Am J Otolaryngol xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Am J Otolaryngol

journal homepage: www.elsevier.com/locate/amjoto

Stereotactic radiotherapy in three weekly fractions for the management of vestibular schwannomas

James A. Gallogly, Mejd Jumaily, Farhoud Faraji, Anthony A. Mikulec*

Saint Louis University School of Medicine, Department of Otolaryngology – Head and Neck Surgery, 3635 Vista Ave, 6FDT, St. Louis, MO 63110, USA

ARTICLE INFO

Keywords:
Vestibular schwannoma
Acoustic neuroma
Stereotactic radiotherapy
Radiosurgery
CyberKnife

ABSTRACT

Purpose: This study evaluates the rates of tumor control, hearing preservation and cranial nerve toxicity with the use of CyberKnife stereotactic radiotherapy consisting of 2100 cGy to the 80% isodose line delivered in three weekly fractions to treat vestibular schwannomas.

Materials and methods: Retrospective chart review of vestibular schwannoma patients treated with CyberKnife stereotactic radiotherapy or undergoing watchful waiting between 2006 and 2017 was performed. For inclusion, patients receiving CyberKnife stereotactic radiotherapy must have had pretreatment magnetic resonance imaging and audiography, and 2 follow-up magnetic resonance imaging and audiograms. Watchful waiting patients must have had a minimum of 2 magnetic resonance imaging and 2 audiograms.

Results: Forty patients met inclusion criteria. Twenty-two underwent CyberKnife stereotactic radiotherapy. Eighteen remain in watchful waiting. Crude tumor control was 86.4% at mean radiographic follow-up of 52.3 months. Kaplan-Meier progression-free survival was 76.9% at 5 years. Kaplan-Meier survival from radiographic growth was 61.5% at 5 years. Kaplan-Meier hearing preservation was 17.5% at 5 years. All patients undergoing watchful waiting presenting with serviceable hearing maintained serviceable hearing. Serviceable hearing among CyberKnife stereotactic radiotherapy patients was 42.9% prior to treatment and 14.2% through mean follow-up of 53.7 months. One patient experienced trigeminal nerve toxicity 45 months after SRT. 95.5% of CyberKnife stereotactic radiotherapy patients were complication-free.

Conclusions: Our fractionation regimen provides tumor control consistent with current literature. Hearing outcomes, however, should be discussed with patients prior to CyberKnife stereotactic radiotherapy.

1. Introduction

Vestibular schwannomas (VS) are uncommon, histologically benign tumors that have very low mortality rates but can cause a considerable degree of morbidity. This morbidity is due to factors including mass effect on nearby structures such as the brainstem, intrinsic injury to the affected nerve causing hearing loss, and iatrogenic injury due to radiation or surgery during treatment.

Three main strategies have been discussed in the literature regarding the management of vestibular schwannomas, although there is no established treatment algorithm. The decision to undertake one strategy depends on patient preference and tumor characteristics such as growth rate and size. Watchful waiting is preferred for older patients in whom the risk of complications from surgery is increased, and in patients whose tumors are small and stable or whose hearing is still serviceable. The other two strategies are microsurgery, which is often used for large tumors and younger patients, and stereotactic radiotherapy (SRT). SRT using the Gamma Knife (Elekta AB, Stockholm, Sweden) or LINAC-based CyberKnife (Accuray Incorporated, Sunnyvale, California, USA) systems have been able to achieve an excellent tumor growth control rate ranging from 91% to 100% in small tumors [1–4], but hearing preservation rates are much more variable and are heavily dependent on the length of follow-up. With respect to microsurgery, six prospective interventional studies comparing microsurgery to SRT concluded that SRT demonstrated similar progression-free survival with a significantly lower risk of neurological complications [5]. Considering that small tumors account for most lesions, there is a strong recent emphasis on evaluating SRT outcomes.

Although there are several studies showing favorable hearing outcomes with radiation therapy compared to untreated controls, the natural progression of the schwannoma can still cause hearing loss that manifests over time periods longer than the follow-up found in those studies [6–8]. In a meta-analysis by Mahboubi et al., the average

* Corresponding author.
E-mail addresses: jim.gallogly@health.slu.edu (J.A. Gallogly), mejd.jumaily@health.slu.edu (M. Jumaily), farhoud.faraji@health.slu.edu (F. Faraji), anthony.mikulec@health.slu.edu (A.A. Mikulec).

https://doi.org/10.1016/j.amjoto.2018.06.017
Received 8 June 2018

follow-up of the included studies that used SRT was 4 years or less, except for one study [9]. The reported collective hearing preservation rate was 79.1%. In studies that used SRT with a median follow-up ranging from 5 to 10 years, the hearing preservation rate ranged between 24 and 44.5% [10–13]. Evaluating hearing outcomes is also complicated by variation among centers in the number of radiation fractions (single- or multi-fractions), radiation dose per fraction, and the isodose line at which the fractions are given [14].

This study evaluated audiometric and tumor control outcomes in a cohort that had long follow-up and had been treated with 2100 cGy to the 80% isodose line delivered in 3 weekly fractions.

