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Case Report Open Access

Radiation Therapy in Optic Gliomas: A Case Report and a Review of Literature

Fedele D*, Ponti E, Tolu B, Ingrosso G, Hamoud E, Terenzi S, Tortorelli G And Santoni R

Department of Diagnostic Imaging, Molecular Imaging, Interventional Radiology and Radiotherapy, Tor Vergata University General Hospital, Rome, Italy

Abstract

To assess the role of Radiation Therapy (RT), in the treatment of optic glioma analyzing 11 retrospective trials during the latest twenty-five years.

In a 25-year-old woman, referred to our centre because of right optic glioma, fractionated stereotactic radiation therapy (FSRT) was the treatment of choice using a commercial linear accelerator Elekta Synergy beam modulator with an integrated Cone Beam Computed Tomography (CBCT) system. In order to evaluate volumetric changes of the right optic nerve lesion a co-registration of pre-RT Magnetic Resonance Imaging (MRI) and CT planning scan was performed and compared with the co-registration of CT planning scan and MRI performed 3 years after the end of the treatment. A noticeable shrinkage in Clinical Target Volume was found and the patient experienced a complete recovery of the right eye visual deficit.

Successful Progression Free Survival and Overall Survival at 10 years can be obtained using a dose between 52 and 60 Gy. FSRT is advantageous compared to conventional RT because of sparing of normal tissues within the high dose volume. Modern linear accelerators with an integrated Cone Beam system improve treatment set-up and dose delivery.

Keywords: Optic glioma; Fractionated stereotactic radiation therapy; Cone beam CT

Introduction

Optic pathway gliomas are rare and account for 1-5% of all central nervous system (CNS) tumours in the paediatric group (peak age incidence between 2 and 6 years); 75% of all patients are <10 yrs [1-3]. There is a slight female preponderance and a genetic factor has been implicated [4]. They may be divided into three clinical-pathologic entities: anterior lesions, confined to the optic disc and nerve (25%); chiasm lesions, involving or not the optic nerves (20-40%); posterior lesions involving the hypothalamus with possible extension to the optic tracts (33-60%) [2,5]. The most common histotype entity is low-grade astrocytoma [6,7] which in 10-70% of patients is associated with neurofibromatosis [8,9].

With the use of high resolution computed tomography (CT) and magnetic resonance imaging (MRI) scan the diagnosis of optic pathways gliomas no longer requires biopsy in most cases [10].

Symptoms depend on the anatomic site involved: gliomas confined to the optic nerves cause vision impairment and/or proptosis, while chiasmatic-hypothalamic tumours may cause hydrocefalus, focal neurologic deficits, endocrine dysfunction in addition to vision loss.

The disease course is variable. Although some cases may remain stable with no evidence of progression for years without any treatment, others may progress rapidly, resulting in severe morbidity and death [2,3,5,11-13]. The rarity of these tumours and their unpredictable course make assessment and standardization of treatment methods controversial [14]; there has been considerable debate about the roles of radiotherapy, surgery, chemotherapy and simple observation [13,15-24].

Total surgical excision is the treatment of choice but intracranial surgery alone exhibits low survival rate [21,25]. Radiation therapy (RT) is recommended when the total resection is not possible with acceptable morbidity and when intracranial or progressive symptoms are evident [13,15-24] .

Numerous reports document the value of radiation therapy for patients with optic gliomas [2,9,13,26]. Long term survival rates range between 80% and 100% with improvement of symptoms.

RT complications such as calcification, necrosis and chiasmal damage are rare, while endocrine disorders in children are more common [9,27]. Chemotherapy is an alternative choice [28].

We report the case of a young woman with an optic nerve glioma treated with radiotherapy at our Radiotherapy Unit and we show how MRI may be useful to verify quantitative tumour regression during follow-up. We also report 11 retrospective studies about optic glioma irradiation published in the latest 25 years analyzing the assessment of progression-free survival (PFS), overall survival (OS) and side effects in patients treated with radiation therapy [5,9,11,13,14,16,22,23,29-31].

