Chapter

Treatment Practices in Optic Nerve Glioma

Rashmi Singh, Anup Kumar, Payal Raina, Rajanigandha Tudu and Praveer K.S. Munda

Abstract

Optic nerve glioma (OPG) is a rare tumor in children and adolescents. It comprises 1–5% of central nervous system tumors. It can be sporadic or associated with the neurofibromatosis 1 (*NF1*) gene. These are usually slow-growing tumors and may remain localized to the optic nerve or can have encroached upon adjoining structures like optic chiasma, opposite optic nerve, and hypothalamus. So, there may be decreased or loss of vision, proptosis, focal neurological symptoms, precocious puberty, and short stature. Due to the involvement of these critical structures, its treatment should be based on multidisciplinary consensus. The treatment modalities include surgery, RT, and chemotherapy. The aim of the treatment should be to preserve vision. However, the timing and selection of optimal treatment modalities are always a clinical dilemma. Recently, there have been promising results with newer techniques of radiotherapy and chemotherapy.

Keywords: optic nerve glioma, pediatric optic glioma, radiotherapy in optic glioma, challenges in treatment in optic glioma, optic glioma and neurofibromatosis 1

1. Introduction

Optic nerve glioma (OPG) is a rare tumor comprising 1–5% of central nervous system tumors [1]. Child and adolescent patients are most commonly affected [2]. Depending upon the tumor extent as to optic chiasma, hypothalamus, there are symptoms like vision loss, proptosis, hydrocephalous, focal neurological symptoms, precocious puberty, and short stature. Location and also, the volume of the disease are determinants of prognosis. As gliomas limited to only optic nerve (OPN) have better long-term visual outcomes than those with post-chiasmatic disease [3].

OPG has been associated with the neurofibromatosis 1 (NF1) gene in 50–60% of cases [4]. It has been observed decreased visual acuity is a more common presentation in non-NF1 patients than in NF1 positive (90% vs. 72%). However, proptosis has been found in 20–30% of cases with NF1+ and, only in 5–12% cases with non-NF1 [5].

Natural history and growth patterns have been variable for this tumor [6]. Some remain stable for years, while others demonstrate slow or rapid growth patterns.

2. Diagnosis

OPG is a radiological and clinical diagnosis. It is a type of tumor where pre-treatment tissue diagnosis is not mandatory [7]. A biopsy is limited to cases with

unusual clinical and imaging findings. Pilocytic astrocytoma is the most common histopathological variant observed, pilomyxoid astrocytoma and grade II diffuse fibrillary astrocytoma are other variants [8].

A detailed ophthalmological examination including visual clinical examination, fundoscopy, Goldmann visual field, and imaging studies (CT/MRI orbit and brain) [9], all are vital in knowing the tumor extent, response to treatment, and prognosis.

3. Treatment

The aim of the treatment should be to preserve vision. However, the timing and selection of optimal treatment modality are always a clinical dilemma [10] as it is challenging due to tumor location and treatment-related effects. Patients once diagnosed can be kept in surveillance as it remains stable for multiple years. Active intervention is to be taken once there is evidence for progression in diminition of vision or size of the tumor. Choice of the treatment to be assessed in a multidisciplinary clinic and at well-equipped centers having state of art facilities.

3.1 Surgery

Surgery can be curative when the tumor is localized to the optic nerve, [10], it can be offered as palliative treatment in advanced OPGs with no vision, and severe disfiguring proptosis. Also, as most of the time there is an involvement of optic chiasma, hypothalamus, surgery is not attempted avoid to unacceptable adverse effects.

3.2 Radiotherapy

Radiotherapy when started early this could minimize vision loss [11]. There have been reports of stabilization and also improvement in vision in the range of 13–81% post-RT [9, 12].

Long-term results of radiotherapy in a retrospective study including 89 pediatric optic-hypothalamic gliomas patients showed 10-year event-free survival (EFS) of 61.9% in NF1+ and 67.5% without NF1, whereas 10 years overall survival (OS) was 92.3%. The median dose of radiotherapy was 54 Gy/30#. However, there were reports of secondary neoplasms possibly due to RT in eight patients (four in NF1+); also, the 10-year cumulative incidence of vasculopathy was 7%. Older patients without NF1 were at low risk of toxicity [13].

So, caution should be taken while selecting patients as in children less than 6 years, where the risk of precocious puberty, growth hormone deficiency, and cerebrovascular complications has been observed in studies [14].

