The Leeds Teaching Hospitals NHS Trust

Visual outcomes in children treated with chemotherapy for optic pathway glioma in the SIOP LGG 2004: results from the UK multicenter study

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Introduction

Optic pathway gliomas (OPGs) represent 4-6% of all brain tumours in childhood. The European Paediatric Brain Tumour Group, under the auspices of SIOP-Europe, has coordinated two Low Grade Glioma (LGG) trials. LGG1 commenced in 1997 and ran until 2002. LGG2 commenced in 2004 and closed in 2013. The UK has 21 regional paediatric oncology centers. The aim of this study is to present the UK experience of the long-term monitoring of visual acuity (VA) in both NF 1 and non NF 1 children diagnosed with OPGs who had undergone treatment with chemotherapy. In addition, poor prognostic indicators of the final visual outcome were assessed.

Materials & Methods

A search in the national Low Grade Glioma database (LGG-UK) was performed allowing identification of all paediatric patients with OPGs from 21 participating centers in the UK. The study population consisted of a review of 122 patients younger than 16 years of age who had undergone treatment with chemotherapy. Ophthalmic examination records and visual data were prospectively collected from the time of diagnosis and last follow-up. VA was assessed by Teller Acuity cards, HOTV and LogMAR optotypes depending on age and cognitive ability.

A criterion of 2 LogMAR lines was selected as the amount of VA change required for the visual outcome to be classified as improved or worse, therefore suggesting progression sufficient to initiate treatment. Age was divided for analysis into 3 groups (< 2yrs, 2-6 yrs, >6 yrs). Tumour location was described by the original Dodge classification system. Treatment was based on clinical or radiological signs of progressive tumor.

Contingency tables data were analyzed using the Fisher`s exact test. Data were evaluated based on per eye or per subject analysis as appropriate.

Results

75% of the cases were detected before the age of 6 years, whereas 10% were aged over 10 by the time of diagnosis.VA loss was the most frequent clinical presentation. The median interval from OPG diagnosis to the initiation of treatment was 8½ months.

Approximately 80% of children received chemotherapy within 12 months after tumour diagnosis. Non NF1 individuals are more likely to have severe visual loss at presentation (Figure 1) (Table 1).

At last follow-up, VA had improved in 29.50% of subjects, remained stable in 31.14% and declined in 39.34% of subjects (Table 2). VA was deteriorated in 35% of NF1 patients during treatment with only 12.5% of the cases being over 6 years of age. Normal VA at final review was recorded in half of the eyes of the NF 1 Group and was found to be twice the rate recorded in non NF1 individuals

Figure 1

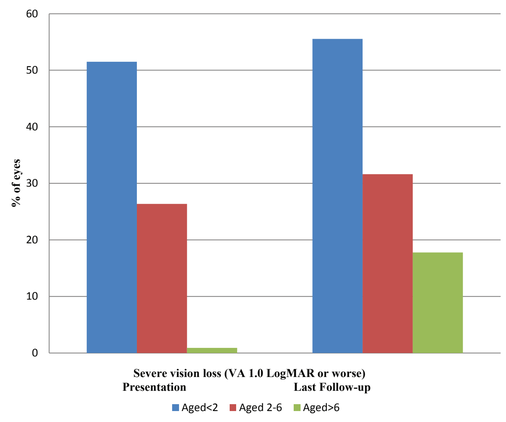

Table 1

	Total with vision loss n [a] (%)		Normal VA 0.2 LogMAR or better n (%)		Severe visual loss 1.0 LogMAR or worse n (%)	
	Presentation	Last Review	Presentation	Last review	Presentation	Last review
NF1 Status						
NF1	69 (57.50)	47 (48.35)	51 (42.50)	62 (51.66)	20 (16.67)	26 (21.56)
Non NF1	96 (77.42)	72 (73.39)	28 (22.58)	33 (26.61)	53 (42.75)	52 (41.93)
Dodge						
1	24 (57.14)		17 (40.47)	22 (52.38)	7 (16.66)	12 (28.57)
2	43 (52.43)		39 (47.56)	49 (59.75)	11 (13.41)	12 (14.63)
3	93 (77.50)		27 (22.50)	31 (25.83)	46 (38.33)	50 (41.66)

Table 2

	VA outcome n [a] (%)		
	Improved	Stable	Worse
Study cohort	36 (29.50)	38 (31.14)	48 (39.34)
NF1 subjects	19 (31.66)	20 (33.33)	21 (35)
Non NF1 subjects	17 (27.41)	18 (29.03)	27 (43.54)
Age at diagnosis			
<2 yrs	12 (38.71)	7 (22.58)	12 (38.71)
2-6 yrs	17 (27.86)	20 (32.78)	24 (39.34)
> 6 yrs	8 (26.66)	13 (43.33)	9 (30)
Dodge			
I	9 (42.85)	6 (28.57)	6 (28.57)
II	12 (29.26)	18 (43.90)	11 (26.82)
III	18 (30)	15 (25)	27 (45)

Table 3

MRI Outcome	VA Outcome n[a](%)		
	Improved	Stable	Worse
Improved (CR+ PR)	6 (22.22)	14 (51.85)	7 (25.92)
Stable (SD)	9 (25)	15 (41.66)	12 (33.33)
Worse (PD)	0 (0)	1 (33.33)	2 (66.66)

Multivariable analysis revealed that VA at last review is dependent on VA at the time of diagnosis. On univariate analysis, severe visual loss was mainly documented in patients aged < 2 at the time of diagnosis as well as in the long term. In contrast, age over 6 years is correlated with normal VA at initial presentation. Anterior gliomas showed the highest rate of VA improvement. Nearly half of the subjects with most posterior tumor involvement demonstrated decline in vision. Tumor involvement in the most posterior portion of the visual pathway was associated with a higher likelihood of VA loss at presentation and last follow-up. Non NF 1 children tend to present with posterior visual pathway involvement in a significantly higher rate. Furthermore, young subjects aged less than 2 years are more likely to have post-chiasmal tumour with/without involvement of the hypothalamus. Correlation between radiographic and VA outcomes was poor (Table 3).

Conclusion

The natural history of OPGs is unpredictable and therefore the preferred initial management is close observation with serial examinations and MRI evaluations. Vision loss has become the primary outcome measure and is the key component in the diagnosis and management of NF1-OPGs.

We clearly documented that there are children who regain vision with treatment therefore supporting the effect of systemic chemotherapy to slow down or suppress tumour growth. There appears to be no absolute age during childhood beyond which the likelihood of visual loss becomes insignificant. Individuals aged < 2 years and with postchiasmatic tumour involvement tend to present with severe visual loss and these factors remain poor prognostic indicators of the visual outcome in the long term. Treatment for radiologic progression was not associated with better VA outcomes that for clinical progression. OPG diagnosis and associated VA loss is most likely to occur during the early childhood years and tumour progression is expected soon in newly diagnosed NF1-OPGs. Close neuro-ophthalmology and neuro-oncology evaluation is required until the age of 16 years. VA is the most robust indicator of clinical progression, stability or improvement. However, for sporadic OPGs, it is still important to follow hypothalamic involvement and radiographic tumor progression.

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