Original Research Paper

Volume-7 | Issue-11 | November-2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

Neurosurgery

ROLE OF GAMMA KNIFE RADIOSURGERY IN MANAGEMENT OF GLOMUS TUMORS : THE INDIAN ARMED FORCES EXPERIENCE

Saurabh Kumar Verma*	Mch Neurosurgery, Senior Advisor Surgery & Neurosurgeon, Department Of Neuro surgery, Army Hospital (research&referral), New Delhi, India *Corresponding Author
MS Sridhar	Mch Neurosurgery, Consultant Surgery & Neurosurgeon, Department of Neurosurgery, Army Hospital (Research&Referral), New Delhi, India
Manoj k Semval	Phd, DipRP, Scientist "G"(Medical Physycist) Army Hospital (Research & Referral), New Delhi, India
J Bhadoria	MS General Surgery, First Year Resident NBE Neurosurgery Department of Neurosurgery, Army Hospital (Research&Referral), New Delhi, India
S Shashivadanan	Mch Neurosurgery, Senior Advisor Surgery & Neurosurgeon, Department of Neurosurgery, Army Hospital (Research&Referral), New Delhi, India
Chinmaya Srivastav	Mch Neurosurgery, Classified Specialist Surgery & Neurosurgeon, Department of Neurosurgery, Army Hospital (Research&Referral), New Delhi, India
Manish Garg	MS General Surgery, Final Year Resident NBE Neurosurgery Department of Neurosurgery, Army Hospital (Research&Referral), New Delhi, India

KEYWORDS : Glomus tumors, Gamma Knife Radiosurgery

INTRODUCTION:

Glomus jugulare tumors are rare & are indolent, with an estimated doubling time of 13.8 years and the annual growth rate to be 0.79 mm/year [1]. Conventional Surgery has been the dominant treatment for glomus jugulare for decades.

Radiosurgery has lately emerged as a treatment option that incorporates the benefits of radiation therapy while minimizing the adverse side effects of conventional surgery & conventional radiotherapy. Radiosurgery is equally effective as surgery for tumor control and possesses lower morbidity and mortality rates. The mechanism by which radiosurgery is effective against glomus jugulare tumors remains unresolved, as these tumors are radioresistant, and radiation probably attacks the highly developed vasculature of the tumors.

We present our series of 14 cases of Glomus Jugulare, treated with GKS over the last 09 years and will present the multimodality treatment algorithms followed in our centre for these complex tumors & would review various treatment modalities currently available.

GLOMUS JUGULARE – AN OVERVIEW:

The word "Glomus" is a misnomer and has its root in the word "a nest" as it was initially considered to be a tumor of blood vessel origin and comprising of "a nest" of vascular tissue. It is also not to be confused with the "Glomangioma or Glomus body tumor" which are vascular tumors of the thermoregulatory bodies of fingers and toes.

The nomenclature of Glomus tumor evolved with time.It was initially called Tympanic body tumor in 1949 and also known Chromaffin paragangliomas based on its location &histological staining properties. In 1958 it was named as Chemodectoma- a name more specific for carotid body tumor or Chemoreceptoma based on its property of assessment of oxygen saturation of blood. It was felt however that none of the above nomenclature could encompass the wide range of the glomus tumors and thus evolved the most acceptable nomenclature in 1974 that is the Paragangliomas.[2]

As the name suggests thesetumors arise from paraganglia cells of neural crest origin. These are specialised neuroendocrine cells which migrate along the cranial nerves, vessels or autonomic nerves. Only about 1 to 3% of these tumors are hormonally hyper secreting to be clinically active.[3][4] Most of these tumors are benign & only about 1 to 4% are metastatic[5]- metastasis being defined as presence of these cells in locations other than expected for example in lymph nodes, bone, liver etc.

Location-Head & Neck Paragangliomas:

I. Carotid body - along the periadventitia of carotid bifurcation
II. Jugular bulb - along the adventitia of the Dome, along the Jacobson's nerve, along the Arnold nerve
III. Middle ear- along the tympanic nerve or the cochlear promontory
IV. Vagus nerve – along the inferior Nodose ganglia usually
V. Laryngeal nerve usually the inferior laryngeal nerve

Rarely thee lesions may also be seen in Orbit, nasal cavity, paranasal sinuses, nasopharynx, trachea and thyroid.

The Ambit of this particular study is however only the Jugular or the Jugulotympanic paraganglioma.

Epidemiology:

These are rare tumors seen in 1 in 1 million population in the community. In the commoner Sporadic varietythe incidence in females is more than the males and the average age at diagnosis is fourth decade. In the familial variety the sex ratio of incidence is equal, with the tumor being diagnosed at an earlier age and with a higher incidence of bilaterality.[6]

These are highly vascular, but indolent tumors with annual growth rate of 0.79 millimetre and doubling time of 13.8 years.The average time to diagnosis from the initial symptoms depends on the site of tumor, however, varies on an average from 4 to 6 years.

