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"INSULAR GLIOMAS INCLUDING VOLUMETRIC STUDY: A SINGLE INSTITUTION EXPERIENCE"

Neurosurgery

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ABSTRACT

OBJECTIVE- Insular gliomas are difficult and challenging area to operate and manage because of its proximity to eloquent areas of the brain. Our aim is to describe and define insular glioma using MRI based volumetric study and to determine the association of overall outcome with preoperative tumor volume of insular gliomas.

METHOD- The study was conducted on patients who were diagnosed as insular gliomas on MRI. All grades of patients treated by microsurgical techniques at our centre from June 2016 to December 2017 were included in the study. Volumetric scan analysis was applied on magnetic resonance images (MRIs) to establish preoperative and postoperative tumor volume.

RESULT- The average age at diagnosis was 36.24 yrs; with 68% were male and 32% were female patients with the ratio of 2.13:1. 56% of patients had right sided tumor. WHO grade 2 was most common grade and constituted 62.50% of all cases followed by 20.83% had grade 4 tumor, 12.50% had grade 3 and 4.17% had grade 1 tumor. The median preoperative tumor volume was 89.72cm^3. The extent of resection (EOR) <70% was 87.50% and EOR between 70-90% was 16.67% of cases. At 6 months follow up 16% patient had motor deficit, 8% had sensory deficit and 8% had language deficit. One patient died in follow up period due to the unrelated cause.

CONCLUSION- A good knowledge of anatomical landmarks and awareness of potential complications can allow surgeons to reduce neurological complications and maximum safe resection of insular gliomas.

KEYWORDS

Insular glioma, Extent of resection (EOR), volumetric study.

INTRODUCTION

Insula earlier also known as island of Reil was first described by Johann Christian Reil, the German anatomist, physiologist and psychiatrist in 1809.[1,2] This anatomically and functionally complex structure is located in the depth of the sylvian fissure, overlies the basal ganglia block, and is hidden by the opercula of the frontal, parietal, and temporal lobes. It is covered by the trunk of the Middle Cerebral Artery (MCA) and its branches, and it has important relationships with the perforating Lateral Lenticulostriate Arteries (LLAs)[2,4,9]

Furthermore, the pyramidal tract runs in the superior posterior part of the insula, the Inferior Fronto Occipital Fasciculus (IFOF) that runs medially to the insula, and the arcuate fibers that runs more superiorly, uncinate fasciculus inferiorly and could be very close to insular tumors.

It is thought to play roles in autonomic sensation, gustatory function, olfaction, memory, drive, auditory-vestibular function, and the motor integration and motor planning of speech in the dominant hemisphere.[3,4] The insula is also associated with cardioregulatory, vasomotor functions, pain perception, and bio-behavioral dysfunction characteristics of schizophrenia.[5] Moreover, the insula is adjacent to essential peri-sylvian language areas(ie, Broca areas and Wernicke areas and their association fibers), the primary auditory area, and the primary motor and sensory areas.Therefore intrinsic tumors located in the insula and peri-insular areas present with a variety of ill-defined symptoms and neurologic signs dominated by a single entity, such as motor dysphasia with or without lower facial paresis[1,6,7].

Insular gliomas are not rare, recent epidemiological study by Duffau and Capelle[10], suggested that the lesion accounted for up to 25% of all low-grade gliomas (LLGs) and 10% of all high-grade gliomas (HGGs) Insular gliomas are difficult and challenging tumors to operate, and radical insula operations to be prohibited among neurosurgeons for a long time and they have often recommended a conservative strategy for the treatment of intrinsic insular tumors.[8] However, since 1992 study by Yasargil and colleagues,[2] which demonstrated that it was possible to operate intrinsic insular mass with less risk than previously thought.

An experienced neurosurgeon has reported favorable outcomes of insular gliomas surgery based on a detailed understanding of the complex anatomy and the use of modern microneurosurgical techniques[4]. Maximum surgical resection and good functional outcome in insular gliomas has been challenging for neurosurgeons. This study is a single institution experience regarding surgical characteristic of insular gliomas and to describe and define insular glioma using MRI based volumetric study and to evaluate the association of overall outcome with preoperative tumor volume of insular glioma, the reported oncological and functional outcomes after insular glioma surgery. We discuss the physiopathological role of insular gliomas and reached to some conclusions about the present feasibility and restriction of insular glioma surgery.

