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Original Article

Stereotactic Radiosurgery in Brain Cavernomas: Single-Center Experience

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ABSTRACT

Objective: In this study, we aimed to present our treatment results involving patients with intracranial cavernomas who were treated with stereotactic radiosurgery (SRS) by using a CyberKnife®.

Methods: Between April 2010 and December 2017, data from 19 patients treated with SRS in our clinic with the diagnosis of cavernomas were retrospectively evaluated.

Results: The median follow-up time was 82 months (range: 9–100 months). SRS was performed in the median 1 fraction (range: 1–3); according to the lesion size, the prescription dose ranged from 12 to 21 Gy (median: 15 Gy). During the post-SRS follow-up period, 6 out of the 10 patients with a headache had a complete response, 3 patients had a partial response, and 1 patient had no response. Further, 3 out of the 4 patients with a seizure had a partial response and 1 patient had a stable response in seizure frequency. Furthermore, 1 out of the 2 patients with a vision problem had a complete response and 1 had no change. Also, 1 out of the 3 patients with hemiparesthesia had a complete response and 2 had no change. Radiological evaluations in the post-SRS follow-up period revealed a complete response in 4 patients, partial response in 3 patients, stable disease in 9 patients, and progression in 3 patients. Rebleeding was detected in 1 (5.3%) out of 3 progressive patients at the 17th month, and radiation-induced radionecrosis was detected in the other 2 patients at the 9th and 11th months. There were no procedure-related complications resulting in mortality.

Conclusion: In cavernoma patients with a high risk for surgical intervention and/or patients with high risk for bleeding, SRS is an effective and alternative treatment to surgery.

INTRODUCTION

Cavernomas, also known as cavernous angiomas, cavernous hemangiomas, or cavernous malformations, are low-stream vascular lesions associated with developmental venous anomalies and capillary telangiectasia.[1] Most of them are intracerebral: 80% are supratentorial; 15%, infratentorial; and 5%, spinally located. Further, 40% lesions are asymptomatic.[1,2] Cavernomas are known to have a bleeding tendency, often causing mild bleeding; however, they can lead to serious disability and death in the event of serious bleeding. The ideal management of intracranial cavernomas is microsurgical resection. However, surgery can be progressively troublesome for cavernomas in the basic zones, similar to the brainstem, basal ganglia, or engine zone.[3] Therefore, stereotactic radiosurgery (SRS) has been regarded as an alternative ideal treatment method. Following SRS, there can be cell proliferation, hyalinization, and thinning of the vessel walls, leading to lumen closure, thereby decreasing the bleeding risk.[4–9] In this study, we aimed to present our treatment results of patients with intracranial cavernomas who are treated with SRS by using a CyberKnife® (CK).

MATERIALS AND METHODS

Between April 2010 and December 2017, data from 19 patients treated with SRS in our clinic with the diagnosis of cavernomas were retrospectively evaluated. All these 19 patients were referred to our department for cavernoma radiosurgery because of deep-seated lesions or comorbidities or refusing surgical management. All the patients undergoing SRS had at least one bleeding episode before radiosurgery along with other related symptoms. Before the SRS treatment, informed consents were obtained from all the patients.

A custom thermoplastic mask was used for the immobilization of patients. Further, 1-mm-thick computerized to-

mography and magnetic resonance imaging (MRI) images obtained in the treatment position were combined for contouring. The target volume was defined as the region of mixed-signal changes surrounded by the hemosiderin ring. We did not give any additional margin to make the Planning Target Volume (PTV). We used the MultiPlan Treatment Planning System (Accuray CyberKnife®) software for inverse planning. Real-time images were obtained through X-ray cameras, and we used bony landmarks to define tumor localization. A representative treatment plan of a patient is shown in Figure 1.

After the SRS treatment, MRI imaging and clinical evaluations were performed at 6-month intervals during the first year and then annually. Ethics committee approval was obtained for this study (2018/514/136/2). All the statistical analyses were performed using the SPSS 17.0 software.

RESULTS

The median follow-up time was 82 months (range: 9–100 months). No patient was lost in the follow-up period. Before SRS, 17 (89.5%) patients suffered hemorrhage only once and 2 (10.5%) patients suffered hemorrhages twice. SRS was performed in the median 1 fraction (range: 1–3); further, according to the size of the lesion, the prescription dose ranged from 12 to 21 Gy (median: 15 Gy). The patient and treatment characteristics for SRS are listed in Table 1. Before SRS, the symptoms of the patients included headache in 10 patients (53%), seizures in 4 patients (21%), visual disturbance in 2 patients (10%), and hemiparesis in 3 patients (16%).

Functional outcome

During the post-SRS follow-up period, 6 out of the 10 patients with a headache had a complete response, 3 patients had a partial response, and 1 patient had no response. Further, 3 out of the 4 patients with seizure had a partial response and 1 patient had a stable response in seizure frequency. Furthermore, 1 out of the 2 patients with vision problems had a complete response and 1 had no change.

