Stereotactic radiosurgery for the treatment of glomus tumors: long-term results

Radiocirurgia esterotáctica para o tratamento de tumores glômicos: resultados a longo prazo

Despite of being a slow growing hypervascular benign tumor, Glomus Jugulare is a challenge for the neurosurgeon, due to its complex localization and relation to the cranial nerves. Microsurgery alone or associated with radiation therapy have been used for decades, and is frequently associated with severe neurological sequelae. In the last decade, radiosurgery has been employed for tumor growth control, but long term follow up is still missing. Objective: The objective is to analyze the late results of radiosurgery alone in the treatment of glomus jugulare tumors. Material and Methods: From a series of 596 patients submitted to radiosurgery at our institution, seven patients with eight complex glomus jugulare tumors were selected. All patients were submitted to radiosurgery, 4 men and 3 women, age 20 to 78. The median volume of the lesions was 12.56 cc (range from 3.06 to 19.6 cc). The primary symptoms were pain and tinnitus, one patient had facial palsy before the initial treatment. Two patients were submitted to surgery before radiosurgery, and both developed lower cranial dysfunction, one of them underwent to conventional radiotherapy before radiosurgery. The patients received a single dose of 18 Gy to 20 Gy, using a LINAC with a conformal shaped beam collimator. Results: All patients had important pain relief (no more medication necessary) and a follow up of 30 to 96 months showed slight reduction in all of eight lesions. No patient suffered a new lower cranial nerve deficit after conformal shaped beam radiosurgery. Conclusion: Despite of the small number of cases, long term follow-up showed that radiosurgery is safe and effective to provide tumor growth control and to reduce pain associated with glomus jugulare tumors.

Key-words: Glomus jugulare tumor, jugular foramen, Stereotactic radiosurgery, Fractionated stereotactic radiotherapy, linear accelerator.
INTRODUCTION

Glomus jugulare tumors are slow-growing benign neoplasms of vascular origin, usually located at the skull base, and almost always associated with the lower cranial nerves. The historical proposal for treatment has always been a complete anatomical resection of the lesion, which is not always possible without leaving serious sequelae.

Due to the lack of success of surgery and the inefficiency of chemotherapy, radiotherapy appeared as a complementary form of treatment. It has been used for many years, especially in cases where there is a post surgical residual lesion or recurrence and, less frequently, as a first therapeutic option. Its use has been widely criticized, especially by the neurosurgical community, whose concern is to obtain a complete resection of the lesion and not just to promote tumor control with the use of radiation.

Towards the end of the last century, with the confirmation of excellent medium and long-term results for Stereotactic Radiosurgery (SRS) in different benign neoplasms, some publications appeared with the use of this technique in cases of glomus tumors. As it is a relatively uncommon disease, publications related to radiotherapy as well as radiosurgical series on glomus tumors contain few cases. Although the initial results of SRS have been quite promising, long-term confirmation of its efficiency and safety are necessary.

We had the opportunity to follow a series of patients with glomus tumors who had undergone stereotactic radiosurgery and we herein present the results obtained in relation to lesion control, efficiency, safety and possible side effects.

MATERIAL AND METHODS

A review was carried out of the records of our series of patients submitted to treatment at the Department of Stereotactic Radiosurgery, Araújo Jorge Hospital, of the Goiás Cancer Association, Brazil, from February 2000 to December 2007. Patients included in the study underwent Stereotactic Radiosurgery or Fractionated Stereotactic Radiotherapy (FSR) as initial treatment or as a complement to surgery, with a minimum two-year follow-up period. Patients were followed with clinical an imaging evaluation.

Out of 596 patients treated in our department, 7 patients harboring eight glomus tumors in different locations were found. There were four males and three females, one of whom presented with two distinct lesions. The patients ranged from 20 to 78 years of age. The volume of the tumors varied between 3.06 and 19.6 cc, with an average volume of 11.52 cc.

These lesions were found in multiple locations, with jugular, tympanic and carotid involvement, as classified by Glasscock & Jackson. The cases can be evaluated in Table 2.

