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Case Report OMICS International

Multisession CyberKnife Stereotactic Radiosurgery for Brainstem Glioma

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Abstract

Adult brainstem glioma is a rare and deadly disease, and optimal treatment has not yet been fully established. Biopsy or surgery is not always possible therefore radiation therapy is the standard treatment. We operated multisession CyberKnife stereotactic radiosurgery for 2 patients of adult brainstem glioma. Both cases have enabled surviving for significantly long terms, and without relapse, for 48 months and 21 months. One of them achieved Complete Remission (CR) and the other achieved Partial Remission (PR). Multisession CyberKnife stereotactic radiosurgery has successfully demonstrated to be substantially beneficial for such a devastating disease.

Keywords: Brainstem glioma; CyberKnife; Stereotactic radiosurgery

Introduction

According to the report from Central Brain Tumor Registry of the USA, brainstem tumors account for 2.0% of all primary Central Nervous System (CNS) tumors, 3.6% of all malignant CNS tumors, and 4.3% of CNS glioma [1]. The median survival time for adult brainstem glioma is 30 months to 40 months, while pediatric Diffuse Intrinsic Pontine Glioma (DIPG) is associated with a dismal prognosis of 10 months to 12 months [2]. Resection is often not possible, and even biopsies are challenging and with significant risk for complications [3]. When biopsy is performed, a low-grade histology (grade Ⅱ glioma) is found in most cases, whereas in children a grade Ⅳ glioma is the most frequent phenotype, which accounts for the better prognosis of the adult cases [4]. Radiation therapy with a dose of 54 Gy to 60 Gy is considered standard upfront therapy [3]. However, no literature in the past has ever reported complete remission by radiotherapy. Guillamo et al. reported that radiotherapy improved clinical status in 61% for 48 adult patients including 46% of DIPG, but a partial radiological response (a decrease of 50% in the T2 hyperintensity in the greatest axial cross-sectional area) was noted in only 19% [5]. Here we report two cases of highly successful treatments for brainstem glioma by multisession CyberKnife stereotactic radiosurgery.

Case Reports

A 17-year-old girl presented with 2-week history of double vision, left facial nerve palsy and numbness in her right extremities. Brain contrast MRI revealed an enhanced tumor of 12 mm × 13 mm with T2WI hyperintensity and DWI hyperintensity in the brainstem (Figure 1). Its margin was unclear, and it was located from the left pons to the left medulla oblongata. She was diagnosed with brainstem glioma, and was referred to our hospital for treatment. Brain biopsy was considered to be unnecessary because the MRI showed typical image of brainstem glioma, and her cranial nerve symptoms supported clinical diagnosis. The patient proceeded with CyberKnife stereotactic radiosurgery. The original plan was 10 fractions with prescription dose of 4000 cGy and prescription isodose line of 71%. However, she had paroxysmal right hemiparesis after the first delivery. She took a break after the 3rd delivery and started taking dexamethasone 0.5 mg/day. Her facial nerve palsy was getting better, but paroxysmal hemiparesis was still observed. Three days later, on the 6th day she resumed CyberKnife stereotactic radiosurgery. The dose was reduced by 2/3 for each delivery, and the fraction was increased by 1.5 times, so that total prescription dose was the same as the original plan. She also started taking Isosorbide 42.0 g/day. The paroxysmal hemiparesis disappeared on the 7th day after the 5th delivery. The left abducens nerve palsy which caused double vision

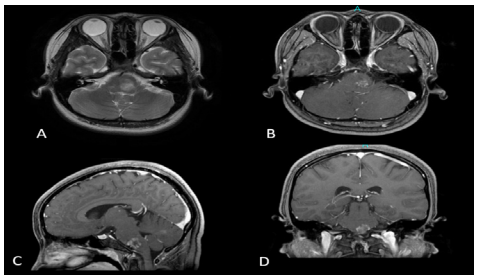

Figure 1: Brain MRI of case 1 before treatment. A: T2WI. B, C, D: Contrast MRI. A tumor is located from the left pons to the left medulla oblongata.

recovered on the 15th day. The radiosurgery completed on the 16th day. She stopped taking dexamethasone and isosorbide on the 23rd day because her cranial nerve symptoms had disappeared.