Case Report

In November 2008, a 25 year-old woman was referred to Radiotherapy Unit of the University of Rome, Tor Vergata, with the diagnosis of a right optic nerve glioma. After the onset of a visual impairment of the right eye, a brain MRI was obtained showing an increased volume of the right optic nerve with moderate ipsilateral exophthalmus. Tumour was limited to the right optic nerve and extended from the optic foramen up to the back of the right eyeball

***Corresponding author:** Dahlia Fedele, Department of Diagnostic Imaging, Molecular Imaging, Interventional Radiology and Radiotherapy, Tor Vergata University General Hospital, Rome, Italy, Tel: +390620904300; Fax: +390620904332; E-mail: dahlia.fed@tiscali.it

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(thickness 8 mm, cranio-caudal extension 10 mm). Before RT an ophthalmological examination showed 5/10 of right eye visual acuity. The patient refused any surgery and, because of its appearance on MRI, a clinical diagnosis of optic glioma was formulated and the patient was referred for radiation therapy only.

We irradiated the optic nerve using high energy photons (10 MV) produced by Elekta Synergy® S with beam modulator that combines a micromultileaf (μMLC) linear accelerator with a kilovolt (kV) imaging system capable of acquiring 3D X-ray volume images based on a kV Cone Beam Computed Tomography (CBCT). We used a fractionated stereotactic radiotherapy (FSRT) delivering 54 Gy (1.8 Gy/fraction) to the tumour.

The patient was immobilized with a thermoplastic mask (Head Mask, Klarity) combined with a bite-block (3DLine®) fixed to a stereotactic frame support (Head Frame, 3DLine®). In addition a frame for stereotactic coordinate generation (Multimodality Localizer CT/MRI, 3DLine®) was applied over the mask in order to define the stereotactic tridimensional Coordinate System.

CT scanning was performed with a GE LightSpeed® Scanner (GE Healthcare Diagnostic Imaging, Slough, UK) with a 1.25 mm slice thickness. MRI was obtained with a 3.0 T Philips Achieva Intera® (Philips Medical Systems, Reigate, UK). CT and MRI images were exported on Syntegra software (Pinnacle, Philips Medical System, and Andover, MA) and the two data sets were automatically fused. Target volume and organs at risk were delineated on each CT scan after fusion with MRI. Eye and lens on both sides, left optic nerve, hypophysis, brainstem, optic chiasm and right temporal lobe were defined as organs at risk.

Clinical Target Volume (CTV) included the Gross Tumor Volume (GTV) visible on MRI plus a 1 mm safety margin to ensure the inclusion of microscopic spread along the optic pathway structures. Planning Target Volume (PTV) was defined as the CTV plus a 3 mm margin. Five photon beams were used for irradiation; the dose to the isocenter was 55.65 Gy. Hypophysis volume was 0.36 cc with a maximum and mean dose of 28.2 Gy and 13.78 Gy.

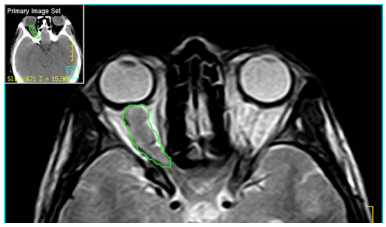

Figure 1A: Pre-treatment T2-weighted MRI showing optic glioma of the anterior right optic nerve.

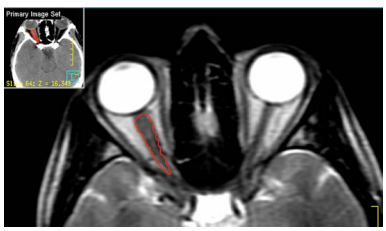

Figure 1B: Post-treatment T2-weighted MRI obtained two and a half years after treatment completion.