2. Method and methods

This retrospective study included 40 patients with unilateral VS that presented for care at our institution from 2006 to 2017. All patients received an initial clinical evaluation including MR imaging and audiometric tests measuring pure tone average and word recognition score. To be included in the study, the patient must have had both baseline audiometry and magnetic resonance imaging (MRI) data available from near the time of presentation and then a minimum of two MRI's, and two audiometric follow-ups unless hearing was unserviceable. If treated, the SRT regimen must have been 2100 cGy to the 80% isodose line (+/−2%) delivered in 3 weekly fractions using CyberKnife technology.

Tumor size was measured as the greatest length, including the internal auditory canal component, among the anteroposterior, craniocaudal, and transverse dimensions. Tumor growth was determined by a change in maximal dimension of greater than 2 mm [15]. Tumor control was determined in two ways: progression-free survival and radiographic progression. Progression-free survival was defined as freedom from further intervention [15, 16]. Radiographic progression was defined as change in diameter greater than 2 mm.

In accordance with the 1995 American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) hearing preservation guidelines for acoustic neuroma, audiometric data was classified into groups A–D (Table 1) [17]. Hearing was categorized into “serviceable” and “unserviceable,” which are classes A–B and C–D respectively. Hearing preservation was determined by classification at last measurement. Audiometric results were taken at presentation or diagnosis, whichever was earlier, and at last follow-up.

Follow up time was calculated from treatment initiation until most recent MRI for tumor growth and audiogram for hearing preservation. Survival rates were calculated with the Kaplan-Meier (KM) method. IBM SPSS Software version 23 (International Business Machines Corporation, Armonk, New York, USA) was used to perform statistical analysis.

Complications of treatment were determined by clinical evaluation of symptoms noted in patient charts. Trigeminal, facial and vestibular nerve dysfunction were noted if new symptoms presented after treatment.

Table 1
Patient characteristics.

Number of patients	40
Male	18
Female	22
Average age	53.65
Extension into cerebellar pontine angle	26
Presenting symptoms	
Hearing loss	32
Tinnitus	18
Imbalance	13
Paresthesia	1
Hearing classification at presentation	
A	17
B	6
C	5
D	12
Average tumor diameter at diagnosis	
All	11.55 mm
SRT[a] treated	13.82 mm
WW[b]	8.71 mm

[a] Stereotactic radiotherapy
[b] Watchful waiting

3. Results

3.1. Patient characteristics

Forty patients were identified meeting inclusion criteria. The average age of the group was 53.7 years at diagnosis. Males and females comprised 45% and 55% of the cohort, respectively. Hearing loss, tinnitus and imbalance were the most common presenting symptoms. One patient presented with paresthesia. At presentation, the hearing quality of 57.5% of patients was serviceable per AAO-HNS guidelines. Twenty-two patients underwent SRT treatment. Eighteen patients remain in watchful waiting (Table 1).

3.2. Tumor control

Of 22 patients receiving SRT treatment, 19 remain free from further intervention following the last obtained imaging study. The crude progression-free survival rate calculated for all patients at last imaging is 86.4% at a mean of 52.3 months. Five-year KM survival is 76.9% (Fig. 1). Radiographic growth after treatment was noted in 5 patients. Three patients underwent surgical resection of growing tumors with subsequent tumor control. The 2 patients not receiving intervention have not experienced changes in symptoms associated with growth and have not required further intervention. One such patient experienced an increase in tumor diameter from 14 mm at the time of treatment to 17 mm over 46 months of follow up. The patient developed ipsilateral trigeminal neuralgia 45 months after SRT, which was the only new symptom. The tumor subsequently shrunk to maximal diameter of 15 mm by 79 months. No further treatment was indicated. The other patient experienced tumor growth 44 months after treatment. Pretreatment tumor diameter was 13 mm. The tumor had remained stable on imaging at approximately 15 mm until growth to 21 mm was demonstrated. The patient's hearing was class D prior to growth and the patient did not experience changes in symptoms. He elected against further intervention given his age of 73. The 5-year KM survival from radiographic progression is 61.5%, with crude control of 77.3% (Fig. 2).

3.3. Hearing preservation

Eleven of 22 patients had AAO-HNS serviceable hearing prior to SRT treatment. At a mean follow up of 36.7 months, 4 patients (36.4%) maintained serviceable hearing. KM preservation of serviceable hearing was 17.5% at 5 years (Fig. 3). When calculated at 3 years, KM preservation of serviceable hearing was 51.1%. One of 6 patients presenting with Class A hearing before SRT maintained Class A hearing through most recent audiogram at a mean of 39.4 months.

Of the 18 tumors managed with watchful waiting alone, 17 were non-growing. The single patient undergoing watchful waiting of a growing tumor was followed radiographically for 17 months with diameter increase from 13 to 16 mm over 3 MRIs. The patient did not experience worsening of symptoms associated with tumor growth. The patient was lost to follow up before treatment was performed. At presentation 8 of 17 patients undergoing watchful waiting (47.1%) had serviceable hearing. At mean follow-up of 48.3 months, all 8 patients maintained serviceable hearing (Fig. 4A). Fourteen of 22 patients receiving SRT had non-growing tumors. At the last audiogram performed