Child's Nervous System (2019) 35:1227–1230
https://doi.org/10.1007/s00381-019-04147-7

CASE REPORT

Twenty-three years follow-up after low-dose Gamma Knife surgery of a brainstem juvenile pilocytic astrocytoma: a case report and review of the literature

J. Sherry Liu[1] · Denise Foo[2] · Tseng Tsai Yeo[2] · Kee Hang Ho[2] · Vincent Diong Weng Nga[2] · Bengt Karlsson[2]

Received: 25 April 2018 / Accepted: 2 April 2019 / Published online: 17 April 2019

Abstract

Juvenile pilocytic astrocytoma (JPA) is a World Health Organization (WHO) grade I tumor that is the commonest to occur in the 0–19 age group, with an excellent prognosis of 96% 10-year survival in pediatric patients. Complete resection is the treatment of choice for JPAs. However, this is not always feasible due to the location of certain tumors, and the management following subtotal resection is controversial. Fractionated radiotherapy, chemotherapy, radiosurgery, and observation have all been used to treat tumor remnants. We report a young patient with good tumor control 23 years following low-dose Gamma Knife surgery (GKS) of a subtotally resected brainstem JPA and recommend that GKS may be a feasible treatment option to achieve long-term tumor control when subtotal resection cannot be achieved, even if the GKS prescription dose must be significantly reduced due to large tumor volume or proximity to critical structures sensitive to radiation.

Keywords Gamma Knife surgery · Pilocytic astrocytoma · Low-grade glioma · Tumor control

Introduction

Juvenile pilocytic astrocytoma is a World Health Organization (WHO) grade I tumor with a slight preponderance for males [16]. CBTRUS statistical report noted juvenile pilocytic astrocytoma (JPA) as the commonest tumor in the 0–19 age group, with a good prognosis of 96% 10-year survival in pediatric patients [17].

Complete surgical excision of tumor generally results in cure for JPA. However, this is not always feasible due to the location of certain tumors. Alternative management strategies include subtotal resection or biopsy, followed by adjuvant therapy or observation. There is still no consensus on how to best manage these patients with tumor remnants.

Stereotactic radiosurgery is conceptually suitable as JPA is a non-infiltrative tumor with well-defined tumor margins. Although sparse, there is data available to support the efficacy of this treatment modality in JPA [1, 7, 12, 20, 23]. The long-term results following Gamma Knife surgery (GKS) in the treatment of JPA are still not clear. The present data suggests that high treatment doses result in high incidences of radiation-induced complications [1] and that the tumor control rate appears to be independent of treatment doses [1, 7, 20, 23]. We here report, to our knowledge, the longest follow-up of a subtotally resected brainstem JPA that was treated with low-dose GKS resulting in excellent long-term tumor control.

Case report

A 13-month-old boy presented with acute signs of hydrocephalus and was initially managed with a ventriculoperitoneal (VP) shunting. On follow-up MRI at 4 years old, a small, 1.5 × 2.5 × 1.5 cm cystic midbrain lesion was discovered. This was managed conservatively with serial neuroimaging until 10 years old, when he began to experience persistent headaches, nausea, and vomiting. MRI then showed significant lesion growth to 3.5 × 4.0 × 3.5 cm, with hydrocephalus. VP shunt was revised followed by subtotal resection of tumor using an interhemispheric transcallosal approach.

✉ Vincent Diong Weng Nga
Vincent_nga@nuhs.edu.sg

[1] Yong Loo Lin School of Medicine, Singapore, Singapore

[2] Division of Neurosurgery, National University Hospital, Singapore, Singapore

Intraoperatively, the tumor was located within the third ventricle, involving the thalamus and cerebral aqueduct. Histological diagnosis was that of JPA. Post-operatively, the patient was neurologically intact apart from a slight upward gaze palsy. Post-operative MRI revealed a 3.3 × 3.0 × 2.9 cm residual tumor in the midbrain. The patient was referred to The Karolinska Hospital for consideration for GKS, as neither chemotherapy nor radiosurgery was the standard of care for JPA in Singapore then. The decision to treat with GKS was controversial at Karolinska. It was recommended due to the low prescription dose that could be used to keep the risk for complications at an acceptable level. GKS was performed based on this recommendation 3 months later. Target delineation was based on stereotactic MRI with the tumor and target volume being 21 cm^3. The prescription dose was 5 Gy, with a maximum dose of 14 Gy. The dose to the brainstem was ≤ 5 Gy. The dose was chosen as it was likely the highest possible dose with acceptable risks, taking into consideration the tumor size and location. Stereotactic MR images performed prior to GKS are shown in Fig. 1a. The patient was discharged well on the day of treatment.

