

Malignant optic glioma – the spectrum of disease in a case series

Ghislaine L. Traber¹ · Athina Pangalu² · Manuela Neumann^{3,5} · Joao Costa⁶ · Michael Weller⁴ · Ruth Huna-Baron⁷ · Klara Landau¹

Received: 20 January 2015 / Revised: 24 April 2015 / Accepted: 29 April 2015 / Published online: 26 May 2015
© Springer-Verlag Berlin Heidelberg 2015

Abstract

Purpose Malignant optic glioma of adulthood is a rare, invasive neoplasm of the anterior visual pathway with 66 cases reported in the literature. It presents as anaplastic astrocytoma (WHO grade III) or glioblastoma (WHO grade IV). The present case series covers the spectrum of disease manifestations, discusses neuroradiological findings, and reviews the current literature.

Methods Retrospective case series of five patients from three tertiary referral centers and literature review.

Results Visual loss with or without pain was the presenting symptom in all patients (two women, three men). Two patients were initially misdiagnosed as optic neuritis, and one patient as atypical non-arteritic anterior ischemic optic neuropathy (NAION). A neoplastic disease was suspected in the two remaining patients. MRI features were iso- to hypointensity on

T1-weighted native images, contrast enhancement, and hyperintensity on T2-weighted images. Biopsy was generally diagnostic; however, one patient required two biopsies for diagnosis. The series includes an exceptional case of intraocular tumor extension and vitreous spread. The disease was lethal within one to two years in all patients.

Conclusions Malignant optic glioma is a diagnostic challenge and remains a devastating and lethal disease. Advances in the understanding of tumor biology have yet failed to translate into effective treatment regimens.

Keywords Malignant optic glioma · Glioblastoma · Anaplastic astrocytoma · MRI · Intraocular tumor extension

Introduction

Malignant optic glioma of adulthood is a rare entity first defined and reviewed by Hoyt et al. in 1973 [1]. The tumor arises in the optic nerve, chiasm, or tract, and may present as a multifocal neoplasm. It is a high-grade astrocytoma, as such either an anaplastic astrocytoma (WHO grade III) or a glioblastoma (WHO grade IV) [2]. In addition to mitotic activity defining high-grade astrocytomas, the presence of necrosis or vascular proliferation is required for grade IV diagnosis. Table 1 gives an overview of the current WHO classification of CNS astrocytic tumors. Patients with malignant optic glioma usually suffer bilateral visual loss within a few weeks and die within one to two years. Upon initial presentation patients are frequently misdiagnosed with optic neuritis, anterior ischemic optic neuropathy, or primary retinal vascular occlusion. Intraocular signs range from a normal fundus to disc edema, disc pallor, and retinal vascular occlusions. Intraocular growth of the tumor is rare. Biopsies need to be obtained to confirm diagnosis. Lateral orbitotomy is performed for tumors

✉ Ghislaine L. Traber
ghislaine.traber@usz.ch

¹ Department of Ophthalmology, University Hospital Zurich, Frauenklinikstrasse 24, CH-8091 Zurich, Switzerland

² Institute of Neuroradiology, University Hospital Zurich, Zurich, Switzerland

³ Institute of Neuropathology, University Hospital Zurich, Zurich, Switzerland

⁴ Department of Neurology, University Hospital Zurich, Zurich, Switzerland

⁵ Department of Neuropathology, University of Tübingen, Tübingen, Germany

⁶ Department of Ophthalmology, Egas Moniz Hospital, Lisbon, Portugal

⁷ Goldschleger Eye Institute, Sheba Medical Center, Sackler School of Medicine Tel Aviv University, Tel Aviv-Yafo, Israel

Table 1 Current WHO classification of CNS astrocytic tumors, modified from Louis et al. (2007) [2]

Astrocytic tumors	WHO grade I	WHO grade II	WHO grade III	WHO grade IV
Subependymal giant cell astrocytoma	•			
Pilocytic astrocytoma	•			
Pilomyxoid astrocytoma		•		
Diffuse astrocytoma		•		
Pleomorphic xanthoastrocytoma		•		
Anaplastic astrocytoma			•	
Glioblastoma				•
Giant cell glioblastoma				•
Gliosarcoma				•

affecting the orbital part of the optic nerve, whereas tumors with intracerebral extension are best accessed by pterional craniotomy [3].

