Objective Visual and Radiological Response to Bevacizumab in a Child with Recurrent Optic Pathway Glioma

IG Simmons, K Falzon, E Drimtzias, S Picton, D Warren, D Guy

The Leeds Teaching Hospitals NHS Trust

Introduction

Chemotherapy has taken on a prominent role in the treatment of paediatric optic pathway gliomas (OPGs). Standard therapy improves visual acuity (VA) in approximately one-third of children with sporadic or neurofibromatosis type 1 (NF1) related OPGs.[1]

While slow-growing and biologically benign tumours, they over-express vascular endothelial growth factor (VEGF) receptor,[2] thus making them an attractive indication for anti-angiogenic therapy. Bevacizumab, a humanized monoclonal antibody that inhibits VEGF activity, has recently been shown to be successful at inducing rapid objective responses in multiply recurrent OPGs.[3-6]

We report the indications and outcomes, both clinical and radiological, for treatment with bevacizumab, in a child with a recurrent, progressive OPG refractory to standard chemotherapy.

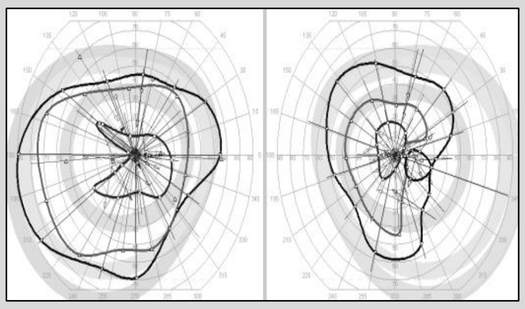
Case Report

An 8-year-old boy with a sporadic (non-NF1-related) chiasmic OPG presented with a decline in VA and visual field (VF) associated with radiographic progression despite second-line chemotherapy with thioguanine, procarbazine, lomustine, and vincristine (TPCV). He first presented at age 3 years with reduced VA (6/36 OD and 6/24 OS), a right convergent squint associated with an abnormal head posture, and pale discs. His height and weight were both above the 98th centile.

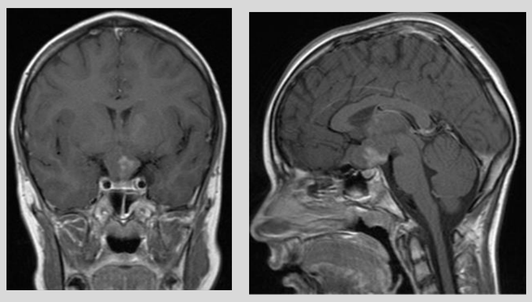
Magnetic resonance imaging (MRI) showed a chiasmic OPG with enhancement. He was initially treated with vincristine and carboplatin. He was allergic to carboplatin and was started on cisplatin instead. After 18 months of chemotherapy he had stable VA (20/126 OD and 20/90 OS) with no evidence of radiographic progression.

At age 7 he presented with acute visual deterioration (6/60 OD and 6/120 OS) and was found to have increased enhancement and growth of his OPG on his MRI. Despite 3 months of second-line chemotherapy with TPCV, there was further decline in both VA and VF. His vision deteriorated to 6/90 OD and 6/180 OS, with worsening in colour discrimination (D-15 Farnsworth test) and contrast sensitivity (Lea^{TM} symbol contrast sensitivity flip chart). Goldmann perimetry demonstrated a right hemi-field defect respecting the vertical meridian. Treatment with bevacizumab 10mg/kg and irinotecan 125mg/m^2 every 2 weeks was initiated instead of TPCV.

