Transtentorial dissemination of optic nerve glioblastoma: case report

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Optic nerve glioblastoma is a rare entity that usually presents with rapidly progressive vision loss, which eventually results in blindness and, ultimately, death. As with malignant gliomas in other anatomical locations, local recurrence is common. Isolated rapid changes in vision, atypical neuroimaging findings, and the rarity of optic nerve glioblastoma may render diagnosis challenging and, thus, delay treatment. The authors present a case of optic nerve glioblastoma that was treated with subtotal resection followed by adjuvant radiation therapy and temozolomide. One year following the initial diagnosis, the patient developed a right cerebellar lesion, which was histopathologically consistent with glioblastoma. This case represents the first report of transtentorial dissemination of an optic nerve glioblastoma. In addition, the authors reviewed the literature regarding optic nerve glioblastomas. Of the 73 previously reported cases of malignant optic nerve gliomas, 32 were histologically confirmed glioblastomas. The mean age at diagnosis was 62 years, and 56% were male; the median survival was 7 months. A malignant glioma of the optic nerve should be considered in the differential diagnosis of a patient with rapidly progressive visual loss. However, the incidence of optic nerve glioblastoma is exceedingly low.

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MALIGNANT gliomas are the most common and aggressive primary brain tumors. They are most often located in the supratentorial compartment.²⁹ Malignant optic nerve glioma (MONG) constitutes a rare entity that typically arises in the optic nerve or chiasm but may also present as a part of a multifocal disease process.³⁷ Patients with MONGs most commonly present with rapidly progressive vision loss, which eventually results in blindness. Similar to malignant gliomas in other locations, these lesions confer a dismal prognosis, with an associated overall survival of less than 2 years.^{35,37} These tumors are frequently misdiagnosed as inflammatory or nongliomatous neoplastic processes on initial presentation; thus, a biopsy is often required to confirm the diagnosis.^{24,28}

While malignant gliomas are considered a diffusely disseminated disease, tumor recurrence most frequently occurs locally, with reported rates ranging from 70% to 100%.^{8,20} As reported by Sherriff et al., the majority of supratentorial glioblastomas with recurrence were observed in the ipsilateral hemisphere, and only 4% of the total re-

currences were found in the contralateral hemisphere.³³ Transtentorial dissemination of malignant glioma is extremely rare, with only 2 case reports in the literature.^{16,36} To our knowledge, we present the first case of transtentorial spread of an optic nerve glioblastoma to the cerebellum.

Case Report

History and Examination

A 66-year-old man presented to the ophthalmology clinic with progressively worsening right monocular nasal hemifield visual deficit and reduced visual acuity in his right eye persisting for approximately 1 year, with subsequent development of visual deficits in his left eye. On ophthalmological examination, the patient's visual acuity was 3/200 and 2/30 in his right and left eyes, respectively, with absent color vision in the right eye and a right afferent pupillary defect. He had a dense nasal defect in the right eye, as well as a relative temporal defect in the left eye, as confirmed by single-field analysis (Fig. 1A).

ABBREVIATIONS MONG = malignant optic nerve glioma.

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FIG. 1. **A:** Single-field analysis at presentation. OD = right eye; OS = left eye. **B:** Preoperative postcontrast T1-weighted MR images (axial, coronal, and sagittal) demonstrating a peripherally enhancing lesion centered on the right side of the optic chiasm, extending into both the pre- and postchiasmatic right optic nerves. The mass abuts the right side of the pituitary infundibulum, the underside of the A₁ segment of the right anterior cerebral artery, and the right carotid terminus. No other intracranial enhancing masses are present. **C:** Postoperative postcontrast T1-weighted MR images (axial, coronal, and sagittal) obtained 10 months following resection, remaining stable and demonstrating small residual contrast enhancement at the base of the right optic nerve that was not changed from prior examination.

MRI revealed a peripherally enhancing lesion centered on the right side of the optic chiasm, extending into both the prechiasmatic right optic nerve and postchiasmatic right optic tract. The mass was adjacent to the right side of the infundibulum, the underside of the A₁ segment of the anterior cerebral artery, and the right internal carotid artery terminus. The lesion was initially thought to be a meningioma, and no other intracranial enhancing lesions were present (Fig. 1B).