The tumor volume on MRI was approximately 7 cm^3 3 years after GKS (Fig. 1b), stable around 4 cm^3 the next 10 years, decreasing to 3 cm^3 15 years post-GKS, and the volume remained the same on the latest scan done 23 years post-GKS (Fig. 1c). Tumor volume on follow-up imaging was estimated as an ellipsoid by multiplying the 3 diameters (assessed by radiologist) and dividing by 2. None of the images showed undue radiation-induced effects. The patient has been clinically stable since GKS with resolution of the gaze palsy 7 years ago. The patient, now 33 years old, remains well and is gainfully employed as a customer relations officer, as of 2016.

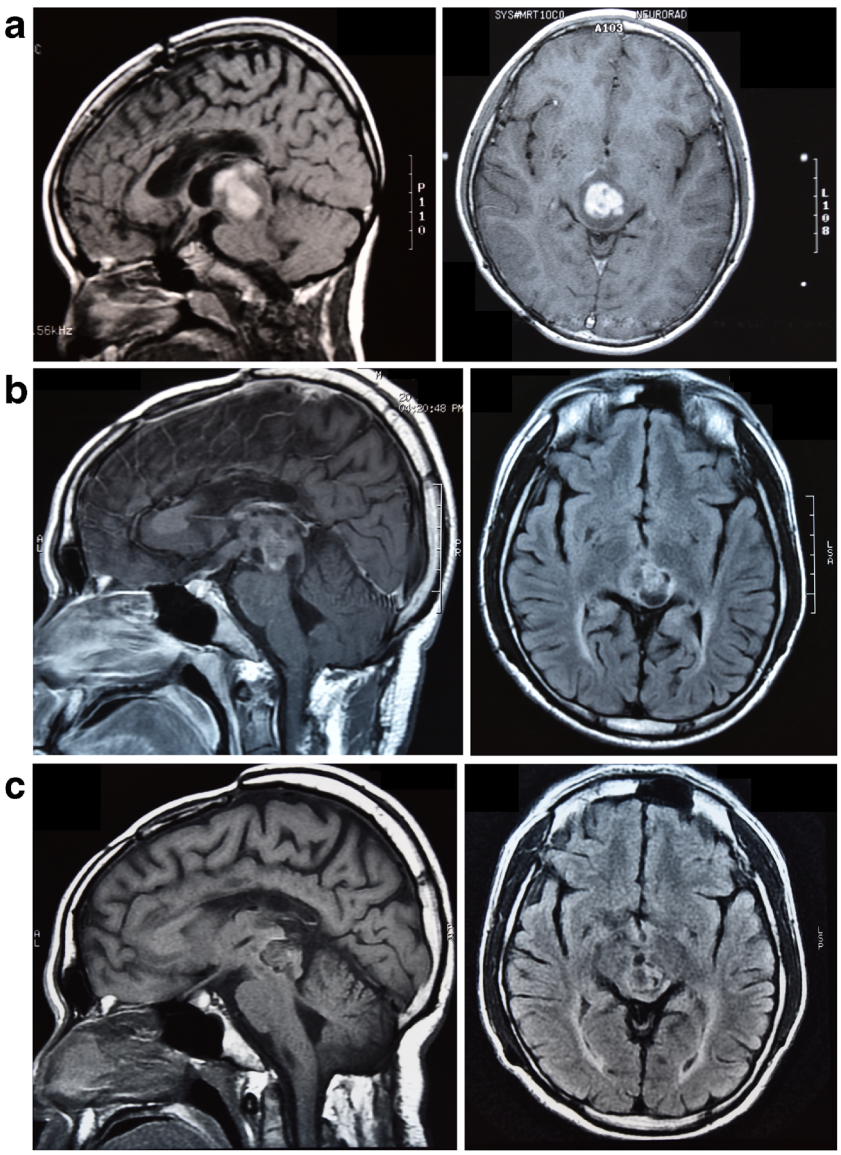

Fig. 1 **a** Gadolinium contrast-enhanced T1-weighted +C (left) sagittal and (right) axial stereotactic MRI images of the tumor taken prior to GKS, showing a 3.3 × 3.0 × 2.9 cm residual tumor in the midbrain; **b** T1-weighted +C (left) sagittal and (right) axial MRI images of the tumor taken 3 years thereafter; and **c** T1-weighted +C (left) sagittal and (right) axial MRI images of the tumor taken 23 years after GKS at the latest follow-up