The present case series covers the spectrum of disease manifestations including one exceptional case of intraocular tumor manifestation, and allows discussion of neuroradiologic findings.

Methods

Retrospective case series of five patients from three tertiary referral centers (1997 – 2011) and literature review. Three patients from the Zurich University Hospital, Switzerland, one patient from the Goldschleger Eye Institute Tel Aviv, Israel, and one patient from the Egas Moniz Hospital Lisbon, Portugal, are reported. All patients underwent biomicroscopy of the fundus and imaging of brain and orbits. In two patients, fluorescein angiography, and in one patient, more extensive work-up with an electroretinogram, genetic testing, and temporal artery biopsy was performed. Diagnosis was confirmed by biopsy in all patients. No ethical board approval was required from our institute when the data was collected (2012–2013).

Results

Three men and two women aged 54 to 76 years (mean 66.8 years) with malignant optic glioma were identified. Table 2 summarizes their disease manifestation and disease progression.

Patient 1 presented with left-sided visual loss to hand movement (HM) level for five weeks. On examination, the patient had a left relative afferent pupillary defect (RAPD), a blurred left disc margin, pain on retropulsion, and a junctional

scotoma. Fluorescein angiography showed unspecific late leakage of the left disc. These findings suggested a retrobulbar and prechiasmatic lesion. MRI showed involvement of the left optic nerve, optic chiasm, thalamus, mesencephalon, and pons with enhancement on T1-weighted images, and hyperintensity on FLAIR and T2 images (Fig. 1). There was progression to disc edema with stasis retinopathy seven weeks later, and to optic atrophy another three months later. The right fundus was normal. Histopathology was obtained from a biopsy via left pterional craniotomy and revealed glioblastoma. The patient received combined temozolomide chemoradiotherapy with irradiation of the involved field (30×2 Gy planned, 24×2 Gy given); however, the patient died during therapy four and a half months after diagnosis, probably due to tumorous infiltration of the brainstem.

Patient 2 presented with painful eye movements, scintillations, right-sided visual loss (20/30), right RAPD, and disc edema. The clinical picture and MRI scan with right optic nerve swelling, enhancement on T1-weighted images, and hyperintensity in T2-weighted images were interpreted as optic neuritis. The patient was placed on intravenous methylprednisolone and oral taper twice with resolution of pain, but had progressive visual loss to hand movements (HM) within two months due to a central scotoma in the right eye. The initial MRI scan had revealed a 2 cm lesion with abnormal signal intensity and a 2 mm enhancing spot in the right medial temporal gyrus of unknown etiology. Four months later, follow-up MRI showed progression of the latter. The subsequent cerebral biopsy allowed diagnosis of a multifocal glioblastoma. Despite combined temozolomide chemoradiotherapy with irradiation of the involved field (30×1.8 Gy), and bevacizumab salvage therapy, the patient experienced progressive tumor growth with bilateral involvement of the optic nerves, chiasm, tracts, as well as left thalamus and right temporal lobe. After seven months, vision in the left eye started to deteriorate, finally resulting in bilateral optic disc atrophy with no light perception (NLP) of the right eye and faint light perception (LP) of the left eye. The patient died within 18 months of disease onset.

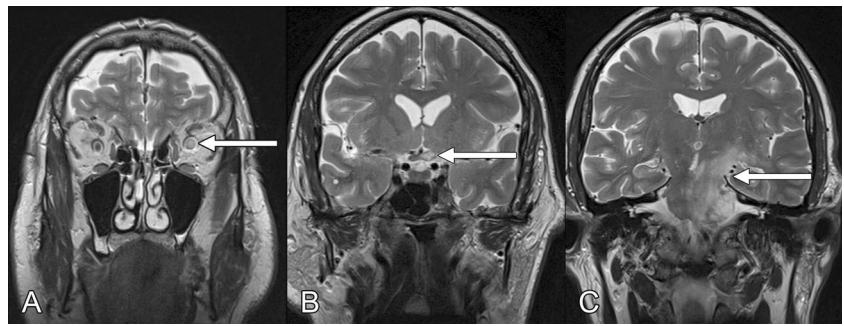
Patient 3 reported painless right-sided visual loss overnight. Initial visual acuity of right eye HM and left eye 20/30 further deteriorated to right eye NLP and left eye 20/400 with temporal hemianopia within six weeks. Fundoscopy showed a membranous structure of the right optic disc (Fig. 2a) with progressive vitreous spread over a four months period (Fig. 2b-c). MRI demonstrated a homogeneously enhancing chiasmatic tumor (Fig. 2d) with extension to both optic tracts and optic nerves (right intraorbital and left intracranial portion). The tumor was hyperintense on T2-weighted images, and isointense on native T1 images. Biopsy via right pterional craniotomy allowed the diagnosis of anaplastic astrocytoma. The tumor progressed despite involved-

