CASE REPORT

Extrascleral Overgrowth of Malignant Choroidal Melanoma after Endoresection

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SUMMARY

Extrascleral Overgrowth of Malignant Choroidal Melanoma after Endoresection (CASE REPORT)

Objective: Course of progression of the malignant choroidal melanoma diagnosed in T2 stage up to stage T4 with infiltration of the orbit. Case report 41 year old patient identified with intraocular malignant melanoma in the year 2005, documentation of disease progression and disease.
Access to treatment of intraocular malignant melanoma in stage T1 - T2 in the last decade has changed from a radical approach (enucleation) towards conservative treatment (brachytherapy, radiosurgical methods) or combined procedures (pars plana vitrectomy and endoresection followed by irradiation or addition of laser treatment). Currently, more than 60% of uveal melanoma is treated by brachytherapy or radiosurgical techniques and combined procedures.
Case report: A 41 years old female patient with malignant melanoma in the choroid stage T2 since 2005. The volume of the tumor was 0.9 cm3, maximal elevation was over 12 mm. The patient refused a radical treatment (primary enucleation). Due to the stage of the melanoma she was recommended to stereotactic radiosurgery and combined therapy. She underwent stereotactic radiosurgery (TDmax – total dose of 35.0 Gy) in 2005. In 2006 pars plana vitrectomy with incomplete endoresection of the tumor and silicon oil instillation was done. In 2006–2007 appeared bleeding into the anterior chamber and she underwent three times an anterior chamber lavage in another department with subsequent development of secondary glaucoma. In January 2010 patient came to our department with the local finding of malignant melanoma in stage T4 with epibulbar growth process and the infiltration of the orbit. In the period have been found two solid liver metastases. Indicated exenteration of the orbit, histopathologically confirmed mixed cell type malignant melanoma.
Conclusion: Progression of malignant melanoma after incomplete endoresection despite previous radiosurgical treatment can be very rapid in the course of the disease documented by ultrasound, computed tomography and magnetic resonance. The patient subsequently passed to another workplace and underwent repeated lavage of the vitreous cavity. During endoresection is opened the package fibrous mesh gateway for the infiltration process in the cavity of the orbit and epibulbar space. In the case of residual melanoma after endoresection even though the tumor was irradiated before the procedure the melanoma might progress very fast into the surrounding tissues.

Key words: malignant melanoma of the choroid, endoresection, stereotactic radiosurgery, exenteration of the orbit

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INTRODUCTION

The clinical stage of development of malignant melanoma in the uveal tract of the eye, in which the patient sought professional medical assistance, connects to localisation of the development of the neoplasm in the uvea. The further the malignant melanoma is from the posterior pole, the smaller the probability that the patient will have subjective complaints. In this the matter, the clinical stage of development of malignant melanoma of the uvea in which the patient sought medical assistance is of fundamental significance for determination of the diagnosis not only in the selection of the treatment procedure, but in particular for determination of the prognosis. At present the applied diagnostic procedures enable determination of the correct diagnosis in almost 95% of cases (19, 21, 22).
A fundamental change in attitudes towards the use of ionizing radiation took place in the last quarter of the 20th century in the approach to treatment of uveal melanomas. In the literature we can identify various attitudes towards the issue of application of ionizing radiation before or after enucleation of the eye. Some authors emphasise that preoperative local irradiation (application of two doses of 400 rad) devitalises approximately 90% of malignant cells and is a significant preventive measure of the possibility of random iatrogenic dissemination of cells of malignant melanoma of the uvea (12).

Combined procedures are usually indicated in order to reinforce the effect or in an attempt to destroy the tumour inside the eye completely. Their target is an increase in the degree and local regression of the tumour, and at the same time a reduction of the possibility of local recurrence of uveal melanoma. In clinical practice the following combinations are frequently used: episclerally fixed irradiator + laser coagulation, transpupillary thermotherapy (by infrared diode laser); episclerally fixed irradiator + hyperthermia; microsurgery (iridocyclectomy, block-excision) plus episclerally fixed ß irradiator (at end of operation); combined partial lamellar sclerouvectomy with pars plana vitrectomy with tamponade by gas and silicon oil (1, 2, 3, 13, 23).

CASE REPORT

The patient, 41 years old at the time of determination of diagnosis (malignant melanoma of the choroidea in stage T2) in 2005.

