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Current management of choroidal melanoma in Serbia
Лечење меланома хороидеје у Србији данас

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SUMMARY

Introduction/Objective Uveal melanoma is the most common primary malignant intraocular tumor in adults, and approximately 90% of uveal melanomas originate from choroid. Nowadays different treatment options for choroidal melanoma are available and an increasing tendency toward eye-sparing therapies is evident.

The aim of this paper is to analyze current treatment of choroidal melanoma in Serbia.

Methods This was a retrospective, observational study. Patients with choroidal melanoma diagnosed between January 2014 and December 2016 were included. Information of patient's age and gender, and suggested and realized therapy were analyzed.

Results During the observation period, a diagnosis of choroidal melanoma was established in 148 patients, 71 (48.0%) males and 77 (52.0%) females. Recommended treatment was enucleation in 108 (72.9%), brachytherapy in 24 (16.2%) and proton beam radiation in 16 (10.8%) patients. Fifteen (10.1%) patients did not accept suggested therapy. Ten (6.8%) patients refused any treatment at all, and five patients insisted on enucleation instead of advised eye-sparing therapies.

Conclusion In our country choroidal melanoma is usually detected late when the possibility of efficient local treatment with preservation of the eye and its function is limited and when patient's prognosis is serious.

Keywords: choroidal melanoma; treatment; Serbia

САЖЕТАК

Увод/Циљ Меланом увеје је најчешћи примарни малигни интраокуларни тумор одраслих, а око 90% меланома увеје су меланоми хороидеје. Данас постоје различите могућности за лечење меланома хороидеје, а све чешће се примењују поступци који поред ефикасне локалне терапије тумора омогућавају очување ока.

Циљ рада је био да се анализира како се меланом хороидеје лечи данас у Србији.

Метод У ретроспективну студију посматрања укључени су болесници код којих је дијагноза постављена у периоду од јануара 2014. до децембра 2016. Анализирани су подаци о полу и узрасту оболелих и о предложеној и спроведеној терапији меланома хороидеје.

Резултати Дијагноза меланома хороидеје је постављена код 148 болесника, 71 (48,0%) мишкарца и 77 (52,0%) жена. Препоручена терапија је била енуклеација код 108 (72,9%), брахитерапија у 24 (16,2%) и терапија умереним снопом протона у 16 (10,8%). Није прихватило саветовану терапију 15 (10,1%) болесника. Десет (6,8%) је одбило било какву терапију, а пет је инсистирало на енуклеацију уместо предложене зрачне терапије.

Закључак Меланом хороидеје се обично дијагностикује касно и могућности за ефикасну локалну терапију тумора уз очување ока и његове функције су ограничене и животна прогноза оболелог је озбиљна.

Кључне речи: меланом хороидеје; терапија; Србија

INTRODUCTION

Uveal melanoma is the most common primary malignant intraocular tumor in adults. Standardized annual incidence rates of a tumor increase from less than 2 per million in south to more than 8 per million in north Europe [1]. Approximately 90% of uveal melanomas originate from choroid [2].

Careful clinical fundus examination with dilated pupille is the most important element in diagnosis of choroidal melanoma, accompany by ancillary methods such as ultrasonography, fluorescein angiography or optical coherence tomography. Despite the fact that the main oncologic principle of histological or cytological evaluation of the lesion is not routinely fulfill in diagnosis of choroidal melanoma, the diagnosis of the tumor is highly accurate [3].

Nowadays a treatment of choroidal melanoma is the main challenge. The main goal of local tumor treatment is to eradicate a tumor locally in order to prevent further tumor dissemination. In addition, the effort is made to preserve the eye and the best possible visual function.

Individual approach to a treatment of choroidal melanoma is necessary. Characteristics of each tumor and diseased eye, the visual function, the patient's general health and its expectations and preferences, the characteristics and availability of the treatment modalities have to be taken into consideration in making a decision of melanoma treatment. Nowadays different treatment options for choroidal melanoma are available and an increasing tendency toward eye-sparing therapies is evident.

The aim of this paper is to analyze current treatment of choroidal melanoma in Serbia.

METHODS

This was a retrospective, observational study. Patients with choroidal melanoma diagnosed in the Clinic for Eye Disease, Clinical Center of Serbia in Belgrade, between January 2014 and December 2016 were included. At this Clinic, all patients with presumed intraocular tumor are presented to the Consultation group that, after detailed patient examination and analysis of his medical papers, recommends treatment. A final decision on a therapy is made in consultation with fully informed patient. Data on patients were obtained from the Consultation group registry. Information of patient's age and gender, and suggested and realized therapy were analyzed.

