Acta Neurochirurgica (2020) 162:839–844
https://doi.org/10.1007/s00701-020-04251-7

ORIGINAL ARTICLE - FUNCTIONAL NEUROSURGERY - OTHER

LINAC radiosurgery for glomus jugulare tumors: retrospective – cohort study of 23 patients

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Received: 2 April 2019 / Accepted: 28 January 2020 / Published online: 11 February 2020

Abstract

Background Glomus jugulare tumors (GJTs) are uncommon and locally disruptive tumors that usually arise within the jugular foramen of the temporal bone. Surgery was the treatment of choice up until recently. In the last decades, however, radiosurgery has surfaced as a promising alternative treatment by providing excellent tumor control with low risk of cranial nerve injuries. Our aim was to examine the results of radiosurgery specifically, linear accelerator stereotactic radiosurgery (LINAC SRS) for GJT treatment. We hypothesized that radiosurgery will reduce the size of the tumor and improve neurological symptoms.

Design and method Between January 1, 1994 and December 31, 2013, 30 patients with GJTs were treated in Sheba Medical Center using LINAC SRS treatment. Comprehensive clinical follow-up was available for 23 patients. Sixteen patients were female and seven males with a median age of 64 years, with a range of 18–87 years. In 19 of the patients, LINAC SRS was the primary treatment, whereas in the remaining four cases, surgery or embolization preceded radiosurgery. The median treated dose to tumor margin was 14 Gy (range 12–27 Gy), and the median tumor volume before treatment was 5 ml (range 0.5–15 ml).

Results Following the LINAC SRS treatment, 14 of 23 patients (60%) showed improvement of previous neurological deficits, nine patients (40%) remained unchanged. At the end of a follow-up, tumor reduction was seen in 13 patients and a stable volume in eight (91% tumor control rate). Two cases of tumor progression were noted. Three patients (13%) had post- SRS complications during the follow-up, two of which achieved tumor control, while in one the tumor advanced.

Conclusions LINAC SRS is a practical treatment option for GJTs, with a high rate of tumor control and satisfactory neurological improvement.

Keywords Linear accelerator stereotactic radiosurgery (LINAC SRS) · Glomus jugulare tumor (GJT)

Introduction

glomus jugulare tumors (GJT), also referred to as paragangliomas, are rare (0.6% of the head and neck tumors), highly vascular tumors and indolent. They usually arise within the jugular foramen of the temporal bone [2, 16, 26]. GJT can derive from several glomic chemoreceptor locations: the carotid body (glomus caroticum), the internal jugular vein (glomus jugulare), the vagus nerve (glomus vagale), or the tympanic cavity (glomus tympanicum) [26]. Several classification systems were developed in the evaluation of GJT and are employed for surgical planning and follow-up of patients. The classification systems of Glasscock–Jackson [16] and Fisch [6] are the most widely used.

GJTs is more prevalent among females than males and among adults in the sixth and seventh decades of life than other age groups. They are slow growing tumors [17] and the interval between the appearance of symptoms and the diagnosis varies from 6 to 15 years. Pulsatile tinnitus, conductive hearing loss, and vertigo are the most common presenting symptoms. Additionally, patients with GJT suffer from cranial nerve deficits (V, VII, IX-XII), headache, and Otorrhea [12, 36].

Until two decades ago, surgery was the first line of treatment for GJT [27], while radiotherapy was offered to patients with poor performance status or as an adjunctive treatment.

This article is part of the Topical Collection on *Functional Neurosurgery – Other*.

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However, incomplete resection, high morbidity rates, and greater risk of cranial nerve injuries resulted in surgery falling out of favor in the treatment of GJTs. The arrival of radiosurgery [both Gamma Knife (GK) and linear accelerator (LINAC) stereotactic radiosurgery (SRS)] introduced a new treatment option in the care of GJTs by reason of lower morbidity and mortality, all while accomplishing marked tumor control [1, 3–5, 7–11, 14, 18–25, 29–35, 37, 38, 40, 41]. Radiosurgery reported to have 0% mortality and 8% treatment related morbidity, compared with more than 1% mortality and 22%–59% morbidity rate associated with surgery [15, 39].

The aim of this study was to retrospectively evaluate the preliminary results in a series of 23 patients treated at the neurosurgery department in Sheba Medical Center for GJT using linear accelerator stereotactic radiosurgery (LINAC SRS). A multi-site prospective randomized study was impossible to establish, considering this tumor grows slowly, uncommon and can easily be overlooked. Therefore, a retrospective case series study was conducted.

The hypothesis was that patients treated with radiosurgery will demonstrate reduced tumor size and improved their neurological symptoms.

