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Original Contribution

CLINICAL, MORPHOLOGICAL AND EPIDEMIOLOGICAL DATA ON EYE TUMORS

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ABSTRACT

The purpose of this study is to investigate the epidemiologic and histological structure of ocular malignancies for a seven year period in the Department of pathology,Sofia 894 ocular biopsies include 242 benignant and 157 malignant tumors of ocular adnexa. Basocellular and spinocellular carcinomas are the most common malignant tumors .Enucleated eyes are 126 with 75 intraocular tumors. The most common cause for enucleation is the uveal melanoma with a higher frequency among men. The mean age for both sexes is similar and is lower than previously described in literature with almost 10 years. We have 13 retinoblastomas with late diagnosis in the majority of cases.

Key words: ocular biopsies, uveal melanoma, retinoblastoma, sebaceous carcinoma, maltoma

Ocular tumors are a heterogeneous group of diseases, relatively uncommon in the daily pathologic practice. They have an enormous social importance because they affect the ability to see. Their great variety comes from the fact that the tree fetal layers take part in the eye embryogenesis.

PURPOSE

To investigate the clinical, morphological and epidemiological structure of eye tumors through analysis of the ocular biopsies in the Department of Pathology, UMBAL "Alexandrovska ", Sofia for the period 2001-2008.

METHODS

We made a retrospective study of the ocular biopsies from year 2001 to year 2008, including 894 cases of eye diseases. All slides were classically stained with hematoxylin – eosin. In some of them we made additional cuts, histochemical (Van-Gieson, Gomori, Sudan4,PAS, Alcian) and immunohistochemical (cytokeratin,LCA,S-100 protein,NSE,GFAP,CD 20,CD 3,CD 5) staining for correct diagnosis. The results from ocular adnexa were divided in three groups: benign and malign tumors and non tumor diseases.

In enucleated eyes we made a comparison between the histological and the clinical diagnosis that prompted the surgical intervention. Six different histological groups were separatedmelanomas. retinoblastomas, intraocular metastases, glaukomas, traumas/ inflammations, Coats' disease. We estimated the percent distribution of melanomas according to their localization (iris, ciliary body and chorioidea), histological type (spindle cell, epitheloid cell or mixed cell) and stage (pTNM).Mean age and sex distribution was calculated. Staging and grading was made for all retinoblastomas.

RESULTS

894 eye biopsies were received and processed in the Department of clinical pathology for the period 2001 – 2008.They included 369 non tumor diseases, 242 benign and 157 malign tumors of the ocular adnexa, conjunctiva and cornea .Enucleated eyes were 126.

In the group of benign tumors papillomas convincingly were the leaders with 171 cases, followed by nevuses (34 cases) and hemangiomas (19 cases) (fig. 1). The most common malign tumors were the basocellular carcinoma (108 cases), followed by the spinocellular carcinoma (19 cases) (fig. 2).

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Figure 1. Percentage of benign tumors



Figure 2. Percentage of malign tumors

In enucleated eyes we found 75 intraocular 59 tumors. including melanomas. 13 retinoblastomas and 3 intraocular metastases (breast, pulmonary carcinoma).Non tumor diseases were 51, among them 20 glaukomas, 30 traumas/inflammations and one case with Coats' disease(fig. 3). Sex distribution for the melanoma group was 61% males (36 cases) and 39% females (23 cases). Mean age for men

was 59, years and 57, 8 years for women. The most common localization was chorioidea - 54 (91, 5%), followed by cliary body -4(6, 78%)and iris -1 case (1,69%). The dominating histological type was the mixed cell -30 cases (50,85%),16 for the spindle cell (27,12%) and 13 for the epitheloid cell (22%). According to pTNM staging 10 melanomas were first stage, 20 - second and 29- third stage.



Figure 3. Findings after enucleation

From the surveyed retinoblastomas we had 5 low grade, 6 moderately and 2 high grade malignant tumors. According to pTNM classification 1 case was pT1, 1 is pT2, 6 pT3a, 1 - pT3c and 4 - pT4.

DISCUSSION

Tumors of the eye and ocular adnexa occupy about 50% of all ocular biopsies. This frequency is higher compared to the ratio of tumor-non tumor diseases affecting other organs, with the exception of the central nervous system lesions. Prevalence of benign tumors is twice that of malign tumors with higher incidence of papillomas. These tumors should not be underestimated because of their frequent recurrence and malignant potential. Surgical excision with subsequent histological examination remains the gold standard and ensures certainty of treatment. (1)



Figure 4a.Sebaceous carcinoma,HEx10

Microscopic the tumor has a solid-lobular appearance with common central necroses. Papillary or mixed types can be seen. The cells have abundant foamy, finely vacuolated cvtoplasm and clear cell borders. In poorly differentiated forms marked nuclear and cell polymorphism can be observed, together with prominent nucleoli and great number of atypical mitotic figures. Additional histo- and immunohistochemical staining like Sudan 3-4, oil red - O on frozen sections, cytokeratin, epithelial membrane antigen (EMA), Ber-EP4,CAM52,HMFG1,helps establish the correct pathohistological diagnosis. Measurements over 10mm, upper lid localization are unfavorable prognostic factors. Tumor differentiation and infiltration of adjacent structures undoubtedly is of major importance.