First Operation and Postoperative Course

The patient underwent a right pterional craniotomy for biopsy sampling and debulking of the optic chiasm lesion under the guidance of frameless stereotactic neuronavigation and intraoperative MRI. Postoperative MRI demonstrated a small amount of residual contrast enhancement at the base of the right optic nerve, which remained stable on repeat imaging at up to 12 months of follow-up (Fig. 1C). The optic nerve lesion was determined to be a glioblas-

toma based on histopathological analysis. Postoperatively, the patient was treated with a course of fractionated radiation therapy (60 Gy) with concomitant temozolomide. On ophthalmological follow-up, the patient developed gradual worsening of his left homonymous hemianopia and worsening of mean sensitivity in his left eye but slightly improved right-eye acuity. Of note, preoperative images demonstrated no evidence of contrast enhancement or hyperintensity to indicate dissemination of glioblastoma to the cerebellum. However, follow-up imaging performed at 12 months demonstrated small foci of hyperintensity on T2-weighted imaging, suggestive of possible initiation of tumor infiltration to the cerebellum (Fig. 2).

Second Operation and Postoperative Course

Approximately 14 months after the initial diagnosis and following completion of 10 cycles of temozolomide, routine follow-up imaging showed a new homogeneously enhancing mass, measuring 2.7 × 2.4 × 2.2 cm, with sur-

FIG. 2. FLAIR (left), T2 weighted (center), and T1-weighted postcontrast (right) preoperative images (A) and postoperative images obtained 12 months after MONG resection (B). The preoperative images demonstrate no evidence of contrast enhancement or hyperintensity to indicate dissemination of glioblastoma to the cerebellum at this time point. Follow-up images obtained at 12 months demonstrated small foci of hyperintensity on the T2-weighted image, suggestive of possible initiation of tumor infiltration to the cerebellum.

rounding satellite enhancing lesions in the right inferior cerebellar hemisphere, extending into the right cerebellar tonsil (Fig. 3A and B). There was no evidence of a direct connection between the previously resected MONG and the newly diagnosed lesion (Fig. 3C). The patient underwent a suboccipital craniectomy for resection of the right cerebellar lesion, and intraoperative MRI did not demonstrate any abnormal residual contrast enhancement (Fig. 3D and E). The histopathological results of the cerebellar lesion were consistent with a glioblastoma. Follow-up imaging at 1 month demonstrated local recurrence (Fig. 3F). The patient was then treated with another course of fractionated radiation therapy (25 Gy) with concomitant temozolomide. The cerebellar tumor progressed, and the patient died 2 months after the second surgery and a total of 16 months from initial diagnosis.

Histopathological Examination

Histopathological analysis of the right optic nerve tumor demonstrated findings consistent with glioblastoma (WHO Grade IV) (Fig. 4). Immunostaining for mutant *IDH-1* (R132H) was diffusely negative, and p53 immunostain was weakly positive. A pyrosequencing assay demonstrated MGMT promoter hypermethylation. The histopathology of the right cerebellar lesion was also consistent with a glioblastoma (Fig. 5). Similar to the optic lesion, there was no evidence of *IDH-1* (R132H) mutation on immunohistochemical analysis, and p53 immunostaining showed minimal positivity.

Discussion

MONG was first described by Hoyt et al. in 1973.¹⁷ Since then, there have been 73 reported cases of MONGs

in the literature.^{35,37} Among these, 32 were confirmed to be glioblastomas, with a mean patient age of 62 years at the time of diagnosis.^{2,4,7,10–13,25,27,28,30,34,35,37,39} Fourteen of the patients were female (44%) and 18 were male (56%). The median overall survival of the reported cases of optic nerve glioblastoma was 7 months (Table 1).