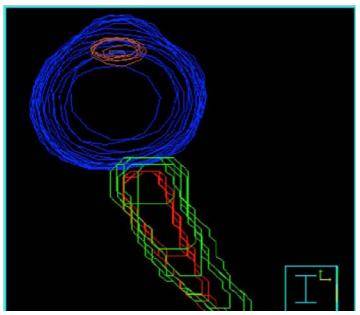

Figure 2: 3D reconstruction of pre-treatment (green) and post-treatment (red) volumes of the optic nerve showing volume reduction following irradiation.

Author	Anterior lesions	Posterior lesion	Neuro fibromatosis	Reduced vision before RT (n)	Endocrine Dysfunction before RT (n)
Bataini (15)	21	36	23	52	29
Tao (28)	4	25	-	22	10
Horwich (12)	19	11	6	29	nr
Jenkin (5)	11	27	nr	27	nr
Pierce (9)	5	19	12	23	9
Sung (21)	36	7	11	40	18
Wong (22)	24	-	8	nr	nr
Debus (10)	10	-	3	10	4
Khafaga (13)	15	13	18	nr	nr
Combs (30)	11	4	3	14	7
Grabenbauer (29)	10	15	3	17	6

Table 1: Patients' lesion characteristics and clinical symptoms before radiation treatment in the literature.

During FSRT, CBCTs were acquired to detect set-up errors and translational errors over 3 mm were corrected on-line before treatment.

Sight of the patient improved at the dose of 25.2 Gy and an ophthalmological examination showed a reduction of right optic nerve edema and blind spot.

The intraorbital tract of the right optic nerve was contoured on pre-RT MRI images, acquired in October 2008, obtaining a CTV volume of 1.201 cc (Figure 1A); the MR performed in July 2011 showed a noticeable shrinkage of the tumour volume (0.615 cc) (Figure 1B and 2). The controlateral (left) disease-free optic nerve was as well measured and resulted to be 0.26 cc.

A complete remission of right eye visual deficit (from 5/10 to 8/10) was obtained and no endocrinological disorders were documented. The patient is pregnant and delivery is foreseen in the middle of July 2012.

Discussion

Optic gliomas amount for <5% of all childhood brain tumours; their prevalence in the general population has been estimated to be about 1/100000 [32]. To date, the treatment of low-grade astrocytomas remains controversial [5,11,24]. Currently, a large randomized trial is underway by the European Organization for Research and Treatment of Cancer to evaluate the role of Surgery, RT and Chemotherapy in the management of optic glioma [31].

To contribute to the debate about optimal treatment of optic glioma eleven retrospective studies published between 1982 and 2005 have been analysed. Primary end-points of all studies are OS and PFS at 10

Author	Patient number	Follow-up (yr)	Dose (Gy)	Progression-free survival 10 yr (%)	Overall survival 10 yr (%)	Visual Improvement (%)	Endocrine Dysfunction (%)
Bataini (15)	57	7.5	51.7	80	83.5	55	37
Tao (28)	29	10	54	100	89	81	72
Horwich (12)	30	10	45-50	90	93	43	33
Jenkin (5)	38		50	73	79	13	nr
Pierce (9)	24	6	54	88	100	30	73
Sung (21)	43	>5	35-60	79	56	49.5	11
Wong (22)	24	9.4	48	55	87	35	8
Debus (10)	10	5	52.4	90	100	30	1
Khafaga (13)	28	10	50	62	75	15	52
Combs (30)	15	8	52.2	72	90	40	7
Grabenbauer (29)	25	9	45-60	69	94	36	48

Table 2: Results after radiation treatment in 11 retrospective studies.

years; secondary end-points are visual improvement and endocrine dysfunction.

The mean number of patients treated is 29 (range 10-57), the mean age ranges between 0-56 yrs with a prevalence of childhood population; the mean follow-up period is 8.2 years.

In each study the number of patients with anterior and posterior lesions and symptoms before treatment is reported (Table 1). Overall Survival (OS), Progression Free Survival (PFS) and clinical symptoms after radiation therapy obtained in the analysed studies are shown in table 2.

