

<https://doi.org/10.31288/oftalmolzh202355658>

Complications after proton therapy of choroidal melanoma: A case report

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Proton beam therapy is a globe preserving treatment method of choroidal melanoma. It is considered to be less harmful for the tissues around the tumour but the complications such as radiation retinopathy and neuropathy occur according to the dosage of irradiation. The visual outcomes after treatment are variable and dependent on the size of tumour.

This article presents a case report of a 44-year-old male with choroidal melanoma in the left eye. Patient was examined in our ophthalmology practice because of photopsia and blurry vision during physical activity. After full ophthalmologic examination, fundus photography, optic coherent tomography, fluoresceine angiography and ultrasonography the diagnosis of malignant melanoma of choroid was set. The patient was referred to a proton center to undergo a proton therapy of choroidal melanoma in the left eye. Follow-up treatment of severe postradiation retinopathy and neuropathy is presented in the article. The patient took intravitreal bevacizumab injections and the panretinal lasercoagulation was performed. After one and half year follow up the melanoma is stable after therapy with no metastases.

Key words: choroidal melanoma, proton therapy, complications

Introduction. Choroidal melanoma belongs to the most frequent primary intraocular malignancies among adult population. It also appears in ciliary body and iris too [6]. It grows from ciliary body, iris and choroid melanocytes [13]. Therapy of choroidal melanoma includes regular observation, transpupilar thermotherapy by using diode laser, radiotherapy which includes brachytherapy and proton therapy and surgical removing of the eye in cases when radiotherapy is not indicated [1]. Proton therapy is considered as a method potentially causing less damage to adjacent tissues because of the very accurate localization of radiation from charged protons. Despite this fact, postradiation retinopathy or papillopathy still frequently occurs in patients who underwent proton beam radiotherapy. Neovascular glaucoma occurs more often in eyes with larger tumours localized close to macula or optic nerve papilla [7].

Case report

A 44-year-old male undertook an ophthalmologic examination because of photopsia and blurred vision during physical activity in his left eye. Otherwise he had no other health problems.

An ophthalmologic examination was performed: Uncorrected distance visual acuity (UCVA) was 1.0 in decimal in right and in left eye. Intraocular pressure was normal. Anterior segment in both eyes and posterior segment in right eye was normal. Fundoscopy in artificial mydriasis on left eye revealed grey tumorous mass. The tumour covered optic nerve papilla, thus the papilla was not visible (Fig. 1 – see cover page 3). The B scan ultrasonography (USG) of left eye showed a

hyperechogenicity above optic nerve papilla with height 4,72 mm and width 7,66 mm (Fig. 2). There was also visible serous retinal detachment inferotemporally to the tumour. The fluoresceine angiography (FA) was performed. FA showed dual circulation in the arterial phase (Fig. 3 – see cover page 3). Examinations revealed that the tumorous mass was choroidal melanoma. The magnetic resonance imaging (MRI) of brain and orbits showed hyperintense mass in the left eye without perineural spreading. Radiography of thorax and USG of abdomen was performed with a negative findings. Due to

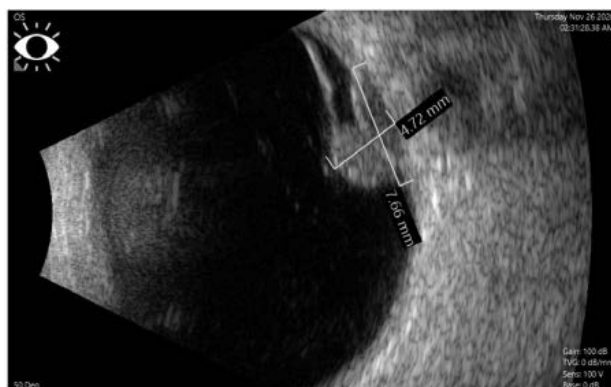


Fig. 3. Ultrasonography B scan shows a hyperechogenic mass with a serous retinal detachment on the posterior pole with the size 7,66 mm on the base and 4,72 mm height.

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Figure 7. Ultrasonography B scan shows smaller size of the tumour and retinal detachment on the top is smaller.

these results in order to restore the eye the proton therapy was chosen.

The patient underwent a proton therapy of choroidal melanoma on the left eye in Department of ophthalmology in Charité Hospital Berlin, Germany. The prognosis of restoring of UCVA in the left eye was poor. The proton centre recommended USG of liver every half a year. Intravitreal application of bevacizumab was recommended.

Three months after proton beam radiotherapy a haemorrhage on the top of tumour appeared (Fig. 4 – see cover page 3). The proton centre recommended 3 intravitreal applications of bevacizumab until the control examination.

Nine months (Fig. 5 – see cover page 3) after proton therapy the nasal 2/3 of tumour were atrophic with haemorrhages and the superonasal part of tumour had hard exsudates around. Lasercoagulation of nasal periphery of retina was performed.

