Ciliary Body Melanoma – A Particularly Rare Type of Ocular Tumor. Case Report and General Considerations

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case report

ABSTRACT
Uveal melanoma is the most common primary malignancy of the eye in white adults. Frequently, uveal melanoma arises from choroid or iris. Ciliary body melanoma is a rare if not exceptional subtype of uveal melanoma. Furthermore, ciliary melanoma is often seen in association with the other two subtypes of uveal melanoma. This paper presents a case of primary ciliary melanoma with invasion of the iris. The patient presented with blurred vision, but this symptom could not doubtless be related with the existence of the tumor, because of the small dimension of the malignancy and the lack of medical history of the patient.

This tumor was included in the category of “very small ciliary melanoma”, a rare diagnosis considering the fast local invasion and the lack of symptoms in such a small tumor. Histopathological and immunohistochemical examinations confirmed the diagnosis of ciliary melanoma.

This type of ocular melanoma has a low prognosis due to early metastases.

Keywords: ciliary body, uveal melanoma, genetic predisposition, unfavorable prognosis

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INTRODUCTION

Uveal melanoma is the most common primary intraocular malignancy in white adults. This malignant neoplasia is composed of atypical melanocytes. Melanocytes are cells that are normally found in the iris, ciliary body and choroid. A proliferation of atypical melanocytes that appear in any of these three structures forms an uveal melanoma. However, depending on its location and structure, each tumor has some particularities.

Intraocular melanoma incidence varies from 4.3 to 6 cases per 1 million people in the U.S., reaching 7.5 cases per 1 million population in Scandinavian countries. In other European countries, epidemiological data suggest an incidence between 5.3 to 10.9 cases per 1 million population (1-3).

Choroidal melanoma is the most common subtype of uveal melanoma. Melanoma of ciliary body is rarely seen, this tumor being reported in 1 of 10 cases of all intraocular melanomas (1, 2). If the melanoma of the iris has the best prognosis, the ciliary body and anterior choroidal melanomas have the worst prognosis of all intraocular melanomas (2). The anatomical location seems to be the key outcome. Hematogenous metastasis is faster in ciliary body melanoma as a result of continuous contractions of the ciliary muscle and of the particularly rich vascularization of this anatomical region (1). At the same time, the late diagnosis of the tumor is due to the absence of clinical signs in the early stages and anatomical localization, making it harder to identify in an usual eye examination. The average age of patients with ciliary body melanoma is between 55 to 62 (2). The 10 year mortality rate reaches values between 30-50%, the main cause of death being due to the impairment of other organs by vascular metastasis (1). Metastases are frequently discovered in the first year after diagnosis, but there are also cases of developing metastases many years after diagnosis and treatment.

The incidence of this type of cancer is greater among Caucasians, northwestern Europeans, populations with light phototype, people excessively exposed to ultraviolet radiation, those with family history of congenital ocular melanosis, xeroderma pigmentosum, dysplastic nevi syndrome, history of uveal nevus or other uveal melanoma (8, 10).

CASE REPORT

The experience of the Department of Pathology of the Emergency University Hospital of Bucharest regarding ocular melanoma diagnosis has increased considerably in the last 3 years due to the relatively high number of cases of ocular melanoma identified by histopathological examination. Among these cases, we found a rare subtype of uveal melanoma – a ciliary body melanoma, diagnosed in a 64 years old female. Complaining of blurred vision in the right eye, the patient came to the Department of Ophthalmology of the Emergency University Hospital of Bucharest for expert advice. On this occasion, after clinical examination and additional testing, the suspicion of iris and ciliary body melanoma was raised. The diagnosis was confirmed by the Department of Pathology. After surgical enucleation of the affected eyeball, tissue pieces were sent for histopathological examination and diagnosis.

Tissue samples were processed by conventional histopathological method using inclusion in paraffin and hematoxylin-eosin staining and we also performed immunohistochemical tests for confirmation (S 100, Melan A, HMB 45).

RESULTS

Histopathological examination confirmed and supported the initial diagnosis of iris and ciliary body melanoma. On microscopic examination we identified many tumor cells of different sizes, heavily pigmented, predominantly polyhedral. The cells had nest or island pattern organization or were dispersed, infiltrating the ciliary body. Cells showed marked nuclear atypia, with bulky nuclei. Mitotic rate...
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was increased with numerous atypical mitoses. The tumor had infiltrative nature, invading the anterior chamber of the eye. Considering the tumor sizes (3.6 / 1.9 mm) it could be included in the category of “very small ciliary melanoma” (11).

Due to the small dimensions and the infiltrative nature of the tumor, the blurry vision was probably determined by intraocular hypertension in the context of acute glaucoma. Still, the accidental discovery remains a high probability because of the lack of further information regarding the patient’s medical history.

DISCUSSIONS

Ciliary body melanoma is rarely diagnosed as a single entity; more often this type of tumor is associated to choroidal melanoma or iris melanoma due to the local extension. Generally, ciliary body melanoma has no symptoms for a very long time and is diagnosed, more often than other uveal melanomas, when metastasis is already present.