Median total dose at isocenter is 51.1 Gy (range 35-60 Gy) with a daily fraction of 1.5-2 Gy. External beam irradiation (EBRT) with parallel opposed fields performed with Cobalt-therapy [5,13,16,22,23] or linear accelerators (6-22 MV) is reported in older trials. Three dimensional Conformal Radiation Therapy (3DCRT) performed with fields tailored by cerrobend blocks [9,14,29,30] or with stereotactic techniques using multileaf collimators [11,29,31] is described in the latest studies. In the selected analysed trials the authors reported an OS and a PFS rates ranging between 56-100% and found no differences between RT alone or RT in combination with surgery. The analysis shows that posterior lesions have a worse prognosis than anterior lesions. Posterior chiasm glioma seems to have different histopathology, characterized by transitions between glial and undifferentiated cells.

Preservation of vision is a paramount goal of the treatment. Visual impairment is the most common presenting symptom and most important functional handicap [29].

Visual improvement ranges between 13-81% after RT. In the study by Horwich and Bloom HJ improvement of visual acuity was found in 43% of patients and stable vision in a further 48% [13]. Tao et al. found visual preservation or improvement in 81% of evaluable irradiated patients, but visual preservation or its improvement is possible if the treatment is started prior to severe impairment [29].

Endocrinal dysfunction is an event that occurs overall in childhood population and may arise either as a consequence of the tumour growth, of surgical or radiation treatment or as a combination of these factors [29,30]. Table 1 shows that the percentage of endocrine dysfunction increases in patients with posterior lesions or posterior chiasmatic involvement [9,29,30]. The late effect of RT on hypothalamic structures in children <10 year-old is well demonstrated in the trial of Grabenbauer et al. showing 63% of actuarial 10-year-incidence of endocrine disorder in children versus 10% in older people (p=0.008). This result indicates the higher radiation sensitivity of neural structures in early childhood [30].

The incidence of endocrine dysfunction both pre- and post-treatment is highly variable (from 10% to 70%) [5,9,11,13,14,16,22,23,29-32]. The most frequent abnormalities reported are precocious puberty [33], growth hormone deficiency and growth retardation, being the last one, the most common sign of hypopituitarism after irradiation [16,34]. It has been supposed that the incidence of hypopituitarism increases during follow up after irradiation with RT having a role at long term in the development of endocrine disorder; in the trial of Tao et al. patients with intact endocrine axes, undergoing RT, were followed for a median of 23.6 months. Patients presenting endocrine abnormalities underwent longer follow up (median 75.9 months) [29]. Debus et al. observed a 10% rate of endocrine dysfunction and 30% visual improvement as most of the patients were affected by anterior lesions treated with fractionated stereotactic RT (FSRT) [11]. Combs et al. confirmed the same results with 7% of endocrine dysfunction rate and 40% of visual improvement using FSRT [31].

Table 2 shows that the percentage of endocrine dysfunction is larger in older trials where older techniques were employed [5,13,14,16,22,23].

Endocrinal dysfunctions are registered in literature and its incidence ranges between 3.6 and 8.3% for dose to the hypophysis <40 Gy and >40 Gy respectively [35]. In our report the maximum (28.20 Gy) and mean (13.78 Gy) doses were calculated and the patient didn't show any endocrinal dysfunction.

On the basis of published data and of our limited experience a total dose of 54 Gy delivered in conventional fractions of 1.8 Gy can be recommended; however a dose reduction should be considered in children <5 years of age [36].

Despite a relatively rapid clinical response to radiation therapy the rate of radiographic regression for low-grade gliomas is expected to be slow. Literature contains only case descriptions of radiographic response without any volumetric quantitation. According to Tao et al. stable or minimally responsive disease in the first few years after RT does not reflect ineffective therapy or higher risk for progression. In addition transient increasing tumour size, enhancement, or edema may occur within the first 12 months after completion of therapy [29]. We had a significant volumetric reduction of the tumour 3 years after the treatment. Although our experience has the limit of a short follow-up (3 yrs) we consider FSRT in combination with Image Guided Radiation Therapy (IGRT) as a good choice in optic glioma treatment.