As seen in our case, patients with optic nerve glioblastomas usually present with a progressive decline in visual acuity and visual field deficits, eventually resulting in blindness. While the majority of patients initially present with monocular symptoms, nearly all patients eventually develop bilateral visual deficits due to infiltration of the optic chiasm and contralateral optic nerve.^{26,37} Additionally, symptoms, such as headaches, behavioral changes, and motor deficits, have been reported.^{5,14,23}

Optic nerve glioblastomas most commonly present as primary lesions involving the anterior portion of the optic tract and optic chiasm. Among the reported optic nerve glioblastoma cases, 5 presented with extensive involvement of contiguous structures (16%),^{14,15,23,35} and 5 were a part of multifocal glioblastoma.^{1,24,35}

The diagnosis of optic nerve glioblastoma can be challenging,²⁸ since initial neuroimaging may demonstrate an edematous, thickened optic nerve,^{9,19,21} anterior optic tract contrast enhancement,^{4,28} an enhancing space-occupying cystic⁵ or solid lesion,^{3,7} or multifocal enhancing lesions with optic nerve involvement.^{1,24} Considering that optic nerve glioblastoma is a rare entity, the differential diagnosis in patients suspected of harboring these lesions should remain broad. However, one must keep in mind that the variety of neoplastic, infectious, and inflammatory conditions, such as optic neuritis,³⁵ nonarteritic⁴ or arteritic²⁴ anterior ischemic optic neuropathy, central retinal artery or

FIG. 3. Postcontrast T1-weighted (A) and T2 FLAIR (B) images demonstrating a new homogeneously enhancing mass with surrounding satellite enhancing lesions in the inferior right cerebellar hemisphere extending into the right cerebellar tonsils. The lesion demonstrates a small amount of surrounding edema, which results in mass effect on the fourth ventricle and adjacent brainstem. **C:** Sagittal postcontrast T1-weighted (*left*) and T2-weighted (*center*) images in the plane of the most medial aspect of the cerebellar lesion, as well as a sagittal T2-weighted midline image (*right*), demonstrating no direct connection between the previously resected MONG and the newly diagnosed lesion. **D and E:** Intraoperative MR images obtained immediately after resection of a right cerebellar mass. Postcontrast T1-weighted (D) and T2-weighted FLAIR (E) images demonstrating no abnormal residual contrast enhancement but heterogeneously increased T2 signal intermixed with T2 hypointensity in the right cerebellar surgical bed and in the right middle cerebellar peduncle, indeterminate for residual tumor. **F:** Follow-up MR image obtained 1 month postoperatively, demonstrating enhancing multilobulated mass lesion along the anterior and medial margin of the surgical cavity representing progressive glioblastoma, causing mass effect on the medulla oblongata and fourth ventricle.

vein occlusion,²¹ or neurosarcoidosis,¹⁵ which are included in the differential diagnosis at the time of presentation, may initially lead to the misdiagnosis of this rare condition. Moreover, the differential diagnosis of neoplastic lesions of the optic nerve may include low-grade glioma,¹⁰

meningioma, lymphoma, craniopharyngioma, pituitary adenoma,⁵ and metastasis.¹ Abou-Zeid et al. presented a case of MONG that was initially thought, based on neuroimaging, to represent a metastasis in a patient with an asymptomatic renal mass.¹ To further illustrate the

FIG. 4. Histopathological examination of an optic nerve glioblastoma. **A:** The tumor shows sheets of fibrillary, pleomorphic cells that infiltrate diffusely. **B:** Microvascular proliferation (arrow) and necrosis (arrowheads) are present. **C:** GFAP immunostain is diffusely positive, consistent with glial differentiation. **D:** Immunostain for mutated *IDH-1* (R132H) is negative. **E:** A Ki-67 stain confirms a markedly elevated proliferative index. **F:** Staining for p53 shows positivity in a small percentage of tumor cells. H & E (A and B). Original magnification $\times 10$ (A), $\times 40$ (B and C), $\times 20$ (D–F). Figure is available in color online only.

challenges in the diagnosis of optic nerve glioblastoma, Balachandran et al. reported a case that was initially diagnosed as nonarteritic anterior ischemic optic neuropathy.⁴ The initial histopathological examination of the optic nerve biopsy demonstrated necrosis and scattered neutrophilic infiltration, without evidence of malignancy. However, subsequent MRI showed optic nerve thickening, and repeat biopsy findings were consistent with glioblastoma.