<table>
<thead>
<tr>
<th>Table 1: Glasscock &amp; Jackson classification of Glomus Jugulare tumors</th>
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<tbody>
<tr>
<td>Type I</td>
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<tr>
<td>Type II</td>
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<td>Type III</td>
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<p>| Table 2 |
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<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Symptoms</th>
<th>Classification</th>
<th>Dose</th>
<th>Volume</th>
<th>Follow-up</th>
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<td>78</td>
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<td>78m</td>
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<td>Hoarsnes</td>
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<tr>
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<td>47</td>
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<tr>
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<tr>
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<td>73</td>
<td>Facial palsy</td>
<td>Type III</td>
<td>60Gy</td>
<td>17.69</td>
<td>30m</td>
</tr>
</tbody>
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Submitted to surgery, radiation therapy, Stereotactic Radiation Therapy.

The most important symptom in all of the patients but one was pain which was frequently refractory to medical therapy. This
was associated with tinnitus in three cases and hoarseness and facial paralysis in two.

Two patients had previously undergone surgical treatment but without complete resection resulting in paralysis of lower cranial nerves. One suffered facial paralysis and IX, X and XI nerves were left paralyzed in the other. The former had also undergone conventional radiotherapy with a total dosage of 60 Gy, and as the lesion progressed after the treatment the patient was referred to radiosurgery. These were the only cases of a confirmed histopathological diagnosis. In the other five cases the diagnosis was based on computerized tomography and cranial magnetic resonance imaging, with classical findings.

The patients underwent SRS and FSR using a Linear Accelerator (Linac 600C, Varian Inc®, Palo Alto, California) in conjunction with a micro multi-leaf collimator and BrainLaB® (Heimsstetten, Germany) planning system.

The radiosurgery technique has already been described elsewhere. It consists of fixing a stereotactic ring to the skull under local anesthesia, obtaining computed tomography (CT), transferring the images to a workstation, fusing with a previously acquired magnetic resonance imaging (MRI), target and structures at risk definition, treatment planning and isodose calculation, using either multiple conformational fields, from 11 to 18 in 6 cases, or conformal arcs (five in 1 case). A dose of 18 to 20Gy was prescribed, with the 80% isodose line always covering the lesion.

After treatment, the patients were followed with imaging control at the first, third and sixth months after treatment and then bi-annually according to its availability. The concern throughout the follow-up was to notice any improvement or worsening of the symptoms and imaging changes of the lesion.

The clinical follow-up of the signs and symptoms of the patients in the post-radiosurgical period along with the findings of serial images show that the results are promising.

The follow-up lasted for a maximum of 96 months and a minimum of 35, or 60.8 months on average, with the exception of the fractionated stereotactic radiotherapy case, which lasted for 30 months.

In six patients with seven lesions, pain was the primordial and most debilitating symptom, with five patients needing opioids before treatment. Pain was totally relieved in all patients and only two patients occasionally presented slight pain, controlled by regular analgesics. Relief of the painful symptoms was mainly obtained progressively after the third month with an occasional short-lived relapse, easily controlled with analgesics.

The tinnitus experienced by three patients continued unchanged during the follow-up period.

Cranial nerve function was clinically evaluated in all patients and no new lesions appeared. The previous cranial nerve deficits, present in three patients, one caused by the lesion and two developed after microsurgery, remained unchanged.

A twenty-year-old female patient had bilateral lesions in the mastoid region. The left side lesion, with a volume of 19cc, was very symptomatic causing severe pain managed just with opioids. As it was the first case to be treated, it was decided to only treat the symptomatic lesion, and observe the contralateral one. After six months, the patient was already feeling pain relief and not taking medication. She was lost on follow-up and only returned because she started with pain in the contralateral mastoid region. In the 57th month of follow-up, a new MRI was performed showing a slight reduction in the treated lesion and considerable progression of the contralateral lesion. The latter lesion was then treated, and at the last follow-up, after 96 and 39 months respectively, the patient was asymptomatic and the lesions have slightly decreased in size.

At the last time they were contacted, all seven patients indicated satisfaction with the treatment that had been used.

Imaging control indicated no significant changes in the lesion patterns, in T1, T2 and FLAIR sequences. The most considerable radiological change was a slight decrease in the volume of the lesions (Figure 1).