Table 2 Summary of patient characteristics, disease manifestation, and disease progression

Patient	Sex/Age	Pain	Suspected Diagnosis	Fundus	Visual Fields	MRI	Time to Blindness	WHO grade	Therapy	Time to Death	Comments
1	M, 65	On retro-pulsion	Tumor	Disc edema OS → stasis retinopathy → disc atrophy Normal OD	VL OS with junctional scotoma OD	T1++contrast ↑ T2↑ / FLAIR↑	5 w (OS) OD unknown	IV, GBM	TMZ/RT→TMZ (24×2 Gy given, 30×2 Gy planned)	4,5 mt	Multifocal GBM
2	M, 54	Yes	Optic neuritis	Disc edema OD → disc atrophy OU	Central scotoma OD	T1+contrast ↑ T2↑	2 mt (OD) 7 mt (OS)	IV, GBM	TMZ/RT→TMZ (30×1.8 Gy), Bevacizumab at progression	18 mt	Multifocal GBM
3	F, 64	No	Tumor	Disc membrane OD → vitreous spread Initially normal OS	VL OD with temporal hemianopia OS	T1→ T1+contrast ↑ T2↑	<1 w (OD) 6 w (OS)	III, AA → IV, GBM	RT (34×1.8 Gy)	6 mt	Intraocular tumor growth; III, AA (biopsy)→IV, GBM (autopsy)
4	M, 75	No	Optic neuritis, CAR	Initially normal OU	OD unspecific OS arcuate scotoma	T1+contrast ↑ T2↑	6 w (OU)	IV, GBM	RT (28×1.8 Gy), patient decided against TMZ	12 mt	Only second biopsy diagnostic
5	F, 76	No	NAION	Disc edema → stasis retinopathy, exudates → CRAO & CRVO OD Initially normal OS	Not documented.	T1↓→ T1+contrast ↑ T2↑	5 w (OD) 4 mt (OS)	IV, GBM	RT (dose not known)	7 mt	Retinal vessel occlusion

Abbreviations: OD right eye, OS left eye, OU both eyes, VL visual loss, AA anaplastic astrocytoma WHO grade III, GBM glioblastoma WHO grade IV, w weeks, mt months, TMZ/RT→TMZ radiotherapy with concomitant and adjuvant temozolomide according to Stupp et al. (2005) [32], RT radiotherapy, TMZ temozolomide, NAION non-arteritic anterior ischemic optic neuropathy, CAR carcinoma associated retinopathy, CRAO central retinal artery occlusion, CRVO central retinal vein occlusion, ↓ hypointense, → isointense, ↑ hyperintense, +contrast ↑ contrast-enhancing

Fig. 1 Coronal T2-weighted images of patient 1 with multifocal glioblastoma show hyperintensity of the left optic nerve (a), left chiasm (b) and infiltration of thalamus, mesencephalon, and pons (c). Four months later the tumor diffusely infiltrated the whole chiasm



field radiotherapy (34×1.8 Gy). The patient became comatose and died from pneumonia six months after diagnosis. Autopsy finally revealed pleomorphic, astrocytic tumor cells, pseudopalisading necrosis, and microvascular proliferation (Fig. 2e-f), consistent with the diagnosis of glioblastoma.