Local recurrences are common in glioblastomas;³⁸ up to 90% of all recurrences occur within 2–3 cm from the primary lesion,¹⁸ while remote recurrences involving the contralateral hemisphere occur in only 4% of cases.^{32,33} Transtentorial spread of malignant gliomas is exceedingly

rare, with only 2 previous reports: one of a left frontal glioblastoma³⁶ and another of a right temporal anaplastic astrocytoma (WHO Grade III).¹⁶ Similar to supratentorial glioblastomas, MONGs also tend to recur locally, with 1 report of supratentorial dissemination of MONG to the ipsilateral thalamus, temporal lobe, and midbrain 7 months after diagnosis.¹⁹ In this report, we present the first case of transtentorial spread of an optic nerve glioblastoma to the cerebellum. Although gliomas arising within the cerebellum account for 0.4%–3.4% of all gliomas and the majority of them are glioblastomas,⁸ the similar histopathology and molecular profiling of the cerebellar lesion and the primary optic tumor, as well as the time course of devel-

FIG. 5. Histopathological examination of cerebellar glioblastoma. **A:** The densely cellular glial neoplasm shows areas of necrosis. **B:** Frequent mitotic figures are present (circled). **C:** GFAP is diffusely positive. **D:** Staining for mutant *IDH-1* (R132H) is negative. **E:** Ki-67 shows brisk proliferative activity. **F:** The majority of tumor cells are negative for p53. H & E (A and B). Original magnification $\times 10$ (A and C–E), $\times 40$ (B), $\times 20$ (F). Figure is available in color online only.

TABLE 1. Review of previously reported optic nerve glioblastoma cases

Authors & Year	Age (yrs), Sex	Areas of Involvement	Initial Diagnosis	Initial Presentation	Survival
Traber et al., 2015	65, M	Lt optic nerve, optic chiasm, thalamus, mesencephalon, pons	Neoplastic process	Lt-sided VL to hand movement level	4.5 mos
	54, M	Bilat optic nerve, optic chiasm, lt thalamus, rt temporal lobe	Optic neuritis	Painful EOM, scintillations, rt-sided VL, rt RAPD, papilledema	18 mos
	64, F	Bilat optic nerve	Neoplastic process	Rt-sided VL, visual acuity OD to hand movement & OS 20/30	6 mos
	75, M	Bilat optic nerve, optic chiasm	Optic neuritis, carcinoma-associated retinopathy	Painless rt blurred vision, impaired color vision, RAPD	12 mos
	76, F	Bilat optic nerve, optic chiasm, optic tract	Nonarteritic anterior ischemic optic neuropathy	OD VL	7 mos
Colpak et al., 2014	47, M	Lt optic nerve	Optic neuritis, inflammatory optic neuropathy	Sudden OS VL, limited lt upgaze	11 wks
Pecen & Bhatti, 2014	61, F	Rt optic nerve, optic chiasm	Optic neuritis	Painless rt blurred vision	10 mos
Caignard et al., 2014	74, M	Lt optic nerve, optic chiasm	Optic neuritis	Progressive lt-sided VL	15 mos
	74, F	Optic chiasm, optic tract, geniculate nuclei	Optic neuritis	Bilat VL & VF defects	11 mos
Ashur-Fabian et al., 2013	64, M	Rt optic nerve, optic chiasm, hypothalamus	Optic neuritis	Progressive rt-sided VL	4.5 yrs
Kang et al., 2012	60, F	Bilat optic nerve, optic chiasm, optic tract, repeat imaging: extension to rt thalamus, rt temporal lobe, & midbrain	Optic neuritis	Painless progressive VL	8 mos
Lincoff et al., 2012	83, M	Lt optic nerve, optic chiasm, lt optic tract	Central retinal artery occlusion, central retinal vein occlusion	Progressive painful lt-sided VL	NK
Matloob et al., 2011	63, F	Rt optic nerve, optic chiasm, multiple periventricular foci, rt lentiform & rt thalamic nucleus, rt cerebral peduncle, rt temporal & parietal lobes	Acute anterior optic neuropathy	Progressive rt-sided VL, lt-sided blurry vision, HA	6 mos
Balachandran et al., 2009	60, M	Lt optic nerve, proximal rt optic nerve, optic chiasm	Nonarteritic anterior ischemic optic neuropathy	Difficulty concentrating, lt-sided frontal HA, OS frosty vision	4 mos
Abou-Zeid et al., 2008	56, M	Bilat optic nerve, optic chiasm, rt parietal lesion	Metastatic renal cell carcinoma	Bilat complete VL, HA	3 mos
Dinh et al., 2007	48, F	Optic chiasm	Ring enhancing lesion	Lt central scotoma	14 mos
Hartel et al., 2006	59, M	Rt optic nerve, optic chiasm, rt optic tract, hypothalamus	Ring enhancing lesion	Rt-sided blurred vision, fatigue	8 wks
Hahn et al., 2004	53, M	Lt optic nerve, optic chiasm, lt optic tract	Neurosarcoidosis	OS visual deficit	NK
Cummings et al., 2000	65, F	Optic nerve (unspecified)		NK	NK
Pallini et al., 1996	59, F	Bilat optic nerve		Bitemporal hemianopia, diabetes insipidus, behavioral changes	7 mos
Woiciechowsky et al., 1995	76, M	Lt optic nerve, optic chiasm, lt optic tract, lt temporal lobe		Progressive lt-sided VL	6 wks
Albers et al., 1988	51, M	Bilat optic nerve, optic chiasm, rt optic tract		Lt temporal field scotoma, lethargy, hypothermia	20 mos
Evens et al., 1987	61, F	Bilat optic nerve, optic chiasm		OD central scotoma, OS loss of superior field	9 mos
Barbaro et al., 1982	26, M	Bilat optic nerve, optic chiasm	Adenoma, craniopharyngioma	Progressive bilat VL, HA	8 mos