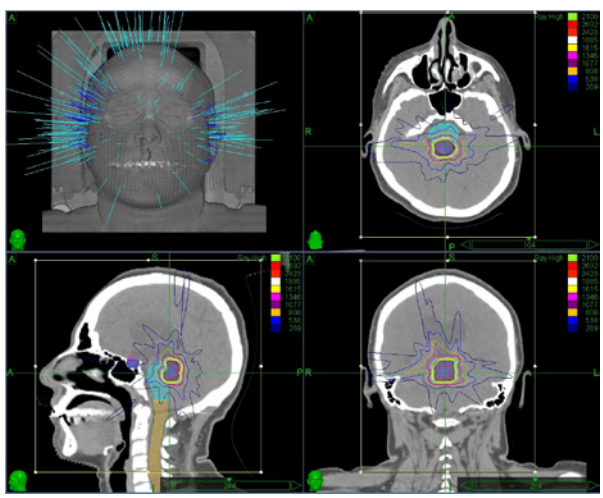

Figure 1. Treatment plan for a patient with cavernoma.

Table 1. Patient and treatment characteristics

	n (%)
Gender	
Male	7 (36.8)
Female	12 (63.2)
Age, median (range)	45 (31–71)
Lesion location	
Basal ganglion/thalamus	5 (26.3)
Frontal lobe	5 (26.3)
Cerebellum	3 (15.9)
Temporal lob	2 (10.5)
Parietal lob	2 (10.5)
Brainstem	2 (10.5)
Symptoms	
Headache	10 (53)
Seizures	4 (21)
Visual disturbance	2 (10)
Hemiparesis	3 (16)
Pre-CK hemorrhagic events	
1	17 (89.5)
2	2 (10.5)
Total dose, median (range)	15 (12–21)
Median Maximum Dose (Gy)	19.23
Fractions number, median (range)	1 (1–3)
Treatment volume (cc), median (range)	1.7 (0.2–7.4)
Isodose level (%), median (range)	83 (73–93)

Also, 1 out of the 3 patients with hemiparesthesia had a complete response and 2 had no change.

Radiological outcome

Radiological evaluations in the post-SRS follow-up revealed a complete response in 4 patients, partial response in 3 patients, stable disease in 9 patients, and progression in 3 patients. Rebleeding was detected in 1 (5.3%) out of 3 progressive patients at the 17th month and radiation-induced radionecrosis was detected in 2 other patients at the 9th and 11th months. These patients received conservative treatment including steroids, analgesics, and anticonvulsant drugs. There were no procedure-related complications resulting in mortality.

DISCUSSION

Although the main treatment is surgery in hemorrhagic and symptomatic patients who have technically accessible cavernomas, the role of SRS has gained importance in symptomatic patients with a high risk for surgery. The most important problem is the lack of prospective, randomized controlled trials evaluating the efficacy of SRS, particularly in high risk surgical patients. In addition, it is not possible to randomize a group of patients who cannot be operated on the follow-up arm for performing such a study. Therefore, several studies conducted on this subject have suffered from defective retrospective evaluations.

In several studies, it has been emphasized that caution should be exercised when treating with SRS, and the most important issue discussed has been radiation-related complications after SRS.[10–13] Despite the administration of similar doses, it is reported that the likelihood of side-effects is higher than those in patients who underwent SRS due to arterial-vascular malformations (AVM).[11–14] Another potential disadvantage is that the bleeding risk does not disappear until vascular obliteration occurs. Also, a close clinical follow-up is necessary since it is not possible to reveal complete obliteration by angiography. In spite of all these problems, SRS is the alternative treatment for surgery in patients that have a high risk for bleeding and in patients who cannot undergo surgery.

Certain recent studies have suggested an early application of SRS due to a possible bleeding risk.[6,14] This recommendation is valid in cases with technically unreachable cavernomas who are more likely to have a risk of death due to recurrent bleeding than those due to SRS. In addition to the decrease in the bleeding risk after SRS, a decrease in the seizure frequency has been reported.[6,15–19]

Despite all the technological developments in the planning and implementation of radiotherapy, side-effects cannot be prevented. It has been reported that the rate of permanent complications after cavernoma radiosurgery can be as high as 41%.[4,5,10–13,20]

Considering this high complication rate, the importance of choosing an appropriate patient for SRS has become imperative. The patient's age, presentation, clinical features, lesion localization, and surgery risk should be taken into consideration during patient selection. Family history and whether there is bleeding before or not is clinically important for assessing the bleeding risk.[9,21–23] Kondziolka et al.[22] and Aiba et al.[23] reported the annual increase in the bleeding risk as 0.6%–4.5% and 0.4%–23%, respectively, if there is no intervention in patients diagnosed with cavernomas. In patients with cavernomas who have been followed-up without any treatment, Li et al.[24] reported that the annual bleeding rate was 18.7% in patients with focal neurological deficit and 12.2% in those without this deficit. This rate is 5% in patients without bleeding at the time of diagnosis. It has been reported that as time passes during the follow-up period, the bleeding risk decreases in patients with focal neurological deficits (12.4%) and the annual bleeding risk increases in patients with no bleeding at the time of diagnosis.