Table 1 Articles reporting results following GKS of JPA

Author	*N*	Dose	Mean follow-up	Tumor control (%)	Cyst progression (%)	Complications (%)
Boethius (1)	17	10–20 Gy	6 years	100	12	30
Hafez (6)	1	12 Gy	3 years	100	0	0
Kano (7)	50	11–22 Gy	4.5 years	96	20	10
Kida (10)	12	Mean 12 Gy	2 years	92	8	17
Trifiletti (23)	28	Median 16 Gy	Median 5.2 years	93	7	0

Discussion

Dose de-escalation

The 25 Gy prescription dose initially given in GKS for all but functional indications was based on an erroneous hypothesis [8]. Serendipitously, the dose turned out to be suitable for small AVMs. Noren et al. [14] started to decrease the prescription dose for acoustic neuromas, resulting in a lower complication rate without compromising tumor control. The point where the tumor control rate drops with lowered prescription dose has yet to be established. It is possible that further dose de-escalation may optimize treatment outcomes.

GKS for JPA

The literature following GKS for JPA is sparse and summarized in Table 1. The reported control rate of solid tumor was high in all studies but the follow-up durations were short [1, 6, 7, 10]. Of interest is the consistently high tumor control rate despite wide variations in prescription doses (10–22 Gy), suggesting that the tumor control rate is satisfactory even at lower doses. The complication rate varied from study to study. Of note, patients treated with 20 Gy in the Boethius study and one patient treated with 20 Gy in the Kano study developed complications [1, 7], consistent with our previous study where 6/6 low-grade glioma patients treated with ≥ 14 Gy developed complications [11].

Results of post-GKS using prescription doses of ≤ 6 Gy

It is unusual to treat tumors with prescription doses of ≤ 6Gy. Ulfarson et al. prescribed GKS of 5–6 Gy for 5 patients with craniopharyngioma and followed them for 4–26 years [24]. The solid tumors were controlled in 4/5 while the cystic portion remained stable in about half. One patient in JPA series by Trifiletti et al. was treated with a prescription dose of 4 Gy, resulting in local tumor control [23].

Reported course of postop JPA remnants

Gunny et al. reported that 6/10 JPA tumor remnants decreased spontaneously [5]. There are several reports of spontaneous regression of JPA tumors following subtotal resection or biopsy [4, 9, 19].

Regression of subtotally resected JPAs is an uncommon event with a mean rate of 20% (36/166) [3, 5, 13, 15, 18, 19, 21, 22]. The extent of regression of those tumors varied widely between 25 and 100% [3, 18, 19].

While it is difficult to ascertain if the favorable outcome in this patient was indeed due to GKS or spontaneous regression of tumor, studies [2, 5, 21] looking at effect of size of residual tumor size on tumor regression showed a trend towards greater regression rate for those with smaller residual tumor volume. It is worth noting that none of the tumors that regressed spontaneously in literature was > 10 cm^3.

The volume of tumor in our patient is approximately 21 cm^3; it is reasonable to postulate that a tumor of this size is unlikely to regress dramatically spontaneously based on findings in literature and that GKS likely played a significant role in the tumor control. This is regardless of whether or not there was any component of spontaneous regression in the 23 years.

Conclusions

GKS using a prescription dose of 5 Gy resulted in long-term tumor control of 23 years in our patient. It is likely but not conclusive that GKS contributed to this favorable outcome. Based on published literature and our observation, a reasonable approach would be to monitor remnants of JPA, especially in young children, until evidence of tumor growth is present. At that time, GKS may be a feasible treatment option even if the prescription dose must be significantly reduced due to large tumor volume or proximity to critical structures sensitive to radiation.