Conclusion

Literature data show that radiation therapy has contributed to the improvement of 10 years PFS and OS in patients treated for optic

glioma. Visual improvement and endocrine dysfunction depend on tumour site, on the total dose delivered and on RT technique. A successful PFS and OS at 10 years can be obtained using a dose between 52 and 60 Gy; visual acuity outcome and endocrine disorder reduction can be obtained using modern techniques that allow high precision in delivering radiation therapy such as FSRT in combination with IGRT. Compared to conventional fractionation FSRT is advantageous because it offers the possibility to minimize the amount of normal tissue within the high-dose volume.

References

1. Danoff BF, Kramer S, Thompson N (1980) The radiotherapeutic management of optic nerve glioma in children. Int J Radiat Oncol Biol Phys 6: 45-50.
2. Weiss L, Sagerman RH, King GA, Chung CT, Dubowy RL (1987) Controversy in the management of optic nerve glioma. Cancer 59: 1000-1004.
3. Alvord EC Jr, Lofton S (1988) Gliomas of the optic nerve or chiasm: Outcome by patients' age, tumor site, and treatment. J Neurosurg 68: 85-98.
4. Janisch Jw, Schneider M, Gerlach H (1976) [Role of genetic factors in the pathogenesis of optic nerve glioma]. Zentralbl Neurochir 37: 169-176.
5. Jenkin D, Angyalfi S, Becker L, Berry M, Buncic R, et al. (1993) Optic glioma in children: surveillance, resection, or irradiation? Int J Radiat Oncol Biol Phys 25: 215-225.
6. Alshail E, Rutka JT, Becker LE, Hoffman HJ (1997) Optic chiasmatic-hypothalamic glioma. Brain Pathol 7: 799-806.
7. Barkovich JA (1997) Pediatric neuroimaging. Lippincott Williams& Wilkins. Philadelphia: 507-509.
8. Slamovits TL (1985) Von Recklinghausen neurofibromatosis. Incidence of optic glioma. Ophthalmology 92: 984.
9. Pierce SM, Barnes PD, Loeffler JS, McGinn C, Tarbell NJ (1990) Definitive radiation therapy in the management of symptomatic patients with optic glioma: Survival and long-term effects. Cancer 65: 45-52.
10. Dutton JJ (1994) Gliomas of the anterior visual pathway. Surv Opthalmol 38: 427-452.
11. Debus J, Kocagoncu KO, Hoss A, Wenz F, Wannenmacher M (1999) Fractionated stereotactic radiotherapy (FSRT) for optic glioma. Int J Radiat Oncol Biol Phys 44: 243-248.
12. Hoffman HJ, Humphreys RP, Drake JM, Rutka JT, Becker LE, et al. (1993) Optic pathway/hypothalamic gliomas: a dilemma in management. Pediatr Neurosurg 19: 186-195.
13. Horwich A, Bloom HJ (1985) Optic gliomas: radiation therapy and prognosis. Int J Radiat Oncol Biol Phys 11: 1067-1079.
14. Khafaga Y, Hassounah M, Kandil A, Kanaan I, Allam A, et al. (2003) Optic gliomas: a retrospective analysis of 50 cases. Int J Radiat Oncol Biol Phys 56: 807-812.
15. Appleton RE, Jan JE (1989) Delayed diagnosis of optic nerve glioma: a preventable cause of visual loss. Pediatr Neurol 5: 226-228.
16. Bataini JP, Delenian S, Ponvert D (1991) Chiasmal glioma: results of irradiation management in 57 patients and review of the literature. Int J Radiat Oncol Biol Phys 21: 615-623.