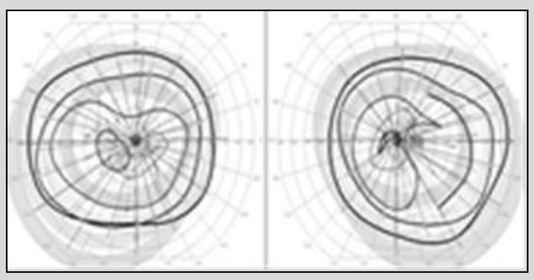
Pre-Treatment



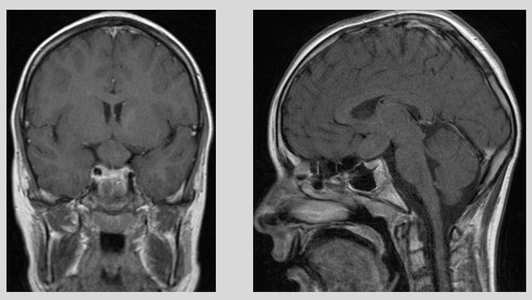
EYE	OS	OD
VA	6/180	6/90
CV	0	5
CS	1	4



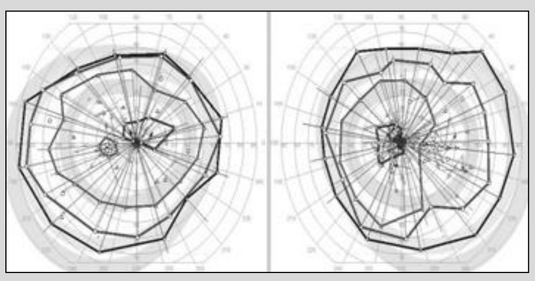
5 Months



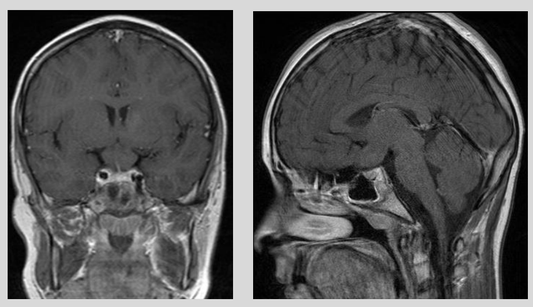
EYE	OS	OD
VA	6/48	6/36
CV	3	11
CS	3	8



14 Months



EYE	OS	OD
VA	6/48	6/36
CV	5	12
CS	5	8



Results

Within 8 weeks VA improved in both eyes to 6/48 OD and 6/60 OS along with a decrease in tumour size and enhancement. Improvement in VF and further reduction in tumuor size was demonstrable after 5 months of treatment.

He completed 12 months of chemotherapy. Adverse events during treatment included recurrent epistaxis and grade 1 proteinuria. Both events resolved after discontinuing therapy. Both VA and VF continued to improve and remained stable 6 months after treatment was discontinued. VA at last follow-up was 6/36 OD and 6/48 OS.

Discussion

Children with OPGs frequently experience vision loss from their tumors.[3] First-line treatment with standard chemotherapy results in modest visual improvement in no more than 30% of children.[1] Long-term sequelae and tumor relapses both remain great concerns.[5] In addition, impending visual or neurologic deterioration requires therapeutic intervention capable of rapid tumor control and protection of function.[4] Bevacizumab-based therapy has recently shown encouraging responses in multiply recurrent OPGs.[3-6] Our patient showed marked improvement in VA, color discrimination and contrast sensitivity, as well as significant recovery of his VF, soon after starting treatment with bevacizumab.

The rapid objective visual and radiologic response provides clear clinical evidence of demonstrable improvement after 8 weeks of treatment. Marked recovery of vision has been similarly reported as early as 6 weeks (range 6 weeks to 5 months) after bevacizumab-based therapy.[3]

Conclusions

Bevacizumab-based therapy was successful at inducing a rapid objective visual and radiological response and was relatively well-tolerated. The encouraging results provide evidence for an alternative or additional therapeutic option for similar patients, including children with NF1, after failing conventional therapy.

References

1. Fisher MJ, Loguidice M, Gutmann DH et al. Visual outcomes in children with neurofibromatosis type 1-associated optic pathway glioma following chemotherapy: a multicenter retrospective analysis. Neuro Oncol. 2012 Jun;14(6):790-7.
2. Bartels U, Hawkins C, Jing M et al. Vascularity and angiogenesis as predictors of growth in optic pathway/hypothalamic gliomas. J Neurosurg. 2006 May;104(5 Suppl):314-20.
3. Avery RA, Hwang EI, Jakacki RI, Packer RJ. Marked Recovery of Vision in Children With Optic Pathway Gliomas Treated With Bevacizumab. JAMA Ophthalmol. 2013 Nov 14.
4. Hwang EI, Jakacki RI, Fisher MJ et al. Long-term efficacy and toxicity of bevacizumab-based therapy in children with recurrent low-grade gliomas. Pediatr Blood Cancer. 2013 May;60(5):776-82.
5. Couec ML, André N, Thebaud E et al. Bevacizumab and irinotecan in children with recurrent or refractory brain tumors: toxicity and efficacy trends. Pediatr Blood Cancer. 2012 Jul 15;59(1):34-8.
6. Packer RJ, Jakacki R, Horn M, Objective response of multiply recurrent low-grade gliomas to bevacizumab and irinotecan. Pediatr Blood Cancer. 2009 Jul;52(7):791-5.