Compliance with ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Boethius J, Ulfarsson E, Rahn T, Lippitz B (2002) Gamma knife radiosurgery for pilocytic astrocytomas. J Neurosurg 97:677–680
2. Buder T, Deutsch A, Klink B, Voss-Böhme A (2015) Model-based evaluation of spontaneous tumor regression in pilocytic astrocytoma. Komarova NL, ed. PLoS Comput Biol 11(12):e1004662
3. Foroughi M, Hendson G, Sargent MA, Steinbok P (2011) Spontaneous regression of septum pellucidum/forniceal pilocytic astrocytomas–possible role of Cannabis inhalation. Childs Nerv Syst 27:671–679
4. Gnekow A, Falkenstein F, von Hornstein S, Zwiener I, Berkefeld S, Bison B, Warmuth-Metz M, Driever P, Soerensen N, Kortmann R, Pietsch T, Faldum A (2012) Long-term follow-up of the multicenter, multidisciplinary treatment study HIT-LGG-1996 for low-grade glioma in children and adolescents of the German Speaking Society of Pediatric Oncology and Hematology. Neuro-Oncology 14:1265–1284
5. Gunny R, Hayward R, Phipps K, Harding B, Saunders D (2005) Spontaneous regression of residual low-grade cerebellar pilocytic astrocytomas in children. Pediatr Radiol 35:1086–1091
6. Hafez R (2007) Stereotaxic gamma knife surgery in treatment of critically located pilocytic astrocytoma: preliminary result. World J Surg Oncol 5:39
7. Kano, Niranjan, Kondziolka D, Flickinger J, Pollack I, Jakacki R, Lunsford L (2009) Stereotactic radiosurgery for pilocytic astrocytomas part 2: outcomes in pediatric patients. J Neuro-Oncol 95: 219–229
8. Karlsson B, Lindquist C, Steiner L (1997) Prediction of obliteration after Gamma Knife surgery for cerebral arteriovenous malformations. Neurosurgery 40:425–431
9. Kernan, Horgan, Piatt, D'Agostino A (1998) Spontaneous involution of a diencephalic astrocytoma. Pediatr Neurosurg 29:149–153
10. Kida, Kobayashi, Mori (2000) Gamma knife radiosurgery for low-grade astrocytomas: results of long-term follow up. J Neurosurg 93:42–46
11. Kihlström L, Lindquist C, Lindqvist M, Karlsson B (1994) Stereotactic radiosurgery for tectal low-grade gliomas. Acta Neurochir 62(suppl):55–57
12. Lizarraga, Gorgulho, Lee S, Rauscher G, Selch M, DeSalles A (2012) Stereotactic radiation therapy for progressive residual pilocytic astrocytomas. J Neuro-Oncol 109:129–135
13. Loh J-K, Lieu A-S, Chai C-Y, Hwang SL, Kwan AL, Wang CJ, Howng SL (2013) Arrested growth and spontaneous tumor regression of partially resected low-grade cerebellar astrocytomas in children. Childs Nerv Syst 29(11):2051–2055
14. Noren G, Greitz D, Hirsch A et al (1993) Gamma knife surgery in acoustic tumours. Acta Neurochir Suppl (Wien) 58:1047
15. Ogiwara H, Bowman RM, Tomita T (2012) Long-term follow-up of pediatric benign cerebellar astrocytoma. Neurosurgery 70:40–48
16. Ohgaki, Kleihues (2005) Population-based studies on incidence, survival rates, and genetic alterations in astrocytic and oligodendroglial gliomas. J Neuropathol Exp Neurol 64:479–489
17. Ostrom, Gittleman, Fulop J, Liu M, Blanda R, Kromer C, Wolinsky Y, Kruchko C, Barnholtz-Sloan J (2015) CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2008-2012. Neuro-Oncology Suppl 4:iv1–iv62
18. Palma L, Celli P, Mariottini A (2004) Long-term follow-up of childhood cerebellar astrocytomas after incomplete resection with particular referenced to arrested growth or spontaneous tumour regression. Acta Neurochir 146:581–588
19. Rozen W, Joseph S, Lo P (2008) Spontaneous regression of low-grade gliomas in pediatric patients without neurofibromatosis. Pediatr Neurosurg 44:324–328
20. Simonova G, Kozubikova P, Liscak R, Novotny JJ (2016) Leksell Gamma Knife treatment for pilocytic astrocytomas: long-term results. J Neurosurg Pediatr 18:58–64
21. Smoots DW, Geyer JR, Lieberman DM, Berger MS (1998) Predicting disease progression in childhood cerebellar astrocytoma. Childs Nerv Syst 14:636–648
22. Steinbok P, Poskitt K, Hendson G (2006) Spontaneous regression of cerebellar astrocytoma after subtotal resection. Childs Nerv Syst 22:572–576
23. Trifiletti D, Peach M, Xu Z, Kersh R, Showalter T, Sheehan J (2017) Evaluation of outcomes after stereotactic radiosurgery for pilocytic astrocytoma. J Neuro-Oncol 134:297–302
24. Ulfarsson E, Lindquist C, Roberts M, Rähn T, Lindquist M, Thorén M, Lippitz B (2002) Gamma knife radiosurgery for craniopharyngiomas: long-term results in the first Swedish patients. J Neurosurg 5:613–622