Visual outcomes after bevacizumab-based therapy for optic pathway glioma

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Abstract

In optic pathway glioma (OPG), bevacizumab-based therapy (BBT) has promising effects on radiographic tumor burden, but impact on vision is less clear. This single-institution study characterized visual acuity (VA) and visual field (VF) outcomes in 17 pediatric OPG patients treated with BBT. VA was stable or improved in 14 patients. Nine patients had evaluable VF data, 6 of whom experienced stability or improvement. Among 6 patients with vision deterioration as a treatment indication, stable or improved was observed for both VA and VF in 5 patients. In summary, BBT was associated with favorable visual outcomes in most patients with OPG.

Introduction

Optic pathway gliomas (OPGs) are low-grade tumors affecting the visual pathways, accounting for 3-5% of pediatric brain tumors. Overall survival is high, but 70-90% experience visual impairment[1,2]. Tumors may occur anywhere along the optic pathway, and those affecting the chiasm and post-chiasmatic structures are associated with increased risk of vision impairment. Radiographic response to treatment is poorly correlated with visual outcome, leading visual acuity (VA) to be included as an outcome in modern clinical trials[3]. Patients with OPG are also vulnerable to visual field (VF) deficits, and there is emerging evidence that VF deficits can be present even in the absence of VA impairment[4].

Biologic therapies have emerged as viable alternatives to traditional chemotherapy for the treatment of OPG. Bevacizumab is a monoclonal antibody against the vascular endothelial growth factor (VEGF) with demonstrated anti-tumor efficacy for progressive low-grade glioma, including OPG[5]. In contrast to traditional chemotherapy, bevacizumab has a direct effect on tumor microenvironment by inhibiting angiogenesis, thereby conferring a theoretical advantage for controlling tumor-related functional impairment. Initial reports of VA outcomes following bevacizumab-based therapy (BBT) are promising. One early case series described favorable vision outcomes in 4 patients with OPG treated with BBT[6]. Another case series included 6 patients with OPG, 4 of whom had vision improvement after BBT treatment[7]. In 2022, Green et al published a multicenter cohort study demonstrating VA stabilization or improvement in 50 of 65 children with evaluable outcomes treated with BBT for OPG[8]. Compared to VA outcomes, VF outcomes are less well-understood, in part because of the relative difficulty of reliable VF assessment and young age of the OPG population. One report of 2 sporadic OPGs with VF deficits, but stable tumor size, had improvement in VF following treatment with BBT[9]. The Green et al cohort study also assessed VF as a secondary outcome. Although less than a third of the overall cohort had evaluable VF data, 23 of 24 patients included had stable or improved VF after BBT[8].

Prospective studies evaluating visual outcomes including VA and VF for patients treated with BBT are

ongoing[10]. In the interim, there is a knowledge gap between the known visual outcomes from traditional chemotherapy regimen and the modern prospective trials of biologic agents. Further characterization of both VA and VF outcomes for patients treated with BBT is needed to inform treatment decisions for patients with vision-threatening OPG. In the present study, we retrospectively assessed visual outcomes for patients treated for OPG with BBT.

Methods

This is a retrospective chart review of patients treated for OPG at a tertiary care pediatric health center from 7/1/2013 to 9/1/2021. The study was approved by an institutional review board. Inclusion criteria included diagnosis of sporadic or NF1-associated OPG, defined as low-grade glial tumor involving the optic nerves, chiasm, post-chiasmal tracts, or optic radiations; age less than 18 years at treatment; receipt of BBT for OPG; and documentation of visual function before and after treatment. Exclusion criteria included comorbid malignant tumor; receipt of chemotherapy for indications other than OPG; and radiation therapy prior to BBT.

VA and VF information were abstracted from clinical ophthalmology notes for baseline and post-treatment timepoints. The baseline timepoint was defined as 3 months before initiation of BBT. The post-treatment timepoint was defined as either the last documented ophthalmology examination or, in the event of disease progression, the last documented ophthalmology exam prior to initiation of a subsequent therapy. Clinically significant change in VA was defined as a change from baseline of 0.2 logMAR[11]. VF data was obtained from formal perimetric techniques including Goldmann and Humphrey perimetry. Clinical evaluations with confrontation alone (without formal perimetry) were excluded. Clinically significant change in VF was defined as change between (1) full field and any field loss, (2) quadrantic and hemifield loss, or (3) generalized constriction or expansion of VF[4]. Radiographic response was assessed from clinical notes and radiology reports at baseline and at the end of BBT.

Results

During the study period, 228 patients with OPG were identified. Of these, 134 received treatment, 38 of whom received BBT. Eleven patients were excluded due to incomplete ophthalmologic records, and 6 were excluded due to early discontinuation of BBT secondary to intolerance. An additional 4 were excluded due to young age at treatment initiation and inability to complete quantifiable VA assessments. The remaining 17 patients were included in the study analysis.