The patient refused the proposed radical treatment (primary enucleation). With regard to the stage of the disorder, stereotactic radiosurgery and combined therapy is recommended (fig. 1a, b, c, 2, 3). In 2005 the patient underwent stereotactic radiosurgery (in a dose of TDmax – 35.0 Gy) in co-operation with the Stereotactic Radiosurgery Clinic at the St. Elizabeth Oncological Institute in Bratislava. In 2006, after an interval of more than 6 months, pars plana vitrectomy was performed with incomplete endoresection of the tumour and implantation of silicon oil. The patient was observed in a clinical workplace also according to her place of residence. In 2006-2007 repeated lavage of the vitreous cavity and anterior chamber was performed (three times) at another workplace, with subsequent development of secondary glaucoma (fig. 4). In January 2010 – two years later – a follow-up check at our workplace was performed, with a finding of malignant melanoma in stage T4 with epibulbar growth of the intraocular process and infiltration of the orbit. The local finding progressed over the course of a number of weeks (fig. 5, 6a, b, 7). Indication of exenteration of the orbit, upon request from the patient the area of the eyelashes was preserved (fig. 8, 9). Mixed cell type malignant melanoma confirmed by histological examination, grading and staging pT4 Nx Mx G2, stage III, ICD – 8770/3, examination on VIM: +++, S100: +++, HMB45 and MelanA: +++, Ki67: 1-2 % of nuclei. Postoperative healing without complications (fig. 10, 11). During this period two solid liver metastases were found. The overall condition of the patient was stabilised 6 months after exenteration, applied individual prosthetic eye to herself without difficulty (fig. 12).

DISCUSSION

The treatment of uveal melanoma in principle requires a causal approach. It involves the endeavour to completely remove the tumour as a whole and prevent the development of later consequences – development of metastases. In many cases even timely removal of the eye or complete destruction of the tumour (with a "clinically healed" uveal melanoma) does not provide a guarantee that metastases will not appear. On the basis of 10-year observation of large number of patients, some authors state that mortality is within the range of 40-60% (4, 5, 6, 11).

At the beginning of the 1960s, discovery of the development of primary uveal melanoma in the eye almost exclusively meant enucleation of the eye or even exenteration of the orbit. Current modern technical possibilities applied in the treatment of malignant melanoma of the uvea, certain dia-

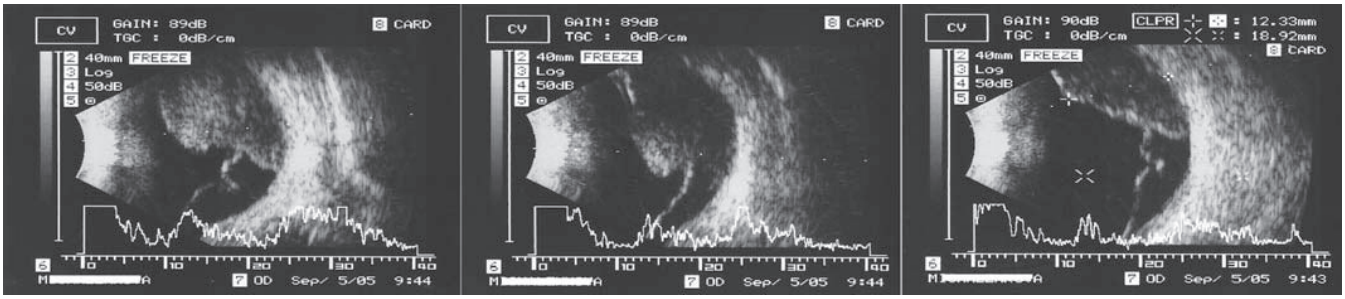

Fig. 1a, b, c Ultrasound examination – Bscan: deposit of malignant melanoma of the choroidea with maximum elevation more than 12 mm, secondary amotio – condition before stereotactic radiosurgery in 2005

Fig. 2 MRI examination 1 year after pars plana vitrectomy, endoresection of tumour and application of silicon oil (in 2006)

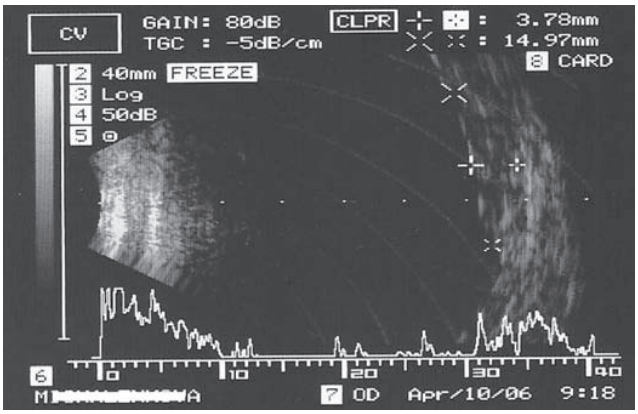

Fig. 3 Ultrasound recording – Bscan – image of residual deposit under silicon oil with thickness of up to 3.8 mm more than 1 year after endoresection (in 2006)