Materials and methods

Patients

Between January 1, 1994 and December 31, 2013, 30 patients with GJT underwent treatment at the neurosurgery department in Sheba Medical Center. All patients were treated using LINAC SRS either as primary or complementary treatment. Clinical outcome for retrospective analysis was determined using medical records and telephone interviews. Seven patients were part of medical tourism and, therefore, were lost to follow-up after their treatment despite attempts to contact the patients in their countries. Collected data included patient demographics (age, gender), disease characteristics, SRS treatment, and dosimetric parameters. Comprehensive follow-up was available for 23 patients with a median follow-up of 5 years (range 1–10 years). Male to female ratio was 7:16. Median age was 64 years, with a range of 18–87 years. Most patients presented with conductive hearing impairment ($n = 16$) and pulsatile tinnitus ($n = 11$). Conductive hearing impairment was documented by an otolaryngologist examination. Nine patients displayed cranial nerve deficits other than the acoustic nerve. Among those nine, five patients had hoarseness and dysphagia (X cranial nerve), four patients with tongue atrophy (XII cranial nerve), three patients with mild unilateral facial weakness (VII cranial nerve), and one patient presented with paralysis of muscles innervated by the XI cranial nerve [Table 1].

Table 1 Presenting features and symptomatic response to SRS

Symptoms	Pre-SRS	Post-SRS improvement	Post-SR Morbidity
Hearing loss	16	5	1
Pulsatile tinnitus	11	5	–
Cranial nerve deficits (V, VII, IX-XII)	9	3	1
Vertigo	3	2	–
Headache	5	4	1
Otorrhea	2	1	–

This study was approved by the Internal Review Board – Helsinki committee of Sheba Medical Center.

Procedure

All patients received treatment with a linear accelerator (LINAC) based system. For the first cases, multiple isocenters with cylindrical collimators were used for target coverage. Since 1999 irradiation was carried out with a computer-driven mini-multileaf collimator (mMLC) using multiple, non-coplanar dynamic arcs, as described in [36]. Briefly, the dosimetry planning was done using the best available MRI modality available (currently contrast-enhanced T1 3D with fat suppression, and FIESTA [Fast Imaging Employing Steady-state Acquisition] sequences fused to a stereotactic computed tomography (CT) scan obtained on the day of treatment. The patient's head was immobilized with a stereotactic frame and in later years with a thermoplastic mask using the ExacTrac localization and tracking system for frameless radiosurgery (Brainlab, Germany). In this series, the median dose to tumor margin was 14 Gy (range 12–27 Gy), and the median tumor volume was 5 ml (range 0.5–15 ml). The median prescription isodose was 80% to the lesion margins. All patients were discharged on the same day after completion of the treatment.

LINAC SRS was the primary treatment in 19 patients. In our cases, surgery (two cases) or embolization (two cases) preceded radiosurgery treatment.

Statistical methods

Dependent variables: tumor volume, neurological symptoms (hearing loss, tinnitus, cranial nerve deficits, vertigo), and other symptoms such as headache and otorrhea. Independent variables: LINAC SRS with or without preceding treatment. Tumor volume was calculated and their symptoms were questioned from the time of treatment until the last follow-up. We used the Kaplan–Meier estimator to estimate the

fraction of patients that improved after LINAC SRS treatment. The statistical calculations were performed with the MedCalc software (version 12.2.1.0, Mariakerke, Belgium).

Results

Demographics and tumor characteristics

The median follow-up was 60 months (range 9–120 months). A clinical and radiological follow-up was done together at the same time. In accordance with the literature [13, 31], most of the patients were female (70%). The median age was 64 years (range 18–87 years). The average tumor volume at the time of treatment was 5 cm^3, varying between 0.5 and 15 cm^3. SRS was the initial treatment for the majority of the patients (80%), whereas two patients (10%) underwent surgery prior to the SRS treatment and an additional two patients (10%) received an angiographic embolization treatment prior to SRS.

Tumor control

Tumor shrinkage was observed in 13 patients, and an unchanged volume was detected in eight patients at the end of their follow-up. Therefore, the total tumor volumetric control rate was 91% [Fig. 1] with a 14 Gy median radiation dose to tumor margin (range 12–17 Gy). Two cases of tumor progression were noted. One of the progression cases received a second LINAC SRS with a higher dose to tumor margin of 18 Gy, while the other underwent an open resection. An example for radiological follow-up is shown in [Fig. 2].