The annual bleeding risk has been reported to decrease from 17.5% to 4.5% in 2 years after SRS.[10] Reduced symptomatic bleeding rates from 8.8% to 1.1% in the first 2 years in patients treated with SRS using a Gamma Knife has been reported.[4] In a more recent study that includes 103 patients who were treated with SRS using a Gamma Knife, it was demonstrated that the annual bleeding rate was 10.8% in the first 2 years after treatment and the annual bleeding rate was 1.06% thereafter.[9] However, it has been understood that the bleeding rate of untreated cavernous malformations exhibits the clustering of all hemorrhages. In this context, the rebleeding rate from untreated cavernous malformations has been initially found to be high. In the first 2.5 years, while the monthly bleeding rate is 2%, the cumulative incidence of rebleeding is 14% during the first year. This rebleeding risk decreases to less than 1% per month after the passage of 2–3 years after the initial bleeding.[25]

The SRS results in cavernomas are controversial. In some publications, it has been reported that there is no decrease in the bleeding risk in deep settlements, such as diencephalon or brain stem, but an increase in bleeding and sequelae due to radionecrosis.[10,20,26,27] In our study, after SRS treatment with median of 15 Gy, 1 (5.3%) patient developed bleeding and 2 (10.5%) patients developed radionecrosis.

CONCLUSION

As a result, the first treatment option for cavernoma is surgery. In our study, a complete radiological response was obtained in 21% patients after median of 15 Gy SRS (8-21), and 42.1% patients had a symptomatic complete response rate. In cavernoma patients with high risk for surgical intervention and/or patients with a high risk for bleeding, SRS is an alternative treatment to surgery.

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Ethics Committee Approval

Informed consent was obtained from all the patients and the study was approved by the Ethics Committee of Kartal Dr. Lütfi Kırdar Training and Research Hospital No:2018-514-136-2 (28.08.2018).

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: G.Y., N.I.; Design: G.Y., N.I.; Supervision: H.D., N.I.; Materials: H.D., Ş.G.; Data: F.T., Ş.G.; Analysis: A.Ö., F.T.; Literature search: G.Y., N.I.; Writing: G.Y., A.Ö.; Critical revision: N.I., G.Y.

Conflict of Interest

None declared.

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Beyin Kavernomlarında Stereotaktik Radyocerrahi: Tek Merkez Deneyimi

Amaç: Bu çalışmada, CyberKnife kullanarak stereotaktik radyocerrahi (SRC) ile tedavi edilen intrakranial Kavernom tanılı hastaların tedavi sonuçlarını sunmayı amaçladık.

Gereç ve Yöntem: Nisan 2010–Aralık 2017 tarihleri arasında kliniğimizde Kavernom tanısı ile SRC uygulanan 19 hastanın verileri geriye dönük olarak değerlendirildi.

Bulgular: Medyan takip süresi 82 (9–100) aydı. SRC tedavisi medyan 1 fraksiyonda (1–3) yapıldı ve lezyonun büyüklüğüne göre reçetelenen doz 12–21 (medyan 15) Gy arasındaydı. SRC sonrası takip döneminde, baş ağrısı olan 10 hastanın altısında tam yanıt, üçünde kısmi yanıt elde edildi ve birinde ise yanıt alınamadı. Nöbet öyküsü olan dört hastanın üçünde kısmi yanıt, birinde ise nöbet sıklığında stabil yanıt elde edildi. Görme problemleri olan iki hastanın birinde tam yanıt saptanırken birinde ise değişiklik saptanmadı. Hemiparestezisi olan üç hastanın birinde tam yanıt saptanırken ikisinde ise değişiklik saptanmadı. SRC sonrası radyolojik olarak dört hastada tam yanıt, üç hastada kısmi yanıt, dokuz hastada stabil hastalık elde edilirken üç hastada ise progresyon saptandı. Progresyon tespit edilen üç hastanın birinde 17. ayda (%5.3) tekrardan kanama, diğer iki hastada ise dokuzuncu ve 11. aylarda radyonekroz tespit edildi. Mortalite ile sonuçlanan işlemle ilgili herhangi bir komplikasyon görülmedi.

Sonuç: Cerrahi müdahale için yüksek risk taşıyan kavernom tanılı hastalarda ve/veya özellikle kanama riskinin yüksek olduğu hastalarda SRC tedavisi cerrahiye alternatif etkili bir tedavi yöntemidir.

Anahtar Sözcükler: Cyberknife, kanama; kavernom; sterotaktik radyocerrahi.