Case 1. Left. Bilateral lesion before radiosurgery on the left side. Center. Slight reduction of the left side, with grow of the contralateral lesion. Right. Important reduction on both lesions.

Although not a common tumor, glomus tumors are the second most frequently found neoplasm of the temporal bone and are the most common type found in the middle ear, with a marked female predominance, of up to 6:1.
The ideal treatment for any solid tumor, whether benign or malignant, in the vast majority of the cases involves surgical resection, if possible with free margins. In the case of neurosurgery this is desirable but not always possible. The glomus tumor, because of its nature and complexity, is a classical example of this situation.

Simple observation\(^4\), radical surgery\(^{17,34}\), radiotherapy\(^6\) and most recently radiosurgery\(^9,11,20,25,29,33,37\) are the current options for treating this disease.

Since it is a benign disease and develops slowly, certain authors suggest that clinical follow-up is the best option, especially in cases of very elderly patients, with clinical comorbidities and in asymptomatic cases. Van der Mey\(^4\), who evaluated 108 patients over a 32 year follow-up period, suggested just a follow-up, because of the high morbidity rate after surgery of lesions at the base of the skull. After a fine review in a series of 53 patients, Brewis\(^5\) found 100 metastases in the bones, lungs and lymphatic system. This finding obliges us to reconsider if glomus tumors are really benign, and if we can afford to merely observe this lesions. In our twenty-year-old patient, with bilateral lesions, a considerable growth after observation during a period of 57 months was documented.

Despite all the technological development of neurosurgery, and adjuvant therapies, such as embolization\(^39\) and neuronavigation, the surgical treatment of glomus tumors is still associated with high morbidity and low resolution levels when a complete resection is sought, even in very specialized centers. In a series of 38 patients, Al-Mefty\(^1\) proposed complete resection in 28 and achieved it in 24, at the cost of various complications. Other authors have suggested surgery. In reviewing 87 cases of operated patients, Kollett\(^19\) achieved 78% complete resection, with recurrence and progression in almost 20%. Jackson\(^41\), who evaluated 182 cases, achieved resection in 85% with an incidence of new lesions in lower cranial nerves between 21 and 35%. Watkins\(^41\) reviewed 61 cases, where he reached total or subtotal resection in 67%, with two post-operative deaths. Borba\(^4\) and Ramina\(^34,35\) obtained excellent results in relation to resection, but all with cranial nerve sequelae, liquoric fistula or death. In our series, the two cases which had been operated on presented cranial nerve lesions. One had a permanent lesion of the facial nerve and the other had IX, X and XI nerves deficits.

Results of glomus tumor surgery are a controversy in the literature, some series reaching high rates of complete resection and others lower success rates. What is common in the majority of published series is the high morbidity rate in relation to new lesions in lower cranial nerves, which in many cases have severe consequences.

Radiotherapy started to be used in the end of the 50’s, as an alternative or nearly always as a complement to surgery. Carrasco and Rosenmann\(^3\) in a series of 299 cases, described residual lesions in 11% of the cases, while recurrence was identified in 8% and death due to progression in 6%. Dall’Igna\(^2\) published a recent review of his cases, after an average eleven-year follow-up with an excellent control and low complications. There is also no consensus regarding to the ideal dose, which varies between 35 and 60 Gy, thereby making an evaluation and comparison of the results even more difficult. In one of our cases, a female patient had previously been treated with radiotherapy and despite having received 60 Gy, the disease progressed in 24 months. With the worsening of the symptoms radiosurgery was chosen as a better option than simple observation, since the patient refused further surgery. The lesion has been controlled, painful symptoms relieved and no long-term radiation induced side-effects were observed.

In the middle of the last century, Lars Leksell\(^23\) introduced the concept of Stereotactic Radiosurgery (SRS), because he believed that a higher, more concentrated and better aimed dose of ionizing radiation could cause more efficient tissue destruction. SRS is a fine, highly efficient and precise technique of applying high ionizing radiation doses to a target volume, with minimal impairment of adjacent structures.