Symptomatic control

Clinical response to the LINAC SRS treatment was achieved in 14 patients (61%) with an overall symptomatic control rate of 87% [Fig. 1]. We defined symptomatic response as improvement or disappearance of these symptoms after SRS treatment. Nine patients (39%) remained unaffected. Unaffected was the absence of symptoms or worsening of symptoms. The most significant improvement was noted in patients who experienced headaches: four out of five patients (80%) recuperated considerably after SRS treatment. The improvement in hearing and the cranial nerve deficits were objectively monitored with the relevant examination, while tinnitus, vertigo, otorrhea, and headache were subjectively reported by the patients and written on the follow-up.

Clinical deterioration post –LINAC SRS treatment was detected in three patients. The three patients (13%) deteriorated within a median of 24 months of treatment (range 24–48). One patient presented with a new – onset headache, while another had a worsening of hearing. This single case of hearing impairment reinforces known data that the risk of hearing loss is low post-SRS treatment in GJT [28]. Despite clinical decline, both cases are followed by tumor volumetric control. However, the third patient, featuring VI cranial nerve palsy, had tumor progression [Table 1].

Discussion

This retrospective-cohort study represents follow up of 23 patients with a median of 5 years investigating the role of LINAC SRS as a treatment option for glomus jugulare tumors.

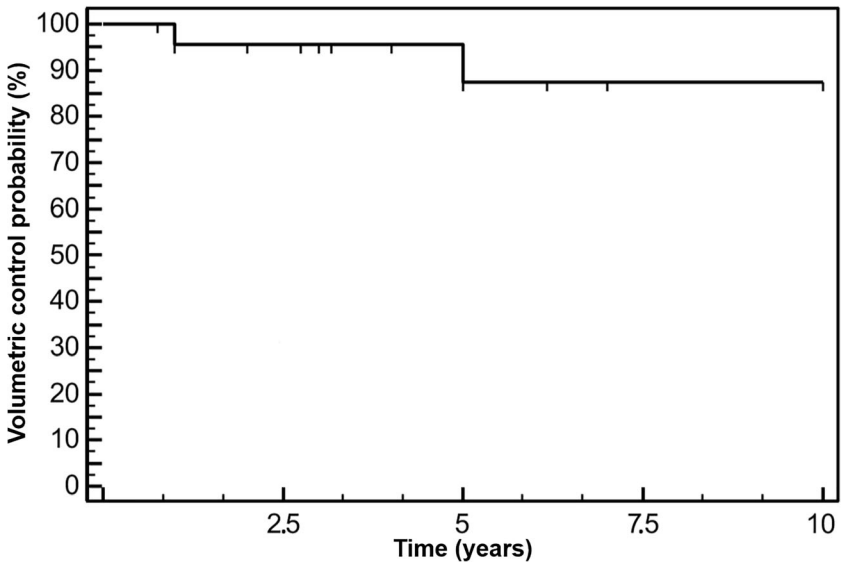

Fig. 1 Kaplan–Meier overall tumor volumetric control curve in the set of 23 GJT Patients