One year after proton therapy (Fig. 6 – see cover page 3) the patients visual acuity was counting fingers in the left eye. Fundoscopy revealed severe ischemy of retina with haemorrhages and hard exsudates. Later a rubeosis of the iris was present. His intraocular pressure remains normal. The intravitreal applications of bevacizumab continue and the lasercoagulation was performed. Results of liver USG remain negative (Fig. 7).

Discussion

Proton beam therapy is a good choice of treatment for big choroidal melanomas located posteriorly close to the optic disc or macula. Reasons for a poor visual outcomes after proton therapy are toxic tumour syndrome, postradiation maculopathy, optic neuropathy or retinopathy as in other methods of radiation therapy [10]. Therapy of choroidal melanoma is dependent on many factors such as location and size of the tumour, visual acuity of the eye and of the contralateral eye, presence of metastases and growth of the tumour into adjacent tissues [12]. Proton irradiation is able to destroy tumour tissues in the depth of 30 cm. The proton beam is concentrated into a narrow beam by strong magnetic field. The protons are absorbed in the tumorous

tissue, the energy is released, ionization occurs, free radicals are destroying the DNA of cells. The main advantage of proton therapy is that the beam is not reaching the healthy tissues. The effect of ionization is mostly significant in the tumour, but adjacent tissues are also affected by the radiation depending on the dose, type or radiosensitivity [11]. Small melanomas with diameter <10 mm and height <3 mm without associated risk factors, clinical changes and growth might be considered for a regular observation. Medium size and large uveal melanomas are indicated for radiology therapy (proton beam therapy, brachytherapy, radiosurgery) or surgical therapy (resection with or without adjuvant radiotherapy, enucleation, exenteration). Studies show comparable results in survival with radiation methods and enucleation [16]. Risks of the proton beam therapy are toxic tumour syndrome, epiphora, keratopathy, cataract, retinal, choroidal vasculopathy [2]. The risk of developing radiation retinopathy is the location of tumour close to foveola or optic nerve head and high dose of radiation. Presence of diabetes mellitus contributes to developing radiation retinopathy [5]. Location of the melanoma of our patient was close to optic nerve head and foveola, therefore the complications such as optic neuropathy and retinopathy with poor visual outcomes occurred. Radiation retinopathy is presented with hard exudates, haemorrhages and macular oedema. The signs of ischaemia are also present. Obliterative arteritis, thickening of the vascular wall, loss of pericytes and endothelial vascular cells occurs. The ischaemic process is very likely caused by higher levels of VEGF. Bevacizumab is an anti-VEGF substance commonly used in ophthalmology to treat age related macular degeneration or different types of neovascularization of the retina. Positive effect of bevacizumab on macular oedema in postradiation retinopathy was published in a few cases. The patients required multiple injections for the effect sustainability and no systemic side effects occurred [8]. Anti-VEGF may improve radiation retinopathy and neuropathy caused by vascular leakage [4]. Visual acuity (VA) in choroidal melanoma patients is dependent on the tumour and treatment zone distance from visually important structures. Toutée et al. compared VA in two groups of patients after proton beam therapy of choroidal melanoma – group 1 – group where the distance of tumour was ≥ 3 mm and group 2 where the tumour was < 3 mm distant from optic disc and foveola. The follow-up had mean duration 122 months without tumor recurrence finding. GSup3 had mean baseline VA 20/25 and mean final VA 20/32. GInf3 had mean baseline VA 20/40 and at the end of follow up the mean VA was 20/80. The groups had significantly different visual outcomes. The risk factors for greater VA loss were age (more than 60), evidence of growth and contact of the tumour with optic nerve head [14]. Pale coloured or oedematous optic disc is a clinical sign on postradiation optic neuropathy. Postradiation maculopathy is presented with macular oedema, haemorrhages and ischaemia. Poor visual acuity is present in both radiation

caused complications. Other complications are dry eye disease or cataract, vasculopathy, retinal detachment, increased intraocular pressure or neovascular glaucoma [3]. Our patient took 4 intravitreal applications of bevacizumab and panretinal lasercoagulation was performed after the anti-VEGF treatment. Melanoma was localized on the optic nerve head and his margins reached close to foveola. His visual acuity was not spared because the radiation was absorbed in the optic nerve and foveola – structures essential for the sight. The treatment with anti-VEGF and lasercoagulation is a prevention of developing complications of radiation retinopathy such as neovascular glaucoma and traction retinal detachment.

Conclusion

Proton beam therapy is a good choice of treatment for medium and big choroidal melanomas with similar survival rates compared to enucleation. Eyes with melanomas located closer to foveola and optic nerve head treated by proton beam therapy have higher risk in developing postradiation complications such as postradiation neuropathy and retinopathy. Postradiation neuropathy is presented with oedematous or atrophic optic disc. Haemorrhages, ischaemia and macular oedema are typical for postradiation retinopathy. Both of these complications cause poor visual acuity.

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Disclosures

Received 01.08.2023

Accepted 31.08.2023

Authors' contributions: All authors contributed equally to this work

Conflict of interest. The authors declare that they have no conflict of interest with this article.

Ethical statement: The written informed consent was obtained from the patient.