One month later she presented with some cranial nerve symptoms. She was not able to close her left eye due to the left facial nerve palsy, had sensory disturbance on the left side of her face due to the left trigeminal nerve palsy, had double vision due to the left abducens nerve palsy, and tinnitus due to the acoustic nerve impairment. She resumed the medication of dexamethasone 1.0 mg/day. These symptoms recovered gradually over 4 months, so that the steroid was reduced accordingly. The steroid was carefully reduced and ultimately discontinued after 22 months. Four years later she visited our hospital. She has no symptoms, and the brain MRI revealed no evidence of relapse (Figure 2). Now she is surviving with no symptoms for 48 months after multisession CyberKnife stereotactic radiosurgery.

Second case is a 43-year-old female. She presented with numbness in the left corner of her mouth. In 6 months, she developed left hemiparesis including face, sensory disturbance on the left body including face, and dysarthria. Brain contrast MRI revealed heterogenous enhanced mass of 30 mm × 27 mm × 29 mm with T2WI high intensity and DWI iso

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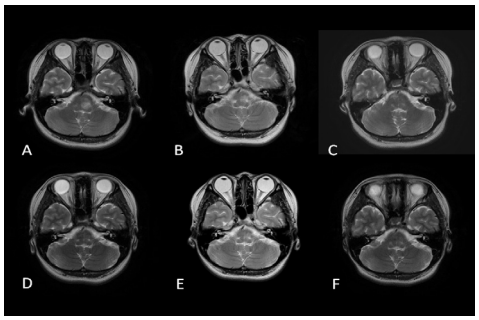

Figure 2: Clinical course of case 1. A: Before treatment, B: After 3 months, C: After 6 months, D: After 18 months, E: After 30 months, F: After 4 years. The tumor in the brainstem has disappeared.

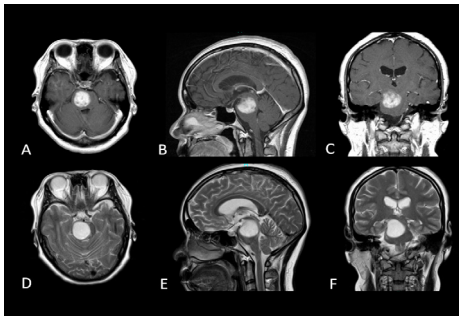

Figure 3: Brain MRI of case 2 before treatment. A, B: Contrast MRI. C, D: T2WI. A tumor is located from pons to midbrain.

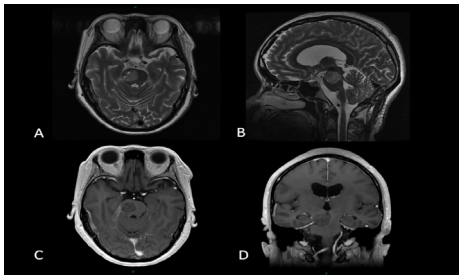

Figure 4: Two months after treatment of case 2. A, B: T2WI. C, D: Contrast MRI. The tumor in the brainstem is smaller than before, and contrast enhancement is poor.

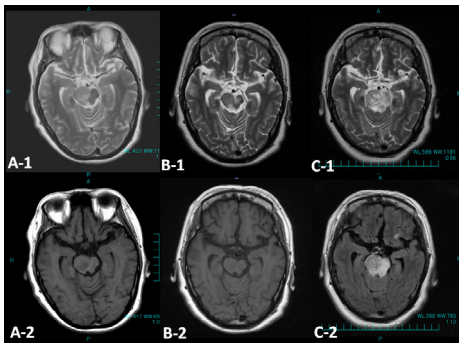

Figure 5: Follow-up MRI of case 2. A-1, 2: After 6 months. B-1, 2: After 36 months. C-1, 2: After 42 months. The tumor in the brainstem is smaller than before, and stable for almost 4 years.

intensity in the brainstem from pons to right midbrain (Figure 3). She was diagnosed with brainstem glioma, and was referred to our hospital for further evaluation and treatment.

She underwent brain biopsy with the right infratentorial supracerebellar approach. Pathological evaluation revealed that the tumor was astrocytoma grade Ⅲ. MIB-1 index was less than 10%, and 1p19q loss of heterozygosity was not observed. CyberKnife stereotactic radiosurgery was performed with prescription dose of 4392 cGy in 12 fractions and 79% of prescription isodose line. Two weeks after the radiosurgery, she started taking Temozolomide 200 mg/m^2 for 5 days and bevacizumab 10 mg/kg twice with 2 weeks interval. Then she was transferred to the local hospital. She continued the chemotherapy with the same doses of temozolomide and bevacizumab for 20 months. Her dysarthria got better, but her hemiparesis remained. However, the brain MRI reveals no relapse, and the tumor became smaller and is not enhanced with contrast (Figure 4).