Fig. 4 Clinical picture of anterior segment of eye – venectasia, anterior chamber after repeated haemorrhage (in 2007)

Fig. 5 Clinical picture of recurrence of malignant melanoma in nasal section of orbit after 5 years

Fig. 6a, b Progression of growth of tumour deposit over the course of several weeks with prolapsed over eyelash opening

Fig. 7 Progression over the course of the following 2 weeks

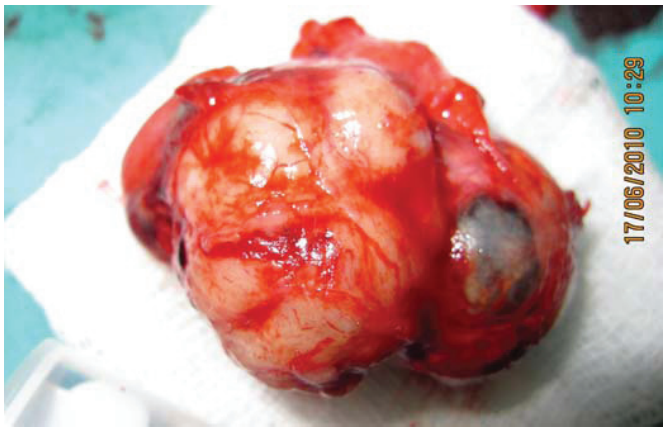

Fig. 8 Macro-photo of eyeball with overgrowing tumour material after exenteration of orbit

gnostic procedures and therapy by ionizing radiation from external sources require wide inter-disciplinary co-operation of experts from various branches of medicine. In the past increased mortality was expected after a deferral of enucleation, there was not a sufficient level of knowledge concerning the character of growth of fusocellular tumours (in which type A fusocellular tumours do not have a tendency to metastasise), there was insufficient knowledge concerning the effectiveness of conservative treatment, in particular by ionizing radiation and the degree of risk of radiation retinopathy (8, 22).

The prognosis is difficult to foresee in the case of malignant melanoma of the uvea, since the prognosis depends on a large number of various factors: size (base and height of tumour), localisation of tumour (iris, corpus ciliare, choroidea), presence of a rupture of the Bruch's membrane, vascularity of tumour, mitotic activity, pigmentation of tumour and histological type of tumour (fusocellular A, fusocellular B, epitheloid and mixed cell type). The following are considered to represent indicators with an unfavourable prognosis: epitheloid type malignant melanoma, high mitotic activity, presence of rupture of Bruch's membrane, high vascularity and low pigmentation of tumour (in connection

Fig. 9 Macro photo of dissected eyeball filled with malignant melanoma, which overgrew into the orbit

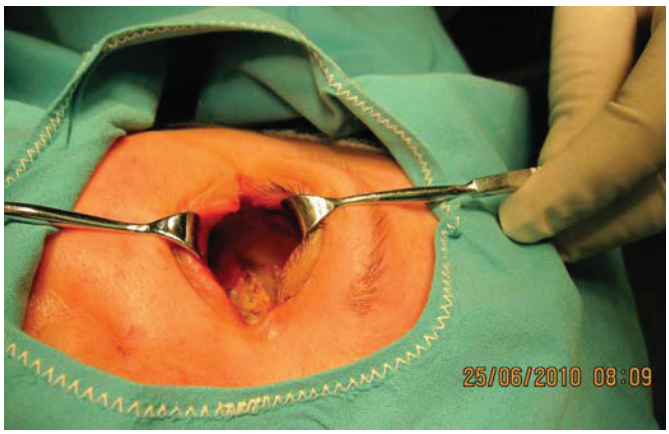

Fig. 10 Clinical picture after exenteration, healing of cavity without complications

Fig. 11 Clinical picture before fitting of individual prosthetic eye

Fig. 12 Clinical picture with applied individual prosthetic eye

with smaller cell differentiation). The clinical course of malignant melanoma of the uvea and the formation of remote metastases in the case of uveal melanoma is practically impossible to predict. Tokošová (2007) presents cases of patients with fusocellular type A malignant melanoma, who died as a result of remote metastases, and by contrast also patients with epitheloid type malignant melanoma who survived for several years without any symptoms of local recurrence or metastatic dispersion. The expression of gene p53 was observed in all enucleated eyes at a certain time interval. In the observed sample of patients, abnormal expression of gene p53 was immunohistochemically demonstrated in 6 out of 36 patients – 16.7% (25). In our conditions at our clinic we introduced this method in 2010 in co-operation with the Pathological Anatomy Institute at the Medical Faculty of Komenius University and University Hospital Bratislava.