Sometimes sebaceous carcinoma develops simultaneously with visceral neoplasms (Muir – Torre syndrome) – rectum, bladder, prostate gland, kidney carcinomas. These tumors have high malignant potential and they can give early lymphogenous metastases. That imposes their early diagnosis and need for radical treatment (2). Unfortunately they are often misdiagnosed by clinicians, because of their resemblance to benign lesions (chalazia), as well as by pathologists. Interesting fact is that we have only to cases up to 2006, when

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In our study we observed a relatively low incidence of sebaceous carcinomas (9 cases for the whole period) (**fig. 4a and 4b**).Clinically the tumor most commonly is presented as a nodular lesion and rarely as a diffuse infiltration of the eyelids with a pagetoid spread. Local loss of eyelashes is an alarm sign and it is due to tumor infiltration of the hair follicle.



Figure 4b.Sebaceous carcinoma,HEx40

for the next two years they are already seven. This includes two relapses with previous histological diagnosis poorly differentiated spinocellular carcinoma and sebaceous type of basocellular carcinoma.

Pigmented tumors of the conjunctiva and eyelids are frequent -34 cases in our survey. Despite their clinical and histological variations, malignisation is rarely observed, mainly in elderly patients.

Uveal melanoma is the most common primary intraocular tumor in adults. According to literature data its incidence is 7 cases /1 million population per year (3, 4, 5). In focused large autopsy studies it reaches 20/1million in people over the age of 70 years (6, 7). This is the most common cause of enucleation in our study with a male preponderance, which coincides with data from other studies (8) (fig. **5a and 5b**). The average age is approximately equal for both sexes, but is lower than that described in literature (9) with almost ten years, which is an alarming trend of rejuvenation of the disease. Even more disturbing is the fact that over one half of the diseased are diagnosed in the third stage and less than 1/5 in the first stage Most common localization of the tumor is the chorioidea (91, 5%), followed by ciliary body (6, 78%) and iris (1, 69%).Perhaps the low incidence of primary iris localization in our study is due to

impossibility to determine the initial origin of the tumor with its advancement and



Figure 5a.Ciliary body melanoma,HEx10

One of the most important prognostic factors is the cell type of melanoma(10). In this study epitheloid cell type ,being the less favorable, is 22% of the total tumors ,while in other surveys it's only about 12%.

Thirteen retinoblastomas are found in the enucleated eyes. Unfortunately again we observed late surgical intervention not because of late diagnosis, but rather because of a delay in parents' decision. We have one registered case in pT1 and pT2, six in pT3 and four in involvement of adjacent structures in pT3 stage.



Figure 5b.Ciliary body melanoma, HEx40

pT4 (**fig.6a and 6b**).Regarding differentiation - five low differentiated, six moderately differentiated and two highly differentiated tumors. Illustration of the enormous importance of multidisciplinary approach in the study of retinoblastoma is the disclosure of the RB-suppressor gene and its relationship to the regulation of cell replication – a universal process. In our study we witnessed a family involvement in one of the children – a sick brother with bilateral retinoblastoma.



Figure 6a.Retinoblastoma infiltrating the optic disc,lamina cribrosa is intact,HEx10

Differential diagnosis of leukocoria includes many diseases, including Coats' disease – exudative retinal detachment, affecting in about 80% small boys (11).We diagnosed this rare disease in a two-year old boy with the



Figure 6b.Retinoblastoma,HEx40

clinical diagnosis retinoblastoma (**fig 7a and 7b**). In such cases correct histological diagnosis would prevent further complications associated with subsequent chemo- or radiotherapy.

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Figure 7a.Morbus Coats,HEx10

Of the surveyed lymphomas prevail maltomas, extranodal marginal-zone B cell non – Hodgkin's lymphoma, expressing CD 20+, negative for CD3-; CD5-.It affects the conjunctiva without systemic involvement (**fig.8a and 8b**).

Conclusion: Unique structure of he eye rises such specific neoplasms as uveal melanoma,



Figure 8a.Maltoma

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Figure 7b.Exudation with foamy macrophages,HEx40

retinoblastoma and sebaceous carcinoma .Specificity of eye pathology requires a thorough knowledge and experience from the pathologist together with close collaboration with the ophthalmologists to achieve optimal results.



Figure 8a. Extranodal marginal zone B-cell NHL

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