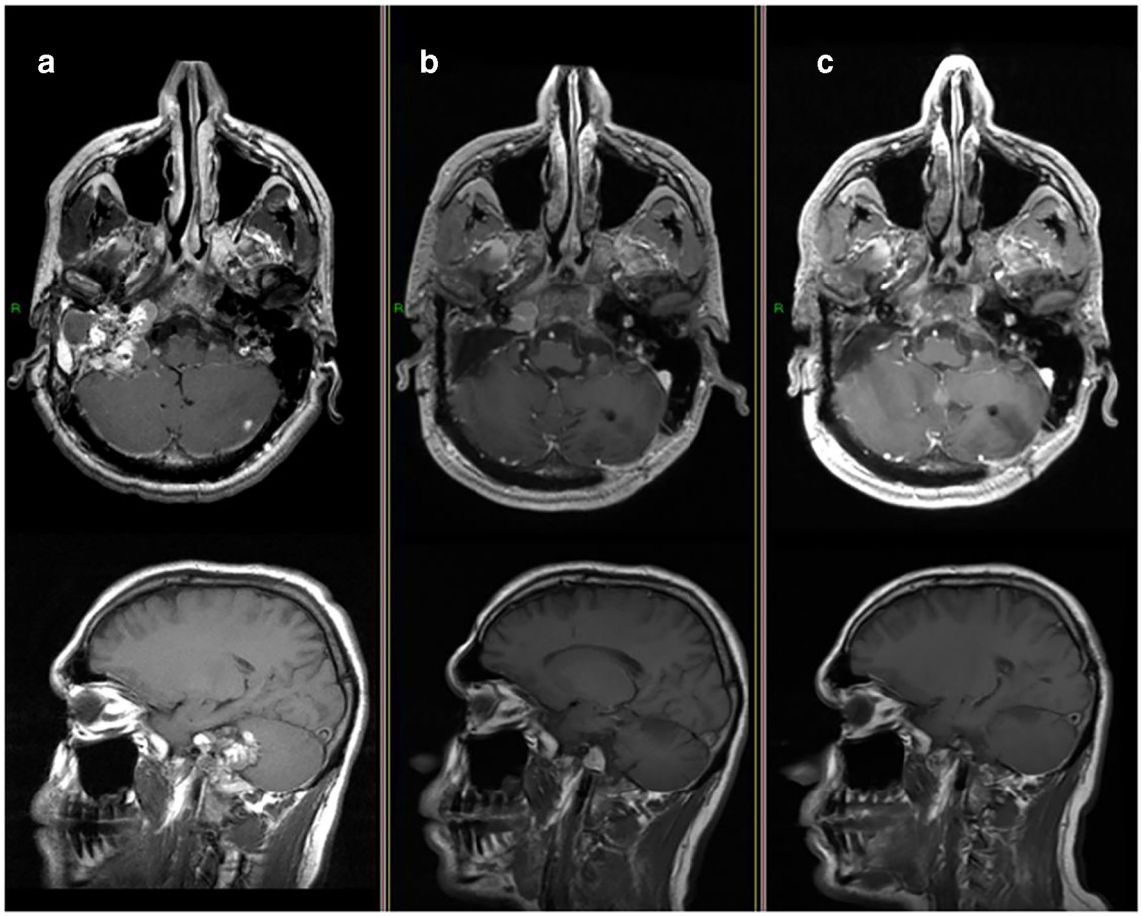

Fig. 2 Longitudinal T1-weighted, with and without gadolinium enhanced MRI follow-up of a 31-year old female with a right-sided GJT. A. pre-LINAC SRS treatment. B. Tumor shrinkage is demonstrated 5 years post-LINAC SRS treatment. C. A complete remission is established 10 years post-LINAC SRS treatment

Treated with a 14 Gy median radiation dose to tumor margin, tumor control was detected in 21 patients and represents a total volumetric control rate of 91%. Clinical response, defined as improvement or disappearance of manifesting symptoms, was achieved in 14 patients (61%) with an overall symptomatic control rate of 87%. The treated group in this study was small (30 patients), of which seven (23%) were unavailable for follow-up. Thus, we are drawing conclusions from a limited study group sample. Additionally, the symptoms were reported subjectively by the patients and are not measured objectively. These two points reflects the limitations of our study.

In a review of 69 studies and 1084 patients treated surgically compared to 254 treated with radiosurgery, Suárez et al. [37] showed that radiosurgery achieved better tumor control rates than surgery (89.6% versus 83.7%) and lower toxicity rate (11% vs 26%). However, the majority of these studies investigated Gamma Knife and not LINAC SRS. Similar results are reported in [12, 13] emphasizing the advantage of SRS in the treatment of GJT. Majority of the publications are on Gamma Knife radiosurgery in the treatment for GJT. Out of 11 series reviewed [4, 8, 14, 18, 20, 21, 25, 33–35, 40], 465 patients underwent Gamma Knife radiosurgery treatment. Follow-up was ranged between 10 and 118 months achieving tumor control rate of 53–100% and symptoms control rate of 40–100%. Thus, Gamma Knife has an excellent tumor reduction and symptom control rates as well as [Fig. 1]. In our institute, we use LINAC- SRS in the treatment of GJTs.

Interestingly, the median dose to tumor margin in Gamma Knife in most of the 11-series mentioned [4, 8, 14, 20, 21, 25, 33–35, 40] is between 15 and 26 Gy, higher doses than our 14 Gy suggested median dose.

The advantage of SRS in GJTs has not been previously researched in Israel; therefore, our research is an addition to the literature. However, due to the small sample size and short follow-up duration, increasing the number of cases and follow-up duration is required. We are continuing our follow up on the patients and an even longer follow-up duration will be the next step in the evaluating the value of LINAC –SRS.

Conclusion

This study found that LINAC SRS is a potential treatment option for GJT. It achieves high rate of tumor control and

neurological improvement with low rates of treatment-related toxicity. Therefore, it offers an important layer in the LINAC SRS modality by demonstrating its treatment effectiveness.

Compliance with ethical standards

Conflict of interest The authors declare that the research was conducted in the absence of any involvement with organization or entity with any financial interest or non-financial interest.

Statement of human rights All procedures performed in the studies involving human participants were in accordance with the ethical standards of the Helsinki and Sheba Medical center research committee (approval number 3207–16-SMC).

For this type of study formal consent is not required.

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