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TABLE 1. Review of previously reported optic nerve glioblastoma cases

Authors & Year	Age (yrs), Sex	Areas of Involvement	Initial Diagnosis	Initial Presentation	Survival
Spoor et al., 1980	60, F	Lt optic nerve		Rapidly deteriorating vision, bifrontal HA	4 mos
Harper & Stewart-Wynne, 1978	75, M	Bilat optic nerve, optic chiasm, bilat optic tract, rt temporal lobe		OS paracentral scotoma, homonymous hemianopia, OS piosis, absent convergence & vertical gaze, lt central cranial nerve VII palsy, lt-sided hemiparesis	3 mos
	79, F	Bilat optic nerve, optic chiasm, bilat optic tract, rt temporal lobe, anterior hypothalamus		Lt hemiparesis, hyponatremia	3 mos
Manor et al., 1976	70, M	Bilat optic nerve, optic chiasm, optic tract, lt thalamus, medial geniculate body	Diagnosed postmortem	Progressive rt-sided VL, led to complete visual loss, frontal HA	4 mos
Hoyt et al., 1973	55, M	Bilat optic nerve, optic chiasm		Rapid OS VL, dyschromatopia, OS RAPD, OS temporal paracentral scotoma, OS papilledema	9 mos
Mattson & Peterson, 1966	59, F	Proximal lt optic nerve, optic chiasm, & bilat optic tract		Painful progressive lt-sided VL	10 wks
Saebø et al., 1949	43, F	Lt optic nerve		Progressive lt-sided VL, OS exophthalmos	12 mos

EOM = extraocular movement; HA = headache; NK = not known; OD = right eye; OS = left eye; RAPD = relative afferent pupillary defect; VF = visual field; VL = visual loss.

opment suggest transtentorial disease dissemination rather than de novo formation of a cerebellar glioblastoma.

Our patient died 4 months after diagnosis of the recurrent cerebellar lesion, which demonstrated aggressive behavior and rapid progression despite gross-total resection. Patients with glioblastoma recurrence after the initial surgery and chemoradiation therapy are offered a second resection in as many as 58% of cases,³¹ with a national reoperation average of 14%,²² but the benefit to survival remains controversial.⁶

Conclusions

We present, to the best of our knowledge, the first case in the literature of transtentorial dissemination of an optic nerve glioblastoma to the cerebellum. Although an optic nerve glioblastoma represents a rare entity and a diagnostic challenge, it should be considered in the differential diagnosis of a patient presenting with rapidly progressive visual loss. Although the overall survival of optic nerve glioblastoma patients may be shorter than that of lobar glioblastoma patients, the management strategies are not substantially different. Specifically, ipsilateral visual preservation should not compromise the extent of resection, and every effort should be made to reduce the risk of disease progression along the unaffected optic pathways to prevent total blindness.