Patient 4 presented with painless unilateral visual blur (right 20/50, left 20/25), impaired color vision, and RAPD in the right eye. Both fundi were normal. Automated perimetry revealed superior constriction on the right and an inferior arcuate defect on the left. MRI was read as suspected vague enhancement of the right optic nerve. Lumbar puncture and laboratory work-up for inflammatory or hematological diseases were normal. Intravenous methylprednisolone for five days and oral taper was initiated without effect. Vision deteriorated to NLP in both eyes within six weeks. At that point an electroretinogram was obtained in order to rule out carcinoma-associated retinopathy. Genetic testing for Leber hereditary optic neuropathy was negative, temporal artery biopsy ruled out arteritis, and fluorescein angiography was normal. A follow-up MRI three months after onset of symptoms showed bilateral optic nerve enhancement on T1-weighted images, and hyperintensity in T2-weighted images. Optic nerve biopsy via lateral orbitotomy was

unrevealing. MRI two months later showed progressive enlargement of the prechiasmatic optic nerves and chiasm suggestive for malignant optic glioma. Biopsy via pterional craniotomy confirmed glioblastoma. Combined temozolomide chemoradiotherapy was recommended. However, the patient decided against temozolomide. The tumor progressed despite involved-field irradiation (28×1.8 Gy), and the patient died one year after presentation.

Patient 5 noticed painless visual loss in the right eye for five weeks. Visual acuity was 20/100 with impaired color vision and RAPD in the right eye, and 20/30 with normal color vision in the left eye. Fundoscopy revealed optic disc swelling with hemorrhages and exudates in the right eye. An arteritic cause could be ruled out, and a diagnosis of atypical NAION was made. Four months later, the patient was referred with progressive deterioration to LP in the right eye and visual loss in the left eye to finger counting level. Fundoscopy revealed shunt vessels and a combined retinal artery and venous occlusion in the right eye, whereas the left fundus was normal. Visual fields were not tested because vision was too low. The MRI was suggestive for malignant optic glioma with bilateral thickening and enhancement of the prechiasmatic optic nerves, chiasm, and tract on T1-weighted images, T1

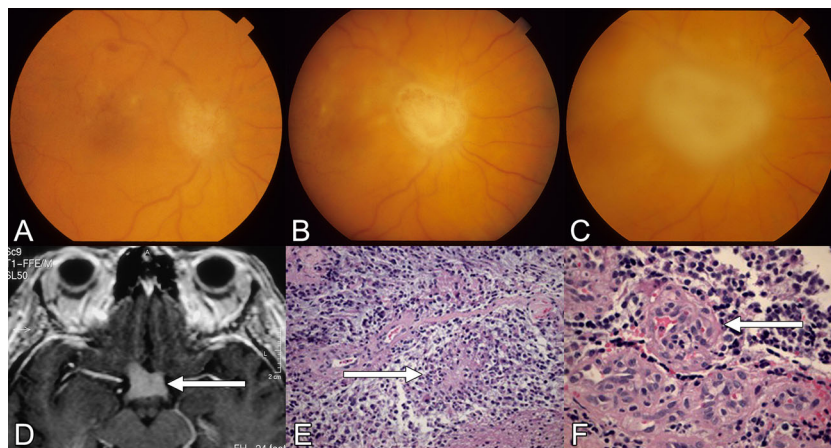


Fig. 2 (patient 3): A membranous structure of the right optic disc (a) progressed in size (b) and resulted in vitreous spread (c) over a four months period. The left optic nerve was unremarkable. The axial (d) MRI scan shows impressive thickening of the chiasm with homogeneous contrast enhancement on T1-weighted images. Autopsy

revealed diffuse infiltration of the optic nerve and chiasm with pleomorphic, astrocytic tumor cells, with pseudopalisading necrosis (e) and microvascular proliferation (f), the two features distinguishing glioblastoma from anaplastic astrocytoma

iso- to hypointensity on native images, and hyperintensity on T2-weighted images (Fig. 3a–c). The diagnosis of glioblastoma was confirmed by right optic nerve biopsy via pterional craniotomy. The patient underwent involved-field radiotherapy. However, the patient died within seven months of symptom onset. Precise information about radiotherapy dose could not be retrieved from the records.