We have reported a case of bilateral OPG in an 18-year-old patient who was treated with intensity-modulated radiotherapy (IMRT). 54Gy/1.8 Gy/#, x 30 fractions over 6 weeks was prescribed to the planning target volume (PTV). Organs at risk (OARs) were taken care off for their tolerance. The patient had only mild irritation and watery discharge in bilateral eyes during radiotherapy with onset after 4 weeks of RT which resolved with symptomatic treatment. We observed stabilization of vision at 8 weeks follow-up [15].

In centers, where fractionated stereotactic radiotherapy (FSRT) [16] is available, the dose to the organs at risk (OARs) can be minimized by a smaller clinical target volume (CTV) margin of 1 mm and planning target volume (PTV) of 3 mm. Radiotherapy should be done by using a conformal newer technique, for example

proton therapy (PRT), intensity-modulated radiotherapy (IMRT), FSRT, and Gamma knife surgery (GKS)/Cyberknife. The patient's MRI can be fused with the planning CT scan for better delineation of the tumor.

An earlier study published in 1999 by M Fuss et al. compared the dosimetric difference between PRT, 3-dimensional radiotherapy (3-D RT), and lateral photons in cases of OPG. Gross tumor volume (GTV) ranged from 3.9 cm^2 to 127 cm^2. PRT gave the advantage of covering the smallest volumes of normal tissue at all isodose levels that will extrapolate as resulting in decreased long-term toxicity. With PRT a 47–77% dose reduction to the contralateral optic nerve (OPN) was observed in comparison as to be received by 3-DRT and lateral photons. Similarly for optic chiasma and pituitary glands doses were reduced with PRT [17].

Another study involved 22 patients' majority having an extension to Chiasma/hypothalamus and five having disease limited to OPN treated with GKS. The median age of the patients was 16 years, with tumor volume 3.1 cm^3 (0.15–18.2 cm^3), prescription dose of 11.5 Gy (8–14 Gy), and mean follow-up (FU) was 43 months. Two patients were progressed, two died, the tumor shrank in 12 patients and remained stable in six patients, a controlled rate of 90% could be achieved. The authors concluded GKS to be a safe and effective treatment for OPG [18].

GKS has also shown promising results in another report where two patients of pilocytic astrocytoma of optic apparatus were treated with a dose of 11–15 Gy to 50% isodose line. Near complete response was observed in both of them at 60 months of FU [19]. Other reports using FSRT and Cyberknife in a young patient have shown a significant reduction in tumor size post-RT on FU MRI [20].

3.3 Chemotherapy

Chemotherapy has been an effective treatment in young children to preserve and stabilization of vision and delays radiotherapy [14]. It is indicated when there is a progressive disease which is evident by substantial tumor progression on MRI and or worsening of visual acuity. Although chemotherapy shrinks the tumor, up to 60% of children have tumor progression after 5 years [21].

The most common combination regimen is vincristine and carboplatin with 3–5 years progression-free survival (PFS) 77–69% respectively, although these results are from studies where the disease was extending beyond the optic nerve [22]. Other regimens with cisplatin and etoposide with 3-year PFS up to 78% have been reported [23]. In recent times monotherapy with temozolomide (TMZ) [24], vinblastine, and vinorelbine has been used for progressive or refractory disease with positive results and low toxicity. Although TMZ should be avoided in patients with NF1+.

MEK inhibitors, for example selumetinib have been reported to give 2-year PFS of 78% in a phase 2 study involving 25 patients with recurrent/progressive optic-hypothalamic gliomas. Common toxicities were grade 1–2 fatigue, asthenia, liver enzymes and creatinine phosphor kinase (CPK) elevation, diarrhea, rash, etc. [25].

OPGs are highly vascular tumors and in other tumors increased microvascular density has been associated with worse PFS. By inhibiting vascular endothelial growth factor (VEGF), neovascularization, vascular permeability, and tumor growth are inhibited with bevacizumab. In a refractory setting bevacizumab-based therapy has been reported to result in objective response and rapid improvement in visual symptoms in up to 86% of cases [26]. Adverse effects of hypertension, fatigue, bleeding have been associated with bevacizumab.

4. Conclusion

OPG is rare and difficult to treat the tumor. Improvement in vision and/or checking further progression should be the aim of selecting a treatment modality. Results with advanced techniques of radiotherapy and newer chemotherapy regimens are promising.

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Conflict of interest

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