Demographic and clinical information for each patient is displayed in Table 1. Median age was 5.6 years (IQR 2.6-8.8 years) at OPG diagnosis and 7.9 years (IQR 3.8-12.8 years) at BBT initiation. Fourteen had sporadic OPG and 3 had NF1. All but one patient had prior treatment failure, and 9 had multiple prior treatment failures. Indications for BBT included radiographic progression alone (N=11), vision decline alone (N=2), and both radiographic progression and vision decline (N=4). Median follow-up time at last vision assessment was 12.9 months (IQR 11.0-16.6 months).

At baseline, 15 of 17 patients had impairment in VA, VF, or both (displayed by-eye in Figure 1). Ten of 17 patients had at least moderate VA impairment and 8 of 9 patients with evaluable VF had defects at baseline.

Following BBT, 14 of 17 (82%) had stable or improved VA and 6 of 9 (67%) had stable or improved VF. Among the 6 patients with vision decline as the indication for BBT, all but one experienced vision stabilization or improvement in both VA and VF (Table 1). VA and VF outcomes were discordant in 2 patients. Eight (47%) patients had radiographic progression during BBT, 5 of whom had stable vision at time of progression. Vision and radiographic outcome were discordant in 7/17 (41%).

Discussion

Vision impairment represents a major cause of morbidity in children with optic pathway glioma. Biologic therapies including bevacizumab have demonstrated promising results for radiographic tumor burden, but the effect on visual function is less well understood. In the present study, we describe a cohort of children

with OPG treated with BBT, a majority of whom had progressive disease, clinically significant baseline visual impairment, and predominantly chiasmatic/post-chiasmatic tumors. The rate of VA stabilization or improvement in the cohort was 82%, consistent prior reports of VA in pediatric low-grade glioma treated with BBT[8]. By comparison, visual outcomes for carboplatin and vincristine, the traditional first-line chemotherapy regimen for OPG, has more modest effect on vision, with VA stabilization or improvement between 59 and 66%[12-14].

The effect of BBT on VF outcomes is not well described, although recent reports have identified VF deficits to be prevalent in OPG even in the absence of VA impairment[4]. In our cohort, baseline VF deficits were common, occurring in 8 of 9 patients with evaluable fields, and stable or improved VF was observed in 6 (66%) of these patients. Notably, 2 patients experienced deterioration in VF despite stable VA, highlighting the importance of monitoring VF to assess response in OPG-directed therapies.

In conclusion, BBT is associated with favorable visual outcomes for both VA and VF in most patients with OPG in this retrospective cohort. Larger, prospective studies are needed to better understand patient and tumor characteristics that predict favorable response to BBT; however, the results of this cohort, and from other published reports, suggest that bevacizumab is a promising biological therapy for vision preservation.

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Figures and Tables

TABLE 1 Demographic and clinical features

Case
Patients with vision decline as indication for BBT, N = 6
1
2
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4
5
6
Patients with radiographic progression alone as indication for BBT, N = 11
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17
Follow-up time from treatment start to last vision assessment; +Visual acuity (VA) and visual field (VF) assessments at las

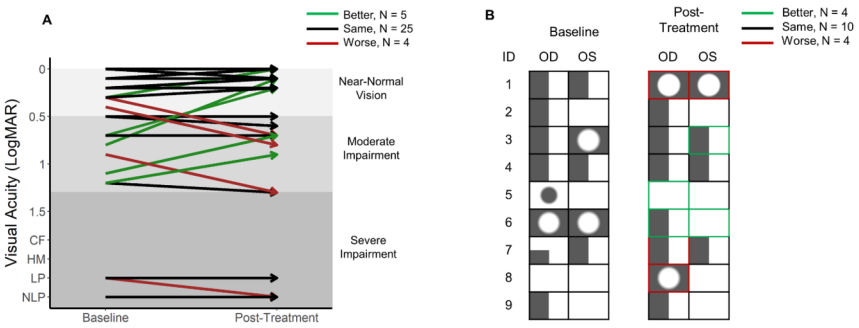

FIGURE 1 Visual outcomes displayed by eye. (A) Change in visual acuity across 34 eyes. 18/34 (53%) had moderate or severe impairment at baseline. 30/34 (88%) eyes were stable or improved post-treatment. (B) Change in visual fields for 18 eyes with evaluable visual field data. Baseline deficits included hemifield defects (N=8, half-shaded boxes), quandrantic field defect (N=1, quarter-shaded box), generalized constriction (N=3, white circle), and central scotoma (N=1, gray circle). Stable or improved visual fields was observed in 14/18 (78%) eyes.

Abbreviations: VA = visual acuity; CF = count fingers; HM = hand motion; LP = light perception; NLP = no light perception; OD = right eye; OS, left eye