Discussion

Malignant optic glioma of adulthood is a rare, invasive neoplasm of the anterior visual pathway with 66 cases reported. By 2004, Wabbels et al. [4] reviewed 45 cases. Including our five patients, 21 additional cases have been published since (Tables 2 and 3) [5–18]. Mean age of onset of all 66 cases is 57 years (standard deviation ± 15 ; range 22–83), with women and men almost equally affected (30 females and 36 males). It rarely occurs in paediatric populations, either as a primary high-grade glioma [19–22] or as malignant transformation of low-grade gliomas [20, 23–25].

Patients suffer from rapidly progressive visual acuity and visual field loss, usually leading to blindness. Depending on tumor localization and extension, visual field defects might be unspecific or show localizing patterns.

With onset of symptoms, all our patients experienced visual loss within one to two months in at least one eye. Patient 2 had a delayed involvement of the fellow eye after seven months. Patient 1 initially seemed to have a strictly unilateral infiltration of the chiasm (Fig. 1) with preserved visual function of the fellow eye. However, there was neuroradiologic evidence of diffuse chiasmatic infiltration and extension to both optic tracts within four months of disease onset, two weeks before the patient passed away. Interestingly, purely unilateral involvement of the anterior visual pathway has been reported in one patient described by Wabbels et al. [4] with a follow-up period of 12 months until death.

At an early stage, clinical findings might suggest anterior ischemic optic neuropathy (patient 5) or inflammatory neuropathy (patient 2 and 4) with minimal neuroradiologic

findings and transient responsiveness to steroids. However, progressive visual acuity and visual field deterioration, progressive dyschromatopsia, subsequent retinal vascular occlusions (patient 1), ocular ischemia as well as ocular pain, headaches, ophthalmoplegia, proptosis, and other neurological deficits depending on tumor localization and extension [4] point towards a possible malignant infiltrative disease, and a follow-up MRI should be obtained.

Neuroradiologic findings are unspecific, usually described as contrast enhancement and eventual thickening of the optic nerve, chiasm or tract in T1-weighted images [4, 26], with iso- to hypointensity on native T1 images [27, 28]. T2 hyperintensity of the affected anterior visual pathway is a matter of debate [27]. It was first described by Albers et al. [29] in one patient. Friedman et al. [28] presented a second case, and suggested T2 hyperintensity as a possible distinguishing feature of malignant optic glioma versus sarcoidosis with its tendency to hypointensity on T2-weighted images. However, T2 signal intensity is variable in sarcoidosis [30]. Most authors did not comment on neuroradiologic findings of T2-weighted images in malignant optic glioma. In two more recent cases [5, 15] T2 hyperintensity was described, whereas Wabbels et al. [4] explicitly did not find T2 hyperintensity of the optic nerve and chiasm. Our case series supports T2 or FLAIR hyperintensity as a characteristic, albeit unspecific finding of malignant optic glioma, since it was evident in all five patients. This is consistent with neuroradiologic findings in the better-characterized cerebral high-grade gliomas [31]. With regard to imaging features, differential diagnosis of a suspected malignant optic glioma still includes demyelinating, infectious, granulomatous, vasculitic, and infiltrative optic neuropathies [30]. CT imaging is not helpful in diagnosing malignant optic glioma.

So far, obtaining a biopsy is mandatory for diagnosis, and in case of an unspecific inflammatory histopathologic result, the biopsy might have to be repeated in a patient with a progressive, presumably neoplastic disease as in our patient 4 [13]. Interestingly, patient 3 had documented progression of a grade III glioma (biopsy) to a grade IV glioma (autopsy), which is unique in the current literature on adult malignant optic glioma. However, it might also simply reflect the tumor heterogeneity with sampling bias.