In 2001 Garcia described endoresection without prior and subsequent irradiation in 25 patients and over the course of 12-72 months did not observe local recurrence of a tumour (16). However, it is generally recognised that endoresection is to be performed after prior irradiation, since it has been demonstrated that non-irradiated melanoma cells proliferate considerably more rapidly than irradiated cells. Mitotic activity of melanoma cells is substantially reduced after irradiation.

Prior irradiation by gamma-knife before resection and endoresection was introduced by Bornfeld in 2002 (3). He performed endoresection of uveal melanoma on 29 patients, in whom the volume of the tumour ranged from 0.2 to 1.4 cm3. In 17 patients irradiation of the tumour deposit was completed by a ruthenium irradiator. Later enucleation was required in only 5 patients.

The dose of radiation before endoresection is in different every ophthalmo-oncological centre, in our conditions in Slovakia we apply 35.0-38.0 Gy in one session by stereotactic radiosurgery (9, 14, 15). Upon irradiation by gamma-knife in one session it is possible also to apply a higher dose and fixation procedure – immobilisation of the eye is possible by another method (17, 18, 20). Upon fractionated treatment by stereotactic radiosurgery using an external optic fixation system in Vienna, the method of non-mechanical but optic fixation of the eye is applied, which enables fractionation and thus also an increase in the total dose of radiation (7). In our conditions it is not currently possible to perform fractionation for technical reasons, and we continue to perform stereotactic radiosurgical operations by fixation of the eye by means of a mechanical procedure (immobilisation via direct extraocular muscles) and subsequent fixation to a stereotactic ring (24).

In a retrospective study in 1990-2000, Cohen et al. (2003) analysed 198 patients with choroidal melanoma who were treated by stereotactic radiosurgery – 78 patients, or enucleation – 118 patients. In all patients with confirmed metastases within the observation interval from treatment, metastases of the liver were confirmed sonographically or by CT examination – 53 patients (27%). In 8 patients enucleation was required after treatment by stereotactic radiosurge-

ry. The duration of observation was from 1 month to 10 years, 7 patients left the observed sample in the group of enucleated patients, no patients left the group in which stereotaxy had been performed. This study was the first analysis of survival of patients following enucleation and following stereotactic radiosurgery. No significant influence on the interval without the presence of metastases after treatment was demonstrated depending on age, sex, presence of extrascleral spreading or secondary amotio. This study and others confirmed that the largest size of the tumour and localisation of the tumour are independent prognostic factors in the survival of patients (4, 10).

From our clinical experience it ensues that identification of initially diagnosed malignant melanoma of the choroidea in stage T4 with overgrowth into the orbit is very rare. Unfortunately, even despite the developing diagnostic procedure as well as the newly emerging socio-economic problems experienced by patients, when the first examination by an ophthalmologist still demonstrates the process of overgrowth into the orbit at the beginning of the 3rd millennium, is realistic (10). The clinical course of development of choroidal melanoma up to progression with overgrowth into the orbit, as presented in this case report, is very rare, though unfortunately not unrealistic. Neglect of regular examinations by the patient or refusal of a radical procedure by the patient may have the final result of the development of malignant melanoma of the choroidea to this stage.

CONCLUSION

The progression of malignant melanoma following incomplete endoresection, even despite prior radiosurgical treatment may be very rapid.

In the case of residual melanoma following endoresection, opening of the fibrous mesh of the eye is a gateway for the infiltration of the process into the orbital cavity and epibulbar space. Observation of the patient at the same workplace with indication of a radical procedure in the case of progression is very important, because substantial progression may occur in the case of an interval of more than one year.

