Journal of Neuroimaging and Neuromedicine

Research Article

Gamma Knife Radiosurgery for Vestibular Schwannoma: Predictive Factors and First Experience from Saudi Arabia

Bilal Muhammad[1]*, Abdulaziz AL Hamad[1], Marouf Adili[1], Faiza Salim[1], Mansoor Wahid[1]

Department Radiation Oncology, Prince Sultan Military Medical City, Riyadh, KSA

Abstract

Introduction: This study is aimed at an institutional review of Vestibular Schwannomas (VS) treatment with the first Gamma Knife machine in the Kingdom in order to describe expected goals of outcomes.

Methods. The clinical information of VS patients from the prospective database of Gamma knife Radiosurgery (perfexion) were reviewed and analyzed through SPSS v22 for outcomes. A total of 47 consecutive patients were reviewed and 35 got selected for final review considering at least one or more year of post radiosurgery follow up. All the patients were treated between the year 2013 and 2019 completing machine's first Cobalt sources half-life

Results. A total of 35 patients were reviewed. The cohort consisted of 13 males and 22 females with a median age of53 years (23-80 years). 22 patients had no comorbidity and the rest had at least one including DM, HTN or both. 7 patients had post-operative Radiosurgery to their residual disease and 28 were treated with Radiosurgery alone. 34 patients presented with symptomatic disease. Mean follow up duration for < 2yrs group: 13.8 months, while > 2 yrs: months. Hearing deficiency; Sever SN hearing loss: 15 patients, Mild to moderate: 15 and normal hearing: 5 patients. Tinnitus: 20 patients and Vestibular dysfunction: 23 patients. Duration of follow up time (more than 2 years) isthe single predetermining factor associated with improved outcomes (P<0.001

Conclusion. Gamma knife Radiosurgery is an effective treatment modality with expected treatment goals to achieve requires at least a period of 2 years to become clinically appreciable

Keywords: Vestibular Schwannoma (VS) • Gamma Knife (GK) • radiosurgery

Introduction

. Vestibular Schwannomas (VS) share a large contribution of benign brain tumors (Joshua B. Greene 2018). There is areported increase in incidence during the last two decades that could easily be attributed either to a certain receptive change in genetic profile or simply an increase in radiological detection of incidental cases. (John P. Marinelli) Middle Eastern population, with better health care facilities is expected to follow numbers of Western world with a growing access to Gadolinium enhanced MRI brain scans that objectively accounts for a standard in diagnosing VS. (MARKET RESEARCH FUTURE 2016) There is a lack of local data about VS in KSA. Apart from very scanty reports which don't virtually describe real prevalence or annual incidence of the disease, can hardly be found searching regional literature. A report on sensorineural hearing deficiency reported 2.7% incidence of VS in a suburban region as a cause of hearing deficiency in a single cohort from Southern KSA. (Khurayzi 2018) (Yardımcı 2019) (AF.Alahmari 2020 July) (Almutrafi, 2020) With the growing trends in use of stereotactic radiosurgery for pathologies in brain, it is imperative to share experience globally in order to improve understanding of etiology and pathogenesis of disorders like VS with no known reason of origin, alongside geographic trends and variations in outcomes amongst various populations, as evident from regional variations seen in many other benign and malignant pathologies. (Mohammed, 2013) (AR 2019 Jul) (Rottenberg 2019) (Moller 2018) (Wanner 2020) (McKinney 2004) The incidence of NF2 with associated bilateral VS poses difficulty in management plans where relatively younger patients face a competition of choice between diminishing hearing potentials and progressively growing bilateral tumors. (Lloyd 2013) The first ever Gamma knife radiosurgery machine was installed at this tertiary care center in Oct 2013 and this review represents its first outcomes describing details of VS in terms of incidence, characteristics, treatment details, factors associated and exclusive radiosurgical

Methods

2.1 Patient population:

There is a prospective database of Gamma knife radiosurgery cases which was used to identify cases alongside their treatment details. Hospital information system was used to collect clinical information through documented follow up summaries. ARIA system (2nd back up at the facility) needed to be reviewed for 20 earlier patients whose treatment data went missing from main GK server following a break down. During a period from Oct. 2013 and Oct 2019, 45 patients with AS were reviewed and managed at Radiation Oncology department, 35 were found evaluable for having past at least 12 months of post-treatment follow up. All the patients were seen in the combined clinic where they were reviewed by a Radiation Oncologist and a Neurosurgeon with occasional presence of a Base of skull/ ENT surgeon on need basis. Clinical features of the patients at presentation are described in Table 1.

***Address for Correspondence:** Bilal Muahmmed, Department of Radiation Oncology Prince Multan Miltray Medical City, Riyadh, KSA*

Received: Feb 4 2024, **Accepted:** Mar 10 2024; **Published:** Mar 15, 2024, DOI: 10.59462/jninm.1.1.102

Citation: Bilal Muhammed (2024), Gamma Knife Radiosurgery for Vestibular Schwannoma: Predictive Factors and First Experience from Saudi Arabia, Journal of neuroimaging and neuro medicine, 1(1):102

Table 1. clinical features of patients at presentation.

Gender	**Male: 13**	**Female: 22**		
Dose	≤12.5 Gy: 29 (82%)	15 Gy: 6 (18%)		
Comorbidity	Yes: 12 (34%)	None: 22 (63%)	Unknown: 1 (3%)	
Tinnitus	Yes; 20 (57%)	No: 15 (43%)		
Vestibular dysfunction	Yes: 23 (65%)	No: 12 (35%)		
Hearing at presentation	Normal: 5 (14%)	None: 15 (43%)	Serviceable: 15 (43%)	
Facial compromise	Yes: 6 (17%)	No: 29 (83%)		
Trigeminal compromise	Yes: 1(3%)	No: 34 (97%)		
Koos Grading	G1: 9(25.7%)	G2: 12 (34.3%)	G3: 8 (22.9%)	G4: 6 (7.1%)
Intracanalicula rcomponent	None: 6(17.1%)	Complete:24 (68.6%)	Partial: 5 (14.3%)	
Surgery	Yes: 7(20%)	No: (80%)		
Lesion side	Right: 18(51.4%)	Left: 15 (42.9%)	Bilateral: 2 (5.7%)	

All the patients went through baseline audiology and MRI Brain scan with Gadolinium enhanced thin slices, called IAM (Internal auditory meatus) protocol. Elekta "Perfexion" GK machine was used to treat all the cases. Decision on Radiosurgery were made at combined Neuro Oncology meeting and patients were offered informed consent with details of procedure, outcomes, expected complications and routines of follow up while they were reviewed first in the clinic. Patients were also informed of their data utility while writing reviews for scientific and academic purposes. All the patients who lost to follow up or remained on observation without getting Radiosurgery treatment were excluded. Patients underwent Koos grading documentation for staging of size. Surgical cases who underwent post-operative radiosurgery were included. NF2 with bilateral AS but received single sided radiosurgery were also included for review. Facial, trigeminal nerves or any other neurologic disability at presentation was documented pre and post treatment during follow up. All the patients were prescribed a dose at 50% isodose line (dose range; 12Gy to 15 Gy) Figures 2,5. All the data was collected, reviewed and analyzed on SPSS software. This review was approved through local IRB for publication.

Results:

The goals of managing VS in a patient range from simple observation for incidentally found asymptomatic cases, to restricting growth of tumor and associated symptoms in a relatively stable but moderately symptomatic patient. Surgical candidates are usually with larger compressing tumors that need to undergo excision (complete or partial) depending on the safety of nearby structures in an unstable and highly symptomatic patient with an intent to achieve quick symptoms relief. (Golfinos, 2016) (Wanner, 2020) Hence clinical response of treating VS is defined as a gain in any of the

affected vestibular or cochlear function without being detrimental to nearby organ functions including brain stem, facial and trigeminal nerves etc. Preservation of residual vestibulocochlear functions (tinnitus, vertigo or cerebellar symptoms and hearing decline) are also considered the goal to achieve after treating with Radiosurgery or other treatment entities. (Carlson 2015) (Golfinos 2016) As with all the available entities of treating VS, there is no predictable and predetermined outcome associated with the type of modality used. The results are considered a numeric function of multiple factors described in the literature. In this study (table 3), clinical benefit of therapy was defined as a benefit in the degree of improvement in any one or more forms of parameters after radiosurgery during patient's follow up. Individual parameters were assessed through standard assessment tools; including regular 1 yearly follow up audiology through Audiology department. Vertigo and tinnitus were assessed during patient's clinical follow up in combined Neuro- Oncology clinics. Responses were recorded against the past recorded grades of disability. As patients had yearly follow

up, their course of benefit and complications were recorded as described by the patients and through medical reports available (if any). The recorded responses are displayed in table 2

Table 2: overall response of radiosurgery.

Feature	**Stable**	**Improved**	**Deteriorate**
Post Treatment size	Stable: 23(65.7%)	Decreased: 11(31.4%)	Increased:
			None (2.85%)
Tinnitus	Stable: 28(80%)	Better: 7 (20%)	Worse:
			None (0%)
Hearing	Stable: 22(62.8%)	Better: 10(28.6%)	Worse: 3(8.6%)
Vestibular response	Stable/worse: 21(60%)	Better: 14(40%)	None (0%)
Overall clinical response	Stable: 14(40%)	Response+: 18(51.4%)	Worse: 3(8.6%)
		Improved:	
Radiological response	Stable: 19(54.3%)	16(46.7%)	None (0%)

Increased vacuolations (Figure 1,2,3,4) found on follow up MRI scans, were in majority of cases, not reported by radiologists during initial reporting

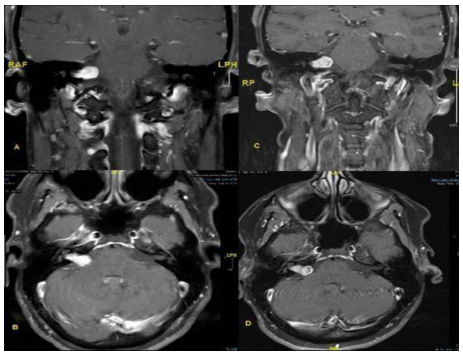

Figure 1: A, B pre radiosurgery volumes and C,D; post radiosurgeryshrinkage and internal vaculation changes in 1year.

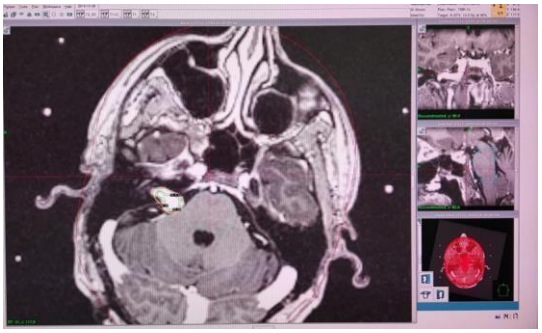

Figure 2: Snapshot taken at Gamma Knife radiosurgery day

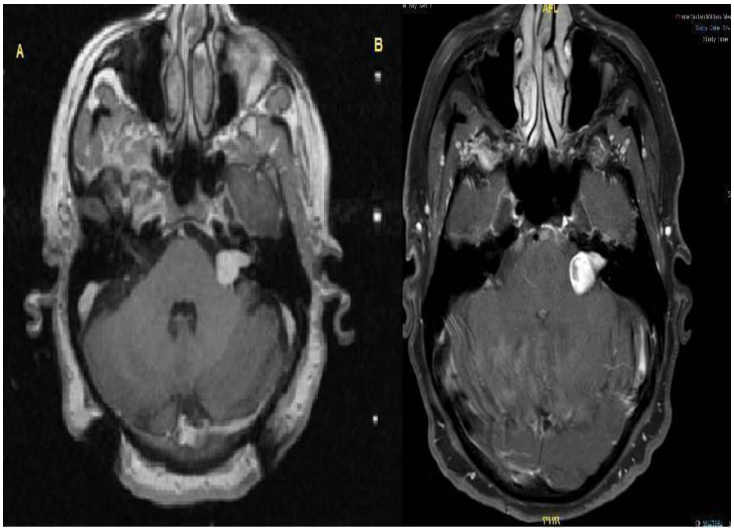

Figure 3: Pre (A) and Post (B) radiosurgery increased vacuolation and increase in volume

conservatively and resolved spontaneously. Pneumocephalus has occurred in all cases and needs no surgical intervention [5].

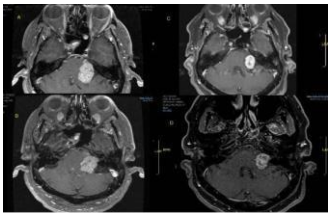

Figure 4: Pre (A,B) and Post (C,D) radiosurgery changes with reduction in size and increased vacuolation at 3.5 years follow up

Figure 5: Snapshot taken at day of Radiosurgery (12 Gy at 50% Isodose line

So, the responses were recollected by reviewing with Neuroradiologists in the Hospital at the time of this review. Overall clinical response was found significantly associated (p :< 0.004) with increased vacuolation, though individual functions did not express that association (Tinnitus: P; 0.42, hearing: P; 0.54, Vestibular function: P; 0.055). A thorough significant association was found in favor of patients who completed 2 years or more of their clinical and radiological follow up; tinnitus: P; <0.001, hearing :P; <0.001, Vestibular function: P;<0.001 and clinical response: p;<0.01,) when analyzed giving weightage for the duration of follow up in months. Age as a factor for outcome didn't show association with any of the functions with P values showed in (table 3), except for clinical response when adjusted for follow up duration. Lesionside, Koos grading and its size also did not show any significant association. Overall stability in clinical symptoms including tinnitus, hearing and vestibular functions amounted 67.6%, while improvement was found in 29.5% of patients. Only 2.9% suffered certain degree of permanent worsening (Table2). Higher doses 15 Gy versus low (≤ 12.5 Gy) also couldn't find any significant difference in outcomes, though the numbers for comparison were also not significant. Clinical response in outcomes was found associated with radiological shrinkage as adjusted for follow up duration with p; <0.001. Individually there was no association found between any of quality parameters and tumor shrinkage (Table 3).

Parameter	Hearing	Tinnitus	Vest. response	Overall clinical response	Radiological response	Vacuolation
Follow up time (More or less than 2 years)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Age (More or less than 50 years)	0.4	0.1	0.1	0.27	0.5	0.02
Vacuolation (present vs absent)	0.54	0.42	0.055	0.003	0.001	
Koos Grading	0.7	0.34	0.36	0.7	0.15	0.32
Radiological response	0.4	0.26	0.4	0.09		0.002
Intracanalicular component(complete, absent or partial)	0.5	0.4	0.08	0.1	0.4	0.6

A total of 5 patients were seen with Neurofibromatosis 2 and bilateral Vestibular Schwannomas. 2 of them received radiosurgery and both had eventual decreased in auditory potentials. Other 3 patients were opted to go on expectant observation while 2 of them received a trial of Bevacizumab with marginal benefit.

Discussion

Acoustic Schwannomas are one of the commonest benign tumors of brain. Their diagnosis, care and outcomes are important from very pertinent quality of life measures that may get affected not only by the tumors but also by modalities in use to treat them (McKinney 2004) (Marinelli 2018 Oct) (Rosenberg 2000 Apr). It is quite relevant not only for treating physicians but also for the patients to know and understand the pros and cons of each modality, related outcomes and particularly associated complications with the passage of time. (Bennett 2007) (Boari 2014 Dec) (Noren 1998) Unfortunately, the treatment outcomes not just simply depend upon the genetic, morphological or biological features of presenting tumors, but quite inconsistently at the level of expertise from center to center, type and availability of treating modality in use, variable selection procedures and range of choices available for the patients to pick from. (Apicella 2016) (Kondziolka 2015) (Bhandare 2012) Physicians most commonly go by the severity of symptoms and size of tumor with related signs that dictate an inclination towards available choices including observation, surgical excision, fractionated radiotherapy or Radiosurgery. (Apicella 2016) (Tsao 2017) Incidence and prevalence of this tumor in Gulf region is not very much known. Few local reports account very scanty information about this disease entity. (AF.Alahmari 2020 July) (Abdulrehman 2006 May) This study, will presumably make the first of its kind from this region to describe experience of management of Vestibular Schwannoma using its first Gamma knife Radiosurgery machine in the country. The VS treatment data mostly comes from US, japan or European centers that may represent geographical variations across the regions as seen amongst the other known benign and malignant tumors with regional attributes in term of morphology and outcomes. So, it is highly pertinent to contribute and describe treatment related outcomes for Middle Eastern community which is expected to have higher incidental presentation on account of access to better healthcare facilities. (MARKET RESEARCH FUTURE 2016) The range of outcomes are usually not perfectly predictable but the toxicity, on the contrary, is a non-stochastic feature based on the experience of modalities used over the last many decades of VS care. (Noren 1998) (Quaranta 2001 Oct) (Bhandare 2012) Hearing decline, tinnitus, vestibular dysfunctions and brainstem or ventricle compressions can present in a range of contributory symptomatology Surgical outcomes beyond usual post-operative complications include nerves and nearby structural damage that becomes eminent in no time after surgery, while Radiosurgery effects are not immediate, but take months to appear. (Quaranta 2001 Oct) (Noren 1998) This factor has also been considered by physicians and many patients at the decision time before undergoing treatment. The other side of comparison is that surgical approach provides a chance of complete or partial removal of tumor, while Radiotherapy or Radiosurgery induce a stable disease without further progression as the primary goal of treatment. Sometimes we observe reduction in size with the passage of time, as in this study, but it took at least 2 years of follow up time to express radiosurgical gains. Clinical response was defined to have a clinical or measurable improvement in one or more of the three quality parameters; hearing, tinnitus and vestibular dysfunction. Stability in clinical symptomatology (more than two thirds) and some form of improvement (nearly one thirds) as seen in this study amounts 97% of total population which equally matches any international experience. Radiological internal vacuolation (necrotic or cystic changes inside the brighter walled tumor) is frequently used by physicians to understand and share with patients during their follow up as an indication of response, but individually, it hasn't been studied as well in terms of its significance with related outcomes. We reviewed all the MRI follow up scans with our worthy neuroradiologists and tried to find any association with response. It was found significantly associated with improvement in overall response, although Independently, there was no significant association with increased vacuolation. We need to keep in mind that individual parameters comprise further reduced number for any analysis of outcome. (Rosahl 2017) This study also shows that we need at least 2 years of follow up after radiosurgery for nonsurgical VS to mark a response or otherwise. Cutoff of 2 years of follow up was taken from traditional teachings for benign tumors management and in this study it was found highly significant for all forms of treatment outcomes; indicating primarily a very slow growing nature of the disease and even more in terms of its outcomes. Whether there is progressive improvement with passing time and who would acquire that change, is something which needs further longer follow up and larger number of cases to elaborate further. It is worth mentioning here, that it is the patient at the end who needs the information in order to decide what level of disability and compromised quality he/she can stand. (Irving 1995) Various retrospective studies and experiences from larger centers contribute understanding the wide range of outcomes, but unfortunately, don't help an individual patient ascertain subjective degree of outcomes. Assumingly, the data from the larger centers may be compiled in an Artificial Intelligence algorithm where certain typical biological, morphological and/or radiological features can help predict an individual's subjective outcomes. (Shapey 2019).

Conclusion

This study entails our center's radiosurgical experience and outlines similar safe treatment outcomes as seen in many other experienced centers.The observations seen here point towards slower results requiring at least a follow up of 2 years or more to be evident clinically. Whether internal cystic changes amount to be considered for a response predictor, requires further larger scale review and assessment.

References

1. JB, Allibone, Harkness WJ, and Hayward RD. "Craniotomy-related complications in a pediatric neurosurgery unit- A prospective study." *Br J Neurosurg* 13 (1999): 148-153.
2. LE, Becker, and Halliday WC. "Central nervous system tumors of childhood." *Perspect Pediatr Pathol* 10 (1987): 86-134.
3. PC, Bucy. "Exposure of the posterior or cerebellar fossa." *J Neurosurg* 24 (1966): 820-832.
4. R, Hayward. "Posterior fossa craniotomy: An alternative to craniectomy." *Pediatr Neurosurg* 31 (1999): 330.
5. Greenberg, Mark. "Greenberg: Handbook of Neurosurgery, Eighth Edition." (2016): 1-1784.
6. S, Setti. "Rengachary: Principles of Neurosurgery, Second Edition." (2005)
7. DJ, Culley, Berger MS, Shaw D, and Geyer R. "An analysis of factors determining the need for ventriculoperitoneal shunts after posterior fossa tumor surgery in children." *Neurosurgery* 34 (1994): 402-408.
8. KM, David, Casey ATH, Hayward RD, and Harkness WF, et al. "Medulloblastoma: Is the 5-year survival rate improving? A review of 80 cases from a single institution." *J Neurosurg* 86 (1997): 13-21.
9. JR, Farwell, Dohrmann GJ, and Flannery JT. "Central nervous system tumors in children." *Cancer* 40 (1977): 3123-3132.
10. Factors affecting Vestibular Schwannoma radiosurgery outcomes; First Gamma knife experience from KSA.
11. SG, Harner, Beatty CW, and Bersold EMJ. "Impact of cranioplasty on headache after acoustic neuroma removal." *Neurosurgery* 36 (1995): 1097-1100.8. Factors affecting Vestibular Schwannoma radiosurgery outcomes; First Gamma knife experience from KSA.