Fig. 3 (patient 5): The coronal MRI scans show bilateral thickening of the optic nerve with hyperintensity in T2-weighted images (a), iso- to hypointensity in native T1-weighted images (b) and bilateral enhancement (c) five months after onset of symptoms

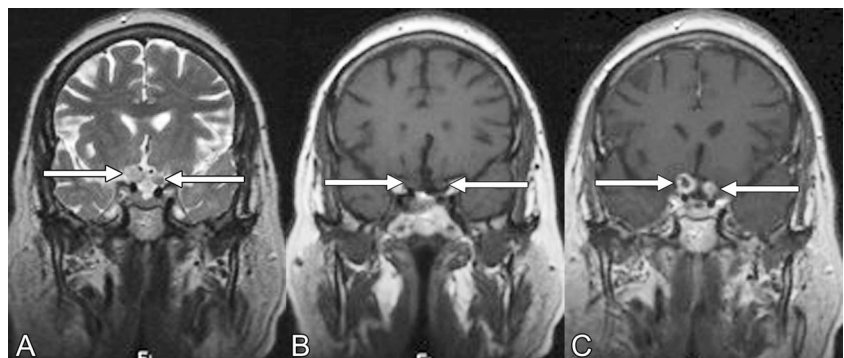


Table 3 Summary of 16 published cases since the review of 45 cases by Wabbel et al. (2004) [4]. A case of gemistocytic astrocytoma was included because it had a rather malignant course with survival of 12 months despite multimodality treatment (Simao et al. 2011)

Author and year	Sex/Age	Eye	Time to blindness	Presumed diagnosis	Histology AA/GBM	Therapy	Time to death
Hahn et al. 2004	M/53	OS	NK	neurosarcoidosis	GBM	chemo (nimustin, temiposid) and RT	NK
Danesh-Meyer et al. 2005	F/77	OU	2 mt OD NK OS	arteritic PION	NK (biopsy done)	chemo and RT (60 Gy)	11 mt
	M/60	OU	NK	inflammatory or infiltrative optic neuropathy	AA	RT (52+15+12.5 Gy)	20 mt
Hartel et al. 2006	F/77	OU	18mt OD NK OS	NAION	AA	RT (50.4 Gy)	30 mt
	M/59	OU	<1 mt OD NK OS	NK	GBM	–	8 w
Dinh et al. 2007	F/48	OU	NK	Optic nerve tumor	GBM	RT (54 Gy)	14 mt
Romano et al. 2007	F/69	OU	4 mt OU	NAION	AA	NK	NK
Abou-Zeid et al. 2008	M/56	OU	<1 mt OU	metastatic brain disease from renal primary	GBM	RT	3 mt
Chacko et al. 2010	M/48	OU	1 mt OD NK OS	optic neuritis	AA	chemo and RT	11 mt
Dumas-Stoeckel et al. 2010	M/73	OU	<1 mt OS 4 mt OD	NAION	AA	chemo/RT	~5-6 mt
Matloob et al. 2011	F/63	OU	<1 mt OD ~3-6 mt OS	optic neuritis	GBM	chemo (TMZ)	6 mt
Simao et al. 2011	M/62	OU	3 mt OD NK OS	optic nerve tumor	Diffuse astrocytoma (gemistocytic)	chemo and RT	12 mt
Lincoff et al. 2012	M/83	OS	<1 mt OS NK OD	large differential for combined CRAO/CRVO	GBM	NK	NK
Kang et al. 2012	F/60	OU	2 mt OU	inflammatory optic neuropathy	AA or GBM (small sample)	TMZ/RT (60 Gy)→TMZ	8 mt
Ashur-Fabian et al. 2013	M/64	OU	~6 mt OS NK OD	NK	GBM	TMZ/RT (60 Gy)→TMZ, propylthiouracil, carboplatin	54 mt
Colpak et al. 2014	M/47	OU	<1 mt OS NK OD	inflammatory or infiltrative optic neuropathy	GBM	–	3 mt

Abbreviations: NK not known, OD right eye, OS left eye, OU both eyes, AA anaplastic astrocytoma WHO grade III, GBM glioblastoma WHO grade IV, w weeks, mt months, chemo chemotherapy (chemotherapeutic agent indicated where available), RT radiotherapy (total dose indicated where available), chemo/RT combined chemoradiotherapy, TMZ temozolomide, PION posterior ischemic optic neuropathy, NAION non-arteritic anterior ischemic optic neuropathy, CRAO central retinal artery occlusion, CRVO central retinal vein occlusion

Considering the aggressively invasive behavior of malignant astrocytomas, intraocular tumor extension is surprisingly rare. While a mechanical barrier at the level of the lamina cribrosa seems plausible, a biological barrier influencing local tumor growth might be suspected as well. Intravitreal seeding of malignant optic glioma of adulthood has not been reported before and makes our case 3 unique. Dumas-Stoeckel et al. [12] presented one patient in the French literature with subretinal tumor extension and combined central retinal vein and artery occlusion. However, neither in this latter nor in our patient was intraocular growth confirmed histologically.