References

1. Abou-Zeid A, Duplessis D, Gnanalingham KK: Blindness from multiple cerebral gliomas mimicking metastatic brain disease. **Br J Neurosurg** 22:772–773, 2008
2. Albers GW, Hoyt WF, Forno LS, Shratter LA: Treatment response in malignant optic glioma of adulthood. **Neurology** 38:1071–1074, 1988
3. Ashur-Fabian O, Blumenthal DT, Bakon M, Nass D, Davis PJ, Hercbergs A: 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, 2013
4. Balachandran C, Millar MJ, Murali R, Bulliard C, Malcolm CM, Maloof A: Malignant optic glioma presenting as an acute anterior optic neuropathy. **Retin Cases Brief Rep** 3:156–160, 2009
5. Barbaro NM, Rosenblum ML, Maitland CG, Hoyt WF, Davis RL: Malignant optic glioma presenting radiologically as a “cystic” suprasellar mass: case report and review of the literature. **Neurosurgery** 11:787–789, 1982
6. Barker FG II, Chang SM, Gutin PH, Malec MK, McDermott MW, Prados MD, et al: Survival and functional status after resection of recurrent glioblastoma multiforme. **Neurosurgery** 42:709–723, 1998
7. Caignard A, Faguer R, Mercier P, Menei P, Milea D: Optic nerve and visual pathways primary glioblastoma treated with radiotherapy and temozolomide chemotherapy. **Eur J Ophthalmol** 24:637–640, 2014
8. Chamberlain MC: Radiographic patterns of relapse in glioblastoma. **J Neurooncol** 101:319–323, 2011
9. Colpak AI, Isikay I, Mut M, Soylemezoglu F, Kansu T, Foroozan R: Acute visual loss: just the beginning? **Surv Ophthalmol** 59:548–552, 2014
10. Cummings TJ, Provenzale JM, Hunter SB, Friedman AH, Klintworth GK, Bigner SH, et al: Gliomas of the optic nerve: histological, immunohistochemical (MIB-1 and p53), and MRI analysis. **Acta Neuropathol** 99:563–570, 2000