The results obtained using SRS were initially promising\(^22\). More recently with the development of imaging technology and the introduction of CT scan, MRI and new radiosurgical equipments, this technique is now widespread and is widely used for the treatment of malignant and benign tumors, arteriovenous malformations as well as for functional procedures. Today it is a fundamental therapeutic tool for the neurosurgeon.

Glomus tumors have become an ideal target for stereotactic radiosurgery because of their vascular and benign nature, their precise and well-delineated limits obtained by imaging and their complex microsurgical management.

The first publication on the use of radiosurgery was made by Pendel\(^12\), and then followed by Hughes-Davies\(^15\) and Kidu\(^18\), who used a Gamma Knife. Radiosurgery based on a linear accelerator has also been used with promising results by Maarouf\(^29\) and Lim\(^30\) all with similar results.

The main objective of radiosurgery in relation to benign tumors is not to make the lesion disappear but rather to prevent its growth. This leads to an improvement in the symptoms which has already been proved through different long-term studies of various tumors. Since benign tumors usually develop slowly, good short-term results are not so significant, as they could be confused with the natural history of the lesion itself. Short-term results have been promising, but with glomus tumors good long-term results are still scarce. Gerosa\(^11\) has recently presented a series with a 50 month follow-up, using a Gamma Knife, with control of 19 out of the 20 treated lesions. Eustacchio\(^9\) managed to control the condition in 18 out of 19 patients, after an average of 7.2 years of follow-up. Using a
linear accelerator, Lim\textsuperscript{24} obtained control of all 16 lesions after a 60 month follow-up. In our experience, despite the reduced number of cases, we obtained control in all 8 lesions after an average follow-up period of 65 months.

There is also no consensus in relation to the prescribed dose for glomus tumors. It varies between 15 and 17 Gy when using Gamma Knife and between 15 and 25 Gy when using a linear accelerator. We opted for an intermediary dose of 18 Gy, which to us, seems adequate to prevent the lesion progressing and not cause a further lesion in lower cranial nerves. Martin\textsuperscript{30} has recently reported on a series of lesions in the jugular foramen, where a 14 Gy dose was used and succeeded in preserving the functions of the cranial nerves in all the cases where there had been no previous lesion.

Just over 30 publications in the radiosurgery literature, the vast majority using a Gamma Knife, have identified almost a negligible risk of early or delayed damage. Gottfried\textsuperscript{12}, who made the fine comparison between radiosurgical and surgical results, concluded that both treatments are efficient. He states, however, that surgery is only efficient when the whole lesion is removed, which increases the risk of lesions in the cranial nerves, leading to very high morbidity rates. In our experience, and after a long follow-up, there have been no new cranial nerve deficits until the present moment, which leads us to believe even more firmly in the safety of this technique.

In the literature, there are few reports of related complications. A secondary induced neoplasm by radiotherapy in the treatment of glomus tumors was reported by Lustig\textsuperscript{28}, with a very severe outcome. With the advent of fractionated stereotactic radiotherapy, and even with radiosurgery, the spreading of radiation around the lesion is minimal, which would reduce even further the risk of a new tumor, if such a risk existed. Hennzel\textsuperscript{13} has recently presented a series of 17 patients with 100% local control after using fractionated stereotactic radiotherapy. We were only able to use fractionated stereotactic radiotherapy in one female patient, whose condition is under control.

When we compared the long-term results of lesion control of radiosurgery with radical surgery, we noticed that they are quite similar. However, the risk of developing cranial nerve deficits and other complications is notably higher with microsurgery. New therapeutic options are always criticized and it is only time, experience and the presentation of results that will give them validity.

A longer follow-up period with larger series will be available in the literature within a few years, and will be fundamental in proving the efficiency and safety of SRS, as happened with the treatment of acoustic neuromas. Today we believe that the safest form of treating glomus tumors with the lowest risk of complications is stereotactic radiosurgery.

**CONCLUSION**

With the introduction of radiosurgery for the treatment of glomus tumors and the presentation of its short-term results, doubts still remained concerning its long-term efficiency. Now with the appearance of medium and long-term results, such as the data from the present study and from other authors, demonstrating that considerable tumor growth control, and a low risk of toxicity, the classical conception that surgery is the only form of treatment with proven curative results should be reviewed.

**REFERENCES**


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