The standard of care for newly diagnosed high-grade astrocytomas consists of surgery or biopsy as feasible followed by radiotherapy alone (WHO grade III) or temozolomide chemoradiotherapy (WHO grade IV). The introduction of temozolomide increased the median survival of glioblastoma patients by 2–3 months and the likelihood of 2-year survival from 10 % to 26 % [32]. In contrast, the standard radiotherapy regimen of 54–60 Gy administered in 1.8–2 Gy fractions has remained essentially unaltered over the last decades. Risk structures such as optic nerves, chiasm, or brain stem commonly receive no more than 54 Gy. Recurrence or progression may be treated with re-resection, a second course of radiotherapy, or most commonly, using systemic alkylating agent chemotherapy or the VEGF antibody, bevacizumab [33]. The course of disease has not considerably improved over the last century [1], and malignant optic glioma remains lethal within one to two years [4]. The latter also holds true for our patients.

Advances in the understanding of tumor biology have yet failed to translate into effective treatment regimens [34]. However as research evolves, it is our hope that patients affected from a disease as devastating as malignant optic glioma will benefit from early diagnosis and treatment in the future.

All authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants, participation in speakers' bureaus, membership, employment, consultancies, stock ownership, or other equity interest, and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

- Hoyt WF, Meshel LG, Lessell S, Schatz NJ, Suckling RD (1973) Malignant optic glioma of adulthood. *Brain* 96:121–132
- Louis DN, Ohgaki H, Wiestler OD, Cavenee WK (2007) WHO Classification of tumours of the central nervous system. IARC, Lyon
- Winn HR (2011) *Youmans Neurological Surgery*, 6th edn. Elsevier Saunders, Philadelphia
- Wabbels B, Demmler A, Seitz J, Woenckhaus M, Bloss HG, Lorenz B (2004) Unilateral adult malignant optic nerve glioma. *Graefes Arch Clin Exp Ophthalmol* 242:741–748
- Hahn U, Ritz R, Ernemann U (2004) Glioblastoma multiforme des Nervus opticus. *Röfo* 176:1700–1701
- Danesh-Meyer HV, Savino PJ, Bilyk JR, Sergott RC (2005) Aggressive glioma of adulthood simulating ischemic optic neuropathy. *Arch Ophthalmol* 123:694–700
- Hartel PH, Rosen C, Larzo C, Nestor S (2006) Malignant optic nerve glioma (glioblastoma multiforme): A case report and literature review. *W V Med J* 102:29–31
- Dinh TT, Wang YY, Rosenfeld JV, Cherny M (2007) Glioblastoma of the optic chiasm. *J Clin Neurosci* 14:502–505
- Romano LM, Gaspari M, Guagnini M (2007) Astrocitoma óptico maligno bilateral del adulto. *Neurologia* 22:389–390
- Abou-Zeid A, Duplessis D, Gnanalingham KK (2008) Blindness from multiple cerebral gliomas mimicking metastatic brain disease. *Br J Neurosurg* 22:772–773
- Chacko JG, Lam BL, Adusumilli J, Dubovy SR (2010) Multicentric malignant glioma of adulthood masquerading as optic neuritis. *Br J Ophthalmol* 94(782–3):812
- Dumas-Stoeckel S, Gambrelle J, Cornut PL, El Chehab H, Vighetto A, Denis P (2010) Central retinal vein and artery occlusions related to intraocular involvement of an anaplastic optochiasmatic glioma. *J Fr Ophtalmol* 33:564–567
- Matloob S, Fan JC, Danesh-Meyer HV (2011) Multifocal malignant optic glioma of adulthood presenting as acute anterior optic neuropathy. *J Clin Neurosci* 18:974–977
- Simao LM, Dine Sultan EN, Hall JK, Reardon DA, Bhatti MT (2011) Knee deep in the nerve. *Surv Ophthalmol* 56:362–370
- Lincoff NS, Chung C, Balos L, Corbo JC, Sharma A (2012) Combing the globe for terrorism. *J Neuroophthalmol* 32:82–85
- Kang JJ, Hou JH, Bui KM, Michals E, Valyi-Nagy T, Koshy M, Munson T, Charbel FT, Villano JL, Moss HE (2012) malignant optic chiasm glioma with initial clinical response to steroids. *Neuroophthalmology* 36:59–63
- Ashur-Fabian O, Blumenthal DT, Bakon M, Nass D, Davis PJ, Herbergs A (2013) Long-term response in high-grade optic glioma treated with medically induced hypothyroidism and carboplatin: a case report and review of the literature. *Anticancer Drugs* 24:315–323
- Colpak AI, Isikay I, Mut M, Soylemezoglu F, Kansu T, Foroozan R (2014) Acute visual loss: Just the beginning? *Surv Ophthalmol* 59: 548–552
- Cirak B, Unal O, Arslan H, Cinal A (2000) Chiasmatic glioblastoma of childhood. A case report. *Acta Radiol* 41:375–376
- Wong JY, Uhl V, Wara WM, Sheline GE (1987) Optic gliomas. A reanalysis of the University of California, San Francisco experience. *Cancer* 60:1847–1855
- Safneck JR, Napier LB, Halliday WC (1992) Malignant astrocytoma of the optic nerve in a child. *Can J Neurol Sci* 19:498–503
- Brooks WH, Parker J, Young AB, Mortara RH (1976) Malignant gliomas of the optic chiasm in adolescents. *Clin Pediatr (Phila)* 15: 557–561
- Wilson WB, Feinsod M, Hoyt WF, Nielsen SL (1976) Malignant evolution of childhood chiasmatic pilocytic astrocytoma. *Neurology* 26:322–325
- de Keizer RJ, de Wolff-Rouendaal D, Bots GT, Thomeer RT, Brouwer OF, Vielvoje GJ (1989) Optic glioma with intraocular tumor and seeding in a child with neurofibromatosis. *Am J Ophthalmol* 108:717–725
- Zoeller GK, Brathwaite CD, Sandberg DI (2010) Malignant transformation of an optic pathway glioma without prior radiation therapy. *J Neurosurg Pediatr* 5:507–510
- Miller NR (2004) Primary tumours of the optic nerve and its sheath. *Eye (Lond)* 18:1026–1037