17. Hoyt WF, Baghdassarian SA (1969) Optic glioma of childhood.Natural history and rationale for conservative management. Br J Ophtalmol 53: 793-798.
18. Imes RK, Hoyt WF (1986) Childhood chiasmal glioma: update on the fate of patients in the 1969 San Francisco study. Br J Ophtalmol 70: 179-182.
19. Janss AJ, Grundy R, Cnaan A, Savino PJ, Packer RJ, et al. (1995) Optic pathway and hypothalamic/chiasmatic glioma in children younger than age 5 years with a 6-year follow-up. Cancer 75: 1051-1059.
20. Mohadjer M, Etou A, Millios E, Baden R, Mundinger F (1991) Chiasmatic optic glioma. Neurochirurgia (Stuttg) 34: 90-93.
21. Rush JA, Younge BR, Campbell RJ, MacCarty CS (1982) Optic glioma: long term follow-up of 85 histopathologically verified cases. Ophtalmology 89: 1213-1219.
22. Sung DI (1982) Suprasellar tumors in children: a review of clinical manifestations and managements. Cancer 50: 1420-1425.
23. Wong JY, Uhl V, Wara WM, Sheline GE (1987) Optic gliomas: A reanalysis of the University of California, San Francisco experience. Cancer 60: 1847-1855.
24. Wright JE, McNab AA, McDonald WI (1989) Optic nerve glioma and management of optic nerve tumors in the young. Br J Ophtalmol 73: 967-974.
25. Tenny RT, Laws ER, Younge BR, Rush JA (1982) The neurosurgical management of optic glioma: results in 104 patients. J Neurosurg 57: 452-458.
26. Flickinger JC, Torres C, Deutsch M (1988) Management of low-grade gliomas of the optic nerve and chiasm. Cancer 61: 635-642.
27. Rappaport R, Brauner R (1989) Growth and endocrine disorders secondary to cranial irradiation. Pediatr Res 25: 561-567.
28. Cohen ME, Duffner PK (1991) Optic pathway tumors. Neurol Clin 9: 467-477.
29. Tao ML, Barnes PD, Billett AL, Leong T, Shrieve DC, et al. (1997) Childhood optic chiasm gliomas: radiographic response following radiotherapy and long-term clinical outcome. Int J Radiat Oncol Biol Phys 39: 579-587.
30. Grabenbauer GG, Schuchardt U, Buchfelder M, Rödel CM, Gusek G, et al. (2000) Radiation therapy of optico-hypothalamic gliomas (OHG)--radiographic response, vision and late toxicity. Radiother Oncol 54: 239-245.
31. Combs ES, Schulz-Ertner D, Moschos D, Thilmamm C, Huber PE, et al. (2005) Fractionated stereotactic radiotherapy of optic pathway gliomas: tolerance and long-term outcome. Int J Radiat oncol Biol Phys 62: 814-819.
32. Singhal S, Birch JM, Kerr B, Lashford L, Evans DG (2002) Neurofibromatosis type 1 and sporadic optic gliomas. Arch Dis Child 87: 65-70.
33. Brauner R, Malandry F, Rappaport R, Zucker JM, Kalifa C, et al. (1990) Growth and endocrine disorders in optic glioma. Eur J Pediatr 149: 825-828.
34. Kovalic JJ, Grigsby PW, Shepard MJ, Fineberg BB, Thomas PR (1990) Radiation therapy for gliomas of the optic nerve and chiasm. Int J Radiat Oncol Biol Phys 18: 927-932.
35. Bhandare N, Kennedy L, Malyapa RS, Morris CG, Mendenhall WM (2007) Primary and central hypothyroidism after radiotherapy for head-and-neck tumors. Int J Radiat Oncol Biol Phys 68: 1131-1139.
36. Parsons JT, Fitzgerald CR, Hood CI, Ellingwood KE, Bova FJ, et al. (1983) The effects of irradiation on the eye and optic nerve. Int J Radiat Oncol Biol Phys 9: 609-622.