RESULTS

During this three-year observation period, a diagnosis of choroidal melanoma was established in 148 patients, 71 (48.0%) males and 77 (52.0%) females. In 39.2% of patients the diagnosis of choroidal melanoma was established in seventh decade of patient's life. The mean age at diagnosis for all patients was 62.5 years, 62.7 for males, and 62.4 for females.

Recommended treatment was enucleation in 108 (72.9%), brachytherapy in 24 (16.2%) and proton beam radiation in 16 (10.8%) patients. Enucleation was advised to 45 males and 63 females, brachytherapy to 15 males and 9 females, and proton beam radiation to 11 males and 5 females.

Fifteen (10.1%) patients did not accept suggested therapy. Ten (6.8%) patients, seven males and three females, refused any treatment at all. Two patients insisted on enucleation instead of advised brachytherapy and three patients wanted enucleation instead of recommended proton beam radiation. Those five patients were treated according to their wishes.

DISCUSSION

The Clinic for eye disease, Clinical center of Serbia in Belgrade has a special unit for ophthalmooncology, the only one in our country. The great majority of patients with intraocular tumors from Serbia are treated in this unit. The records from this unit can be considered as representative for our population.

A standardized incidence rate for uveal melanoma in Central Europe is 4 to 6 per million [1]. This rate remains stable. At the Clinic for Eye Disease Clinical Center of Serbia, in the period from

1986 to 2005, the average of 48.7 new cases of uveal melanoma per year were registered [4]. We registered 49.3 new cases of choroidal melanoma per year. Our findings point out that the incidence of choroidal melanoma in Serbia is in accordance with the incidence of this tumor in Central Europe and that it is relatively stable.

We found more female than male patients with choroidal melanoma, which is unexpected. In a study of 1824 patients with uveal melanoma in 55 year period in Serbia Latkovic [4] found a slight preponderance of males which is in accordance with the literature data.

Over the 40 year study period in USA the mean age of patients at diagnosis of uveal melanoma was 61.4 years [5]. The mean age of our patients at diagnosis was 62.5 years. Our patients were older than patients with uveal melanoma diagnosed between 1951 and 2005 in Serbia with mean age of 54,95 years [4]. Andreoli et al stated that the mean age at diagnosis has increased over the last 37 years [6].

The percentage of uveal melanoma cases managed primary by radiotherapy increased by 62% between 1973-1977 and 2006-2012 time periods according to the Surveillance, epidemiology and End Results database in USA [5]. In United States in 1973-1975 time period 93.8% of patients with uveal melanoma were treated only by surgery, but in 2006-2008 time period just 28.3% of patient were treated surgically. Primary enucleation was performed in 33% of 2384 patients with uveal melanoma between 1996 and 2011 in the United Kingdom [7].

Unfortunately for 73% of patients with choroidal melanoma in Serbia enucleation is still en rational initial treatment of a tumor. It means that in time of melanoma diagnosis a visual function is poor, a tumor is voluminous and secondary changes like total retinal ablation or secondary glaucoma are present. The situation is worse in female patients. Enucleation is recommended in 83% of females and in 63% of males with choroidal melanoma.

In our country only 16% of choroidal melanoma is diagnosed when a tumor is relatively small and the eye is in a relatively good condition with useful function, and when a brachytherapy is advisable.

Various clinical, histopathologic, genetic and molecular parameters are discussed and recognized as predictors of metastatic disease and survival in choroidal melanoma. The tumor size is parameter with considerable influence on melanoma prognosis. A study of 8033 uveal melanoma found metastases at 10 years follow up in 12% of patients with small melanoma and in 49% of patients with large melanoma and the authors concluded that the increase of thickness of the tumor leads to an increase in the risk of occurrence of metastasis [8]. It has been shown that with each 1mm increase in tumor thickness as measured by ultrasonography increases the risk of metastasis for 5% [9].

The fact is that the tumor size is the only parameter important for a prognosis in melanoma on which we can have some influence. Diagnosis of small choroidal melanoma provides the best possible

prevention of metastases development and gives a possibility to apply an eye conserving treatment with potential of salvage useful vision.

In Finland 13% of patients with uveal melanoma were entirely asymptomatic in time of diagnosis [10], and in the United Kingdom even 30.2% of patients were free of symptoms on referral [7]. A delay of less than 4 month from the onset of symptoms to treatment may not always represent a serious hazard [10].

CONCLUSION

The importance and benefits of early diagnosis and treatment of choroidal melanoma are obvious. Unfortunately in our country the tumor is usually detected late when the possibility of efficient local treatment with preservation of the eye and its function is limited and when patient's prognosis is serious.

It is important to give the proper information about choroidal melanoma to general population and to insist on importance of early diagnosis of a disease. A periodic fundus examination in midriasis in persons after the age of 50 years has a great value. Special care must be given to the woman.

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