She was transferred to another hospital for terminal care. Recently we learned that she is still alive with stable disease. She had left hemiparesis and mild dysarthria for 2 years after CyberKnife therapy, and the symptoms had not changed. Then she had a few episodes of stroke in the right medulla oblongata and left posterior lobe. Her left hemiparesis got worse and she developed right abducens nerve palsy. We received her brain MRI of 6 months, 36 months and 42 months after the treatment (Figure 5). To our surprise, she is surviving for 45 months after multisession CyberKnife stereotactic radiosurgery without relapse nor metastasis. She can still speak, eat, and drink.

Discussion

CyberKnife radiosurgery is a minimally invasive hypo fractionated procedure. Since brainstem glioma is a life-threatening disease, it is critical for patients to choose the treatment that provides better quality of life. Our experience with CyberKnife radiosurgery for brainstem glioma has proven highly successful in both clinical outcome and in increasing patients' quality of life (Figure 2).

Case 1 has achieved nearly complete remission. As the T2 hyperintensity is limited, has not changed for one year, and has not shown any clinical symptoms, it is the sole remaining after-effect of radiation therapy. This is absolutely the best outcome of radiotherapy for brainstem glioma documented in the medical literature. Case 2 has achieved PR and surviving for 45 months, without any relapse, and the patient is eating, talking, and enjoying her life.

CyberKnife Radiosurgery usually takes 1 month to 2 months or longer to show its effectiveness. In case 1, the patient had several cranial nerve symptoms for about 4 months after the therapy. She even developed new symptoms 1 month after the therapy (Figure 2), the original tumor in the left brainstem became smaller but remained for 3 months after the treatment which explains the sustained cranial nerve symptoms. The tumor in the left brainstem then disappeared 6 months after the treatment, as did the cranial nerve symptoms. The radiation may have worked slowly over 6 months to destroy the tumor cells, or may have worked sooner and caused the local edema that is shown as T2WI hyperintensity in the left brainstem for 6 months. In (Figure 2), a new T2WI hyperintensity appeared in the right brainstem 6 months after the therapy even though the patient did not display symptoms. Then it disappeared in the subsequent MRI. This points to the patient having some local edema in the brainstem that was caused by the radiation which was completely healed with dexamethazone and isosorbide.

Case 2 also did not show the prompt recovery. The patient was transferred to the local hospital, and her symptoms had not changed until she had a stroke 2 years later (Figures 4 and 5), the tumor was decreased and is not enhanced with contrast medium. CyberKnife could

damage the tumor selectively. A Cochrane review assessing the effects of conventional fractionated radiotherapy versus hyper fractionated or hypo fractionated radiotherapy indicated the dual advantages of hypo fractionated radiotherapy of decreasing the treatment burden as well as increasing the quality of remaining life [6]. The randomized controlled trial in this review is the study of 71 DIPG children randomized into hypo fractionated (39 Gy/13 fractions in 2.6 weeks) and conventional arm (54 Gy/30 fractions in 6 weeks) which concluded that hypo fractionated radiotherapy offers lesser burden on the patients [7]. However, the radiation dose of hypo fractionated radiotherapy in this study may be too small to be effective. CyberKnife radiosurgery is not only hypo fractioned but delivers more radiation dose with minimum toxicity. In our cases, case 1 was treated with 40 Gy with 10 fractions which was calculated to 42 Gy using α/β ratio in the linear quadratic model of 10 Gy. Case 2 was treated with 43.92 Gy in 12 fractions which was calculated to 50 Gy using α/β ratio. CyberKnife radiosurgery was shown to uniquely enable use of optimal radiation dose with less fractions in shorter term without any radiation toxicity.

Conclusion

Multisession CyberKnife stereotactic radiosurgery was highly successful in one case and reasonably successful in the other case of adult brainstem glioma. The patients are surviving long-term without relapse as well as with normal quality of life. Additional cases therefore should further demonstrate and re-confirm the significant benefits of this new approach, which surely brings good news to patients and victims of such a devastating disease.

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