MATERIAL AND METHOD

Present study was carried out in Department of Neurosurgery S.M.S. Medical College & Hospital, Jaipur, India. A total of 25 patients of insular glioma (age >18 years) operated and managed from June 2016 to December 2017, were included in the study. Histopathological tumor grading was done according to the WHO guidelines[13]. Patient with multifocal lesions were excluded from study.

The clinical data included preoperative patient parameters (**Table-1**), Yasargil classification based on preoperative fluid –attenuated inversion recovery (FLAIR), T2 and T1 weighted postcontrast MR images, clinical presentation, age at the time of diagnosis, immediate postoperative MRI, histopathological review were collected from patient record. Low-grade and high-grade gliomas will volumetrically analyzed using FLAIR, T2-weighted image and contrast-enhanced T1-weighted MR imaging respectively.

***Volumetric analysis*:-** Volumetric measurement of pre and post operative imaging was conducted by primary neurosurgeon with the help of radiologist. MRIs in digital imaging and communication in medicine (DICOM) format were used for volumetric analyses of both pre and post operative tumor volume by using MRI images. For the postoperative volume measurement, we used MRI images acquired within 24 hrs after surgery. All preoperative and postoperative tumor volume measurement was performed manually with the *OsiriX* software tool[11].

For LGGs manual segmentation was performed with the region-of-interest (ROI) analysis to measure tumor volume(cm^3) on the basis of FLAIR and T2 weighted axial slice, for HGGs ,similar calculation was made using the volume of contrast enhancing tissue seen on T1 weighted MRI imaging. The extent of resection (EOR) was calculated as described by Smith et al[12], *(preoperative tumor volume – postoperative tumor volume)/preoperative tumor volume*. This study was approved by the institution ethics committee on human research.

Surgical Technique:- All surgical procedures were performed by standard microsurgical technique under general anaesthesia. Due to limitation of resources intraoperative neuronavigation system and neurophysiological monitoring was not used. Awake craniotomy (for sensory-motor and language mapping) could not be done in any of patient. In all cases patients were positioned supine on the table with shoulder elevated with the rest pad and head turned at an angle 60^0 contra lateral to surgical side, with some degree of head extension which allow access to the superior portion of the insula under the frontoparietal operculum. This positioning method allows for the frontal and temporal lobes to separate fall away under the action of gravity so that the sylvian fissure can be exposed easily without applying the retraction and provide more accessible trajectory towards the most posterior portion of insula which is hidden by pre and post central gyri[14].

A standard frontotemporal craniotomy was created in all patients to include the whole perisylvian area from the pars orbitalis of the inferior frontal gyrus to the postcentral sulcus which is the widest sulcus opening in to the sylvian fissure and which limits the posterosuperior corner of the insula. The anatomical landmarks used to limit the extent of resection were perinsular sulcus, limen insulae and Lateral Lenticulostriate Arteries (LLAs). In cases where involvement of eloquent area present the excision of the tumor based on the anatomical landmarks. Gross total removal of the tumor was done and tumor tissue was sent for histopathological examination.

Patient outcome measurement:- Neurological examinations were performed preoperatively and on follow up period. Immediate postoperative neurological examination was performed first 7 days after surgery and long term neurological function determined between 1month, 3 months and 6 months after surgery. Neurological morbidity was defined as new onset and worsening of existing neurological deficit as related to sensory, motor and visual, language function. The neurological outcomes of patients were studied preoperatively

Statistical Analysis

Statistical analyses were done using computer software (SPSS trial version 23 and primer). The qualitative data were expressed in proportion and percentages and the quantitative data expressed as mean and standard deviations or median. The difference in proportion was analysed by using chi square test Significance level for tests were determined as 95% ($P< 0.05$).

Result

Patient population

Table 1 showing patients demographic profile, clinical features and preoperative radiological tumour volume. The total study population included 25, out of them 48% were in 30 to 60 yrs of age groups followed by <30 years age group were 40% and least 12 % were in >60 years of age group. The male prepordance was observed, 17 (68%) were male and rest being the female, with M:F ratio was 2.13:1.The commonest clinical feature was headache observed in 76% cases followed by seizures 68%, 12% had motor deficit and 4% had sensory deficit. According to classification by Yasargil et al[2], 1(4%) glioma involved the sole insular lobe (type 3A), 2(8%) gliomas involved both insula and at least one operculum (type3B) and 12(48%) gliomas involved either frontoorbital or temporopolar areas (type5A) and part of the limbic system (type5B) in 10(40%) cases, type 5A and 5B gliomas occupying all zones as classification given by Berger- Sanai insular gliomas classification system[4], can also be define as giant. All the cases underwent MRI and preoperative tumour volume was assessed, most of cases (84%) had