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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KEY WORDS glioblastoma; optic nerve; case report; review; oncology

Transtentorial dissemination of optic nerve glioblastoma 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).
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 navigational 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 glioblastoma based on histopathological analysis. Postoperatively, the patient was treated with a course of fractionated radiation therapy (60 Gy) with concurrent 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 $2.7 \times 2.4 \times 2.2$ cm, with sur-
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. Among these, 32 were confirmed to be glioblastomas, with a mean patient age of 62 years at the time of diagnosis. 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. Additionally, symptoms, such as headaches, behavioral changes, and motor deficits, have been reported.

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%), and 5 were a part of multifocal glioblastoma. The diagnosis of optic nerve glioblastoma can be challenging since initial neuroimaging may demonstrate an edematous, thickened optic nerve, anterior optic tract contrast enhancement, an enhancing space-occupying cystic or solid lesion, or multifocal enhancing lesions with optic nerve involvement. 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, nonarteritic or arteritic anterior ischemic optic neuropathy, central retinal artery or
vein occlusion,\textsuperscript{21} or neurosarcoidosis,\textsuperscript{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,\textsuperscript{10} meningioma, lymphoma, craniopharyngioma, pituitary adenoma,\textsuperscript{3} and metastasis.\textsuperscript{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.\textsuperscript{1} To further illustrate the

![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.](image-url)
challenges in the diagnosis of optic nerve glioblastoma, Balachandran et al. reported a case that was initially diagnosed as nonarteritic anterior ischemic optic neuropathy. 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; up to 90% of all recurrences occur within 2–3 cm from the primary lesion, while remote recurrences involving the contralateral hemisphere occur in only 4% of cases. Transtentorial spread of malignant gliomas is exceedingly rare, with only 2 previous reports: one of a left frontal glioblastoma and another of a right temporal anaplastic astrocytoma (WHO Grade III). 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. 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, the similar histopathology and molecular profiling of the cerebellar lesion and the primary optic tumor, as well as the time course of develop-

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 x10 (A), x40 (B and C), x20 (D–F). Figure is available in color online only.

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 x10 (A and C–E), x40 (B), 20 (F). Figure is available in color online only.
TABLE 1. Review of previously reported optic nerve glioblastoma cases

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

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Development 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, but the benefit to survival remains controversial.

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


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<th>Initial Presentation</th>
<th>Survival</th>
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</thead>
<tbody>
<tr>
<td>Spoor et al., 1980</td>
<td>60, F</td>
<td>Lt optic nerve</td>
<td>Rapidly deteriorating vision, bifrontal HA</td>
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<td>4 mos</td>
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<td>Harper &amp; Ewing, 1976</td>
<td>75, M</td>
<td>Bilateral optic nerve, optic chiasm, bilateral optic tract, bilateral temporal lobe</td>
<td>Diagnosed postmortem</td>
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<td>Manor et al., 1976</td>
<td>70, M</td>
<td>Bilateral optic nerve, optic chiasm, bilateral optic tract</td>
<td>Diagnosed postmortem</td>
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<td>Hoyt et al., 1973</td>
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<td>Bilateral optic nerve, optic chiasm, bilateral optic tract</td>
<td>Diagnosed postmortem</td>
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<td>Mattson &amp; Peterson, 1966</td>
<td>10 wks</td>
<td>Proximal left optic nerve, optic chiasm, bilateral optic tract</td>
<td>Diagnosed postmortem</td>
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<td>Saebø et al., 1949</td>
<td>12 mos</td>
<td>Painful, progressive left-sided VL</td>
<td>Diagnosed postmortem</td>
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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, Caruso, Ding, Taylor, Lopes. Approved the final version of the manuscript on behalf of all authors: Mastorakos. Study supervision: Lopes, Shaffrey.

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