The most frequent symptoms accused by the patient are represented by local signs as blurry vision due to astigmatism or lens dislocations, floaters, painless visual field loss or pain as a result of an acute glaucoma (1). Dilation of the episcleral vessels (also named “sentinel vessels”) is one of the first ophthalmological sign of this tumor. Another early sign is an unexplained low intraocular pressure compared to the healthy fellow eye of 5 mm Hg or more (1). Weight loss, marked fatigue, cough and gastrointestinal or urinary changes are general signs which can denote the existence of metastases of the melanoma.

The suspicion of ciliary body melanoma is raised after different ophthalmological investigations such as biomicroscopy, ocular CT or MRI, and the diagnosis is confirmed histopathologically. After pupillary dilation, the tumor can be observed as a dome-shaped mass with variable pigmentation which can extend to the iris or to the posterior pole of the eye.

As the choroidal melanoma, the ciliary body melanoma is divided in four histopathological subtypes following the Callender modified classification for uveal melanoma: spindle A and B type melanoma, with the best prognosis, mixed cell melanoma, epithelioid cell melanoma and necrotic melanoma, the last with no identifiable cell type due to the necrosis. The last two have an unfavorable prognosis. Type A spindle cells present small, fusiform nuclei with rare mitoses. The chromatin distribution follows the axe of the nuclei. Type B spindle cells are a little bigger, more pleomorphic, with prominent nucleoli and mitotic activity (4). Epithelioid cells melanomas are the ones with the most unfavorable prognosis. Their cells present intense nuclear pleomorphism, with frequent mitoses and an anaplastic appearance.

Immunohistochemically, ocular melanoma is reactive for S-100 protein, HMB-45, vimentin and different keratins with low molecular weight. The positivity of the last ones seems to be a low prognosis factor and increases the risk of metastasis.

The trigger for uveal melanoma is, at least in some cases, determined by different mutations affecting the regulation of the cell cycle and the control of the apoptosis. The “classical” mutations described and identified in patients with iris and, especially, choroid melanoma are similar to those identified in patients with ciliary body melanoma - GNAQ, GNA11 in the 29 codon (10), the inactivation of INK4A, CDKN2a, CDKN1b and CCND1, p53 gene or the retinoblastoma gene. Other genetic changes are the monosomy 3-BAP gene (BRCA1 associated protein 1 or ubiquitin carboxyl-terminal hydrolase), frequently found in melanoma patients, as well as the duplication of the long branch of the 8th chromosome.

The degree of the aneuploidy is the main cause of the genetic instability. Histopathologically, this instability is correlated with the anaplastic and invasive appearance of the uveal...
melanomas but, at the same time, this degree of aneuploidy is a very important prognostic indicator. These genetic mutations appear to be more often described in the melanomas of the ciliary body, which explains the less favorable prognosis comparing with other uveal melanomas subtypes.

The evolution of the ciliary body melanoma is easily predictable. The tumor can grow and it can be seen biomicroscopically as a variable pigmented mass with diffuse, nodular or mixed pattern situated behind the pupil (1). Also, the tumor can invade the anterior chamber, affecting the iris or it can grow into the posterior pole, affecting the choroid. The metastasis appears after bloodstream dissemination since the eye has no lymphatic vessels. Moreover, as suggested above, the metastases appear earlier in the patients with ciliary body melanoma than other types of uveal melanomas, on the one hand due to the long and silent evolution and, on the other hand, due to the rich vascularization of the ciliary body.

The prognostic factors are classified as clinical, macroscopical and microscopical factors. Among the clinical factors we mention the occurrence of local and general signs, local extension, the presence of metastases, the age of the patient and the presence of dysplastic nevi. Macroscopically, the size of the tumor is the most important factor. Hence, if the tumor’s biggest diameter does not exceed 11 mm, the tumor is considered to be “small”-type and has an 86% survival rate at 5 years. A diameter between 11 and 15 mm is considered “medium” and is associated with a 66% 5 year survival rate (6). “Large” tumors, with more than 15 mm in diameter, have a 56% survival rate (6). From all the microscopical factors, we already talked about the cellular type and mitotic activity. Also, the presence of necrosis, the intense pigmentation and the melanophagic and lymphocytic infiltrate are correlated with the worst prognosis.

CONCLUSIONS

Although the ciliary body melanoma is a rare tumor found in medical practice, this type of neoplasm raises a lot of issues regarding the early diagnosis and further evolution. The most common treatment worldwide is radiotherapy such as plaque brachytherapy or proton beam therapy. Either external beam therapy or brachytherapy can be used for medium-size tumor (less than 15 mm in diameter) (1) with the latter used more often for melanomas and the first for lymphomas (15). Late clinical manifestations, as well as various prognostic factors, determine the management of the disease and can induce a radical and high impact treatment for the patient. In advanced cases, depending on the size of the tumor, the local extension and the cellular type of the melanoma, the treatment is surgical, with enucleation of the eye, block excision or sclerouvectomy consisting in an in-block removal of ciliary body, cornea, iris and sclera following by grafting to close the defect (1). As noted above, the presence of metastases at the time of diagnosis is more common than in other uveal melanomas, therefore an oncologic therapy of high magnitude including radiotherapy, chemotherapy, support group therapy and palliative therapy is required in those particular cases.

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