Presentation:

The lesions may present as lump in the neck if along the carotids or Vagus nerve. The tumor may present with lower cranial nerve deficits, tinnitus, hearing loss, vertigo and features of brainstem compression.Despite the low incidence of metastasis these tumors are locally invasive, expanding within the temporal bone, following the path of least resistance such as air cells, vascular lumen, skull base foramina and eustachian tube.

Treatment Options:

The indolent nature of these lesions frustrates the attempt to determine which treatment is optimal.

Surgery:

Complete surgical resection is off course the ideal management of jugular foramen paraganglioma, however, is seldom possible. Surgical excision has been attempted since 1930, with or without pre operative embolization, with a high incidence ofassociated complications like pulmonary embolism, meningitis, wound infection, lower cranial

nerve palsies[7] - the list is endless; not to mention a delayed recurrence rate of 5.5% in 70 months.[8]

Radiotherapy:
Radiotherapy for these lesions was associated with its own share of controversies. The glomus tumors per se are radio resistant. Then why radiotherapy?

Gamma knife radiosurgery has been proposed as an alternative to conventional surgery. Recommendation as to whether Gamma knife surgery can be delivered as a primary or adjunctive therapy remains unresolved.

MATERIAL AND METHOD:

This retrospective study carried out at the apex tertiary care centre of the armed forces medical setup in India, retrospectively analysed the use of Gamma knife radiosurgery as a primary or adjunctive form of therapy for glomus jugulare offered to patients over a period of 9 years at this centre and compared the same with available national and international statistics. The radiosurgery was carried out using a Leksell Gamma knife Elekta instruments, Stockholm, Sweden, model 4 C, installed in 2007. The gamma knife was planned with safety tolerance limit of dose to brain stem, cranial nerve& Cochlea not to exceed 12 Gy, 20 Gy& 5 Gy respectively. The prescribed tumor margin dose was more than 16 Gy if possible. Aretrospective chart analysis of 14 patients who underwent a radio surgical procedure as a primary or adjunctive therapy was carried out.

Result:

DATE OF SURGERY	SEX	VOLUME	DOSE	COVERAGE
2/2/08	F	6.2	17	95
19/7/08 Primary GKS	F	4.3	17	96
7/2/09 Primary GKS	F	6.9	18	94
12/6/10	M	10.1	20	94
2/2/12 Primary GKS	M	10.4	16	96
5/7/12	F	1.1	18	96
5/1/12	M	8.7	20	94
6/7/13	F	13.0	15	96
13/2/14	F	2.6	18	98
9/7/14	F	8.8	18	94
27/11/14	F	4.1	17	95
31/3/16	F	10.9	17	98
21/4/16	F	3.6	16	99
19/1/17	M	2.5	15	96

Of the 763 cases who received Gamma knife radiosurgery at this centre till Sep 2017, only 14 cases with glomus jugulare underwent the procedure.

3 out of 14 cases received Gamma knife surgery as primary therapy - their tumor volume being 4.3cc, 6.9cc and 10.4 cc respectively. The initial 2 cases where offered primary Gamma knife surgery and the third was offered primary surgery as the patient was unwilling for debulking of the lesion. All the cases of glomus jugulare were of sporadic type. Male is to female ratio was 1 : 2.5. The average tumor volume was 6.66 CC and the average dose of radiation was 17.29 grey with the average tumor coverage being 95.79%. The follow-up has ranged from 6 months to 9 years. There has been no loss to follow up. The three cases which received gamma knife radiosurgery not only exhibited tumour control (defined as unchanged or reduced tumour volume in follow up) but also showed subtle improvement in status viz recovery of lower cranial nerve deficits and improved hearing. The clinical improvement, if any, in cases where gamma knife surgery was offered as adjunctive postoperative therapy for residual lesion, was ignored to offset any confounding factor generated by spontaneous recovery over a period of time from iatrogenic neurological paresis caused by surgery. No case of tumor progression and no radiation-induced adverse effects were noted in this particular series.

DISCUSSION:

It is hypothesized that radiation acts by acting on the rich vascular supply of these lesions akin to its action on cerebral AVMs, against which its efficacy is established beyond doubt. However some post radiotherapy follow-up studies have failed to document this mechanism of action. The external beam radiotherapy and fractionated conventional radiotherapy were found to be attractive alternatives to conventional surgery, with their own share of adverse effects like alopecia, cognitive decline, osteonecrosis, temporal lobe necrosis and neuralgias.[9] Despite the above drawbacks, Springate et al in as early as 1991 documented good tumour control and lesser morbidity with radio therapy than conventional surgery.[10]With the advent of radiosurgery the medical fraternity was able to offer its clientele the advantages of radiotherapy minus the adverse effects of conventional radiotherapy - possible due to sharp drop off in radiation dose outside target area. Gottfried et al in 2004 concluded that radio surgery is as effective as surgery & with lesser morbidity.[11]

INTERNATIONAL STATISTICS:

Authors	Year	Modality	No Of Patients	Months Follow Up	Tumor Control
Milleretal	2009	GKS	5	34.0	80
Ganz & Abdulkarim	2009	GKS	14	28.0	100
Sharmaetal	2008	GKS	24	26.1	100
Limetal	2007	LINAC	18	60.0	100
Henzeletal	2007	LINAC	17	40.0	100
Gerosaetal	2006	GKS	20	50.9	100
Vermaetal	2006	GKS	17	48.0	71
Poznanovicetal	2006	LINAC	18	15.6	100
Shehanetal	2005	GKS	8	28.0	100

An analysis of international statistics show the results to be in sync with those at our centre. Seven out of nine studies concluded a tumor control rate of 100%. Of the two studies that show a control rate of 71% & 80%, one study has been concluded as early as 2006 & the other has a small substrate of only 5 cases.