11. Dinh TT, Wang YY, Rosenfeld JV, Cherny M: Glioblastoma of the optic chiasm. **J Clin Neurosci** 14:502–505, 2007
12. Evens PA, Brihaye M, Buisseret T, Storme G, Solheid C, Brihaye J: [Malignant glioma of the chiasma in adults.] **Bull Soc Belge Ophthalmol** 224:59–60, 1987 (Fr)
13. Hahn U, Ritz R, Ernemann U: [Glioblastoma multiforme of the optic nerve.] **RoFo** 176:1700–1701, 2004 (Ger)
14. Harper CG, Stewart-Wynne EG: Malignant optic gliomas in adults. **Arch Neurol** 35:731–735, 1978
15. Hartel PH, Rosen C, Larzo C, Nestor S: Malignant optic nerve glioma (glioblastoma multiforme): a case report and literature review. **W V Med J** 102:29–31, 2006
16. Hong CS, Hsieh JK, Edwards NA, Ray-Chaudhury A, Zaghoul KA: IDH mutations may not preclude distant, transtentorial spread in gliomas: a case report and review of the literature. **World J Surg Oncol** 14:53, 2016
17. Hoyt WF, Meshel LG, Lessell S, Schatz NJ, Suckling RD: Malignant optic glioma of adulthood. **Brain** 96:121–132, 1973
18. Jansen EP, Dewit LG, van Herk M, Bartelink H: Target volumes in radiotherapy for high-grade malignant glioma of the brain. **Radiother Oncol** 56:151–156, 2000
19. Kang JJ, Hou JH, Bui KM, Michals E, Valyi-Nagy T, Koshy M, et al: De novo malignant optic chiasm glioma with initial clinical response to steroids. **Neuroophthalmology** 36:59–63, 2012
20. Liang BC, Thornton AF Jr, Sandler HM, Greenberg HS: Malignant astrocytomas: focal tumor recurrence after focal external beam radiation therapy. **J Neurosurg** 75:559–563, 1991
21. Lincoff NS, Chung C, Balos L, Corbo JC, Sharma A: Combining the globe for terrorism. **J Neuroophthalmol** 32:82–85, 2012
22. Mahaley MS Jr, Mettlin C, Natarajan N, Laws ER Jr, Peace BB: National survey of patterns of care for brain-tumor patients. **J Neurosurg** 71:826–836, 1989
23. Manor RS, Israeli J, Sandbank U: Malignant optic glioma in a 70-year-old patient. **Arch Ophthalmol** 94:1142–1144, 1976
24. Matloob S, Fan JC, Danesh-Meyer HV: Multifocal malignant optic glioma of adulthood presenting as acute anterior optic neuropathy. **J Clin Neurosci** 18:974–977, 2011
25. Mattson RH, Peterson EW: Glioblastoma multiforme of the optic nerve. **JAMA** 196:799–800, 1966
26. Millar WS, Tartaglino LM, Sergott RC, Friedman DP, Flinders AE: MR of malignant optic glioma of adulthood. **AJNR Am J Neuroradiol** 16:1673–1676, 1995
27. Pallini R, Lauretti L, La Marca F: Glioblastoma of the optic chiasm. **J Neurosurg** 84:898–899, 1996
28. Pecan PE, Bhatti MT: Clinical reasoning: a 61-year-old woman with a swollen optic nerve and progressive visual loss. **Neurology** 82:e205–e209, 2014
29. Rousseau A, Mokhtari K, Duyckaerts C: The 2007 WHO classification of tumors of the central nervous system—what has changed? **Curr Opin Neurol** 21:720–727, 2008
30. Saebø J: Primary tumour of the optic nerve, glioblastoma multiforme. **Br J Ophthalmol** 33:701–708, illust, 1949
31. Saleman M, Scholtz H, Kaplan RS, Kulik S: Long-term survival in patients with malignant astrocytoma. **Neurosurgery** 34:213–220, 1994
32. Seiz M, Nölte I, Pechlivanis I, Freyschlag CF, Schmieder K, Vajkoczy P, et al: Far-distant metastases along the CSF pathway of glioblastoma multiforme during continuous low-dose chemotherapy with temozolomide and celecoxib. **Neurosurg Rev** 33:375–381, 2010
33. Sherriff J, Tamangani J, Senthil L, Cruickshank G, Spooner D, Jones B, et al: Patterns of relapse in glioblastoma multiforme following concomitant chemoradiotherapy with temozolomide. **Br J Radiol** 86:20120414, 2013
34. Spoor TC, Kennerdell JS, Martinez AJ, Zorub D: Malignant gliomas of the optic nerve pathways. **Am J Ophthalmol** 89:284–292, 1980
35. Traber GL, Pangalu A, Neumann M, Costa J, Weller M, Huna-Baron R, et al: Malignant optic glioma—the spectrum of disease in a case series. **Graefes Arch Clin Exp Ophthalmol** 253:1187–1194, 2015
36. van Nifterik KA, Elkhuisen PH, van Andel RJ, Stalpers LJ, Leenstra S, Lafleur MV, et al: Genetic profiling of a distant second glioblastoma multiforme after radiotherapy: recurrence or second primary tumor? **J Neurosurg** 105:739–744, 2006
37. Wabbels B, Demmler A, Seitz J, Woenckhaus M, Bloss HG, Lorenz B: Unilateral adult malignant optic nerve glioma. **Graefes Arch Clin Exp Ophthalmol** 242:741–748, 2004
38. Wallner KE, Galicich JH, Krol G, Arbit E, Malkin MG: Patterns of failure following treatment for glioblastoma multiforme and anaplastic astrocytoma. **Int J Radiat Oncol Biol Phys** 16:1405–1409, 1989
39. Woiciechowsky C, Vogel S, Meyer R, Lehmann R: Magnetic resonance imaging of a glioblastoma of the optic chiasm. Case report. **J Neurosurg** 83:923–925, 1995

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Mastorakos, Chen, Ding, Lopes, Shaffrey. Acquisition of data: Mastorakos, Hays, Caruso, Ding, Taylor, Shaffrey. Analysis and interpretation of data: Hays, Caruso, Chen, Taylor, Lopes. Drafting the article: Mastorakos, Hays, Caruso, Chen, Lopes. Critically revising the article: Mastorakos, Hays, Chen, Ding, Taylor, Lopes, Shaffrey. Reviewed submitted version of manuscript: Mastorakos, Hays, Chen, Ding, Taylor, Lopes, Shaffrey. Approved the final version of the manuscript on behalf of all authors: Mastorakos. Study supervision: Lopes, Shaffrey.

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