27. Chong VF (2006) The orbits in cancer imaging. *Cancer Imaging* 6: S27–S31
28. Friedman DP, Hollander MD (1998) Neuroradiology case of the day. Malignant optic glioma of adulthood. *Radiographics* 18: 1046–1048
29. Albers GW, Hoyt WF, Forno LS, Shratter LA (1988) Treatment response in malignant optic glioma of adulthood. *Neurology* 38: 1071–1074
30. Becker M, Masterson K, Delavelle J, Viallon M, Vargas MI, Becker CD (2010) Imaging of the optic nerve. *Eur J Radiol* 74:299–313
31. Clarke JL, Chang SM (2012) Neuroimaging: diagnosis and response assessment in glioblastoma. *Cancer J* 18:26–31
32. Stupp R, Mason WP, van den Bent MJ, Weller M, Fisher B, Taphoorn MJ, Belanger K, Brandes AA, Marosi C, Bogdahn U, Curschmann J, Janzer RC, Ludwin SK, Gorlia T, Allgeier A, Lacombe D, Cairncross JG, Eisenhauer E, Mirimanoff RO (2005) Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N Engl J Med* 352:987–996
33. Weller M, van den Bent M, Hopkins K, Tonn JC, Stupp R, Falini A, Cohen-Jonathan-Moyal E, Frappaz D, Henriksson R, Balana C, Chinot O, Ram Z, Reifenberger G, Soffiatti R, Wick W (2014) EANO guideline for the diagnosis and treatment of anaplastic gliomas and glioblastoma. *Lancet Oncol* 15:e395–e403
34. Weller M, Stupp R, Hegi M, Wick W (2012) Individualized targeted therapy for glioblastoma: fact or fiction? *Cancer J* 18:40–44