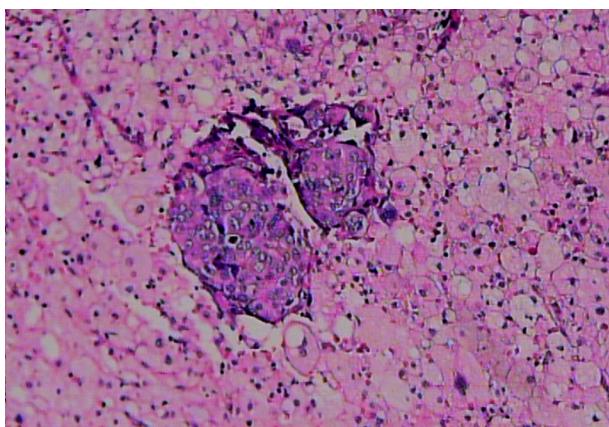
**Figure 10 – Macroscopic aspect of the enucleated eyeball: the aspect and the color of the sclera are modified.**

### Case no. 2

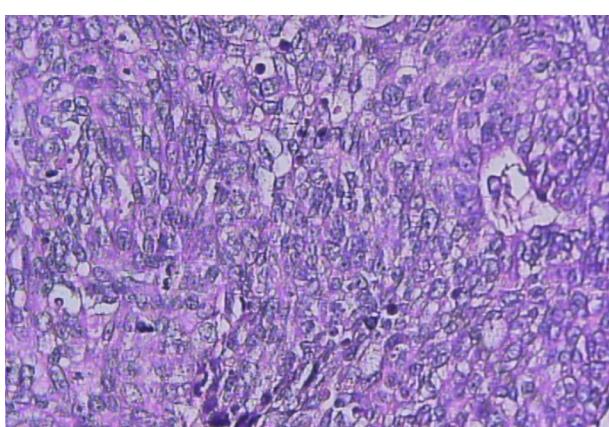
The result of the histopathological diagnosis was that of squamous carcinoma with intra-orbital invasion [5] – details (Figures 11–13).



**Figure 11 – Squamous carcinoma (HE stain, ob. 20×).**



**Figure 12 – Tumoral island surrounded by macrophages (HE stain, ob. 20×).**



**Figure 13 – Details of the tumor (HE stain, ob. 40×).**

### Discussion

In the first case, the child with retinoblastoma, the aggressive progress of the illness is to be noticed and the affection of the second eye in a short period. If at the right eye the tumor formation has limited itself strictly to the ocular globus (the extension was previous, limited inside the vitreous body), thus enabling the enucleation, at the left eye the evolution was completely different.

The tumor formation developed in both the exophytic and endophytic form, to the orbital cavity and the optic canalculus, reasons that imposed the exenteration. The post-operative oncological treatment was efficient, no tumor recidivating appeared or secondary inter-cerebral determinations or with other localization.

In the second case is to be noticed the efficiency of the post-operative oncological treatment (chemotherapy – the 2<sup>nd</sup> protocol has been applied for three months) in the absence of a histopathological diagnosis (the tumor formation considerably decreased in size) enabling the surgical intervention – exenteration, with the total ablation of the tumor.

In addition, post-operation have been taken into consideration more aspects: the possibility of a retinoblastoma recidivating after a long period of time (29 years) [6, 7].

The existence of a local metastasis was infirmed by the absence of the primitive carcinoma: the patient has been generally investigated by complex clinical and paraclinical examinations: thorax CT, abdomen, cranium NMR, oncological periodical checks.

The particular conditions of appearance of the squamous carcinoma are to be noticed in the case presented: the young age, the female sex, the lack of exposure to the UV-rays, the localization at the level of the same orbit [8], as well as the way of progress, not only exophytic (the tumor formation of big sizes, vegetative) as well as endophytic with intra-orbital extension [9], up to the level of the left optic canalculus [10, 11].

### Conclusions

In the first case presented, the child with bilateral retinoblastoma, with enucleation at the right eye and exenteration at the right eye, are to be noticed the following aspects: the genetic field, the genetic “country”, the mother as well as the father being diagnosed with retinoblastoma and enucleated (lack of genetic advice); the aggressive and rapid evolution of the illness, the short interval of appearance between the two eyes and the intra-cranium extension in the case of the left eye.

In the second case, it is rarely met the appearance of another form of carcinoma with the same topographic localization (the left orbit), from structures with pavement epithelium, probably with starting point from the eyelid's integument, the palpebral conjunctiva, etc. It is to be noticed the fact that the post-operation evolution, as well as the periodical checks performed has been favorable.

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