LITERATURE

1. Barraquer, E.J.: Combined pars plana vitrectomy and partial sclerouvectomy for ciliar body and choroidal tumors. Ophthalmic Res, 1999; 31/S1: s. 116.
2. Bechrakis, N.E., Höcht, S., Martus, P., et al.: Endoresection following proton beam irradiation of large uveal melanomas. Ophthalmologe, 2004; 101(4): 370–376.
3. Bornfeld, N., Talies, S., Anastassiou, G., et al.: Endoresection maligner Melanome der Uvea nach praoperativer stereotaktischer Einzeldosis-Konvergenzbestrahlung mit dem Leksell--Gamma-knife. Ophthalmologe, 2002; 99: s. 338–344.
4. Cohen, V.M.L., Carter, M.J., Kemeny, A., et al.: Metastasis-free survival following treatment for uveal melanoma with either stereotactic radiosurgery or enucleation. Acta Ophthalmol Scand, 2003; 81: 383–388.
5. Damato, B., Lecuona, K.: Conservation of eyes with choroidal melanoma by a multimodality approach to treatment. An audit of 1632 patients. Ophthalmology, 2004; 111: s 977–983.
6. Damato, B.E.: Ocular Tumors: Diagnosis and Treatment. Elsevier, 1999: 256.
7. Dieckmann, K., Georg, D., Zehetmayer, M., et al.: LINAC based stereotactic radiotherapy of uveal melanoma: 4 years clinical experience. Radiother Oncol, 2003; 67: 199–206.
8. Edge, S.B., Byrd, D.R., Compton, C.C., et al.: AJCC Cancer Staging Handbook. New York, Springer, 2010: 730 p.
9. Furdová, A., Chorváth, M., Waczulíková, I., et al.: No differences in outcome between radical surgical treatment (enucleation) and stereotactic radiosurgery in patients with posterior uveal me lanoma. Neoplasma, 2010; 57 (4): 377–381.
10. Furdova, A., Chynoransky, M., Krajcova, P.: Orbital melanoma. Bratisl Lek Listy, 2011; 112 (8): s 466–468.
11. Furdová, A., Oláh, Z.: Prežívanie pacientov s malígnym melanómom uvey. Čs Oftalmol, 1995; 51 (5): 289–292.
12. Furdová, A., Oláh, Z.: Malígny melanóm v uveálnom trakte, Asklepios, Bratislava, 2002: 175 s.
13. Furdová, A., Oláh, Z.: Nádory oka a okolitých štruktúr, CERM, Brno, 2010: 151 s.
14. Furdova, A., Strmen, P., Sramka, M.: Complications in patients with uveal melanoma after stereotactic radiosurgery and brachytherapy. Bratislava Medical Journal – BLL, 2005; 106 (12): 401–406.
15. Furdova, A., Strmen, P., Waczulikova, I., et al.: One-day session LINAC-based stereotactic radiosurgery of posterior uveal melanoma. Eur J Ophthalmol, 2012; Mar, 22 (2): s 226–35.
16. Garcia-Arumi, J., Sararols, L., Martinez, V., et al.: Vitreoretinal surgery and endoresection in high posterior choroidal melanomas. Retina, 2001; 21: 445–452.
17. Modorati, G., Miserocchi, E., Galli, L., et al.: Gamma knife radiosurgery for uveal melanoma: 12 years of experience. Br J Ophthalmol, 2009; 93 (1): 40–44.
18. Mueller, A.J., Schaller, U., Talies, S., et al.: Stereotaktische Konvergenz--bestrahlung grosser uvealer Melanome mit dem Gamma-knife. Ophthalmologe, 2003; 100: s 122–128.
19. Oláh, Z., Furdová, A., Pecháň, J., a kol.: Významnosť diagnostických postupov pri malígnom melanóme uvey. Slovenský lekár, 1994; 4 (1–2): s 29–32.
20. Pochop, P., Pilbauer, J., Křepelková, J., a kol.: Dva roky zkušeností s léčbou Leksellovým gama nožem, Česká a slovenská oftalmologie, 54, 1998, 42 (4), s. 222-234.
21. Prečinský, P., Oláh, Z., Furdová, A.: B-scan sonografia malígneho melanómu chorioidey. Čes-Slov Radiol, 1993; 47 (2): s 107–112.
22. Shields, J.A., Shields, C.L.: Intraocular tumors: an atlas and textbook. Kluwer Health, Lippincott Williams & Wilkins, 2007: 574 p.
23. Strmeň, P., Furdová, A.: K liečbe malígnych melanómov chorioidey transpupilárnou termoterapiou diódovým laserom, Čes a Slov Oftalmol, 1999; 55 (3): 176–180.
24. Strmeň, P., Šramka, M., Schreinerová, P., a kol.: Stereotaktická rádiochirurgická a kombinovaná liečba malígnych melanómov uvey. Transacta Ophthalmologica Slovaca, 2004; 4 (1): 15–23.
25. Tokošová, E.: Malígny melanóm uvey. Doktorandská dizertačná práca v odbore oftalmológia, Masarykova Univerzita, Brno, 2007, 78 s.