INDIAN STATISTICS:

In a study published in the year 2008, a retrospective analysis of 24 patients treated with gamma knife between 1997 to 2006 was carried out. 15 out of these were knifed primarily.The study concluded a control rate of 100%. One patient developed trigeminal neuralgia post knifing.[13]

Amongst all radiosurgical modalities, maximum data is available for Gamma knife surgery. Sparse data is available for Linux and cyberknife. However data for all three seem to be encouraging as far as glomus jugulare is concerned.

CONCLUSION:

- There may be a controversy regarding the modality of action on these tumors by radiosurgery – however- evidently, there seems to be no controversy about the efficacy of the same.
- Conventional Surgery is associated with a significantly higher morbidity as compared to radiosurgery
- Radiosurgical treatment is strongly recommended for small tumors < 3 cm in average dimension, residual or recurrent tumor after surgery [14]
- Fractionated radiosurgery is recommended for unresectable large tumors.
- Large symptomatic tumors with significant mass effect on the brainstem however may need to be surgically debulked.
- In a benign disease, *tumor control and quality of life indices* are probably more significant than eradication and morbidity.
- The overall quality of life appears to be significantly better with GKS as a primary and is an effective adjunct as a secondary modality of therapy.

ACKNOWLEDGEMENTS:
Department of Radiology, Army Hospital (Research & Referral), New Delhi, India

REFERENCES:

1. Jansen JC, van den Berg R, Kuiper A, van der Mey AG, ZwindermanAH, Cornelisse CJ: Estimation of growth rate in patientswith head and neck paragangliomas influences the treatmentproposal. **Cancer 88:**2811–2816, 2000
2. Gavin W. Britz, H Richard Winn. Glomus Tumor . Youmans Neurological Surgery, Seventh Edition. 1251-67
3. Netterville JL, Jackson CG, Miller FR, Wanamaker JR, GlasscockME: Vagal paraganglioma: a review of 46 patients treatedduring a 20-year period. **Arch Otolaryngol Head NeckSurg 124:**1133–1140, 1998
4. Pavai Z, Orosz Z, Horvath E, Seres-Sturm L, Jung J: Immunohistochemical features of paragangliomas. **J Cell Mol Med**
5. Brewis C, Bottrill ID, Wharton SB, Moffat DA: Metastasesfrom glomus jugulare tumours. **J Laryngol Otol 114:**17–23,2000

6. Alford BR, Guilford FR: A comprehensive study of tumors ofthe glomus jugulare. **Laryngoscope 72:**765–805, 1962
7. Green JD Jr, Brackmann DE, Nguyen CD, Arriaga MA, TelischiFF, De la Cruz A: Surgical management of previously untreatedglomus jugulare tumors. **Laryngoscope 104:**917–921,1994
8. Green JD Jr, Brackmann DE, Nguyen CD, Arriaga MA, TelischiFF, De la Cruz A: Surgical management of previously untreatedglomus jugulare tumors. **Laryngoscope 104:**917–921,1994
9. Welzel G, Fleckenstein K, Schaefer J, Hermann B, Kraus-TiefenbacherU, Mai SK, et al: Memory function before and afterwhole brain radiotherapy in patients with and without brainmetastases. **Int J Radiat Oncol Biol Phys 72:**1311–1318,2008
10. Springate SC, Haraf D, Weichselbaum RR: Temporal bonechemodectomas—comparing surgery and radiation therapy.**Oncology 5:**131–137, 1991
11. Gottfried ON, Liu JK, Couldwell WT: Comparison of radiosurgeryand conventional surgery for the treatment of glomusjugulare tumors. **Neurosurg Focus 17(2):**E4, 2004
12. Zachary D. Guss, A.B., Sachin Batra, , Gordon Li, Steven D. Chang, Andrew T. Parsa, Daniele Rigamonti, Lawrence Kleinberg,Michael Lim:Radiosurgery for glomus jugulare: history andrecent progress **Neurosurg Focus 27 (6):**E5, 2009
13. Sharma MS, Gupta A, Kale S S, Agrawal D, Mahapatra A K, Sharma B S. Gamma knife radiosurgery for glomus jugulare tumors: Therapeutic advantages of minimalism in the skull base. Neurol India [serial online] 2008 [cited 2017 Aug 8];56:57-61
14. Sheehan J, Kondziolka D, Flickinger J, Lunsford LD: Gammaknife surgery for glomus jugulare tumors: an intermediatereport on efficacy and safety. **J Neurosurg 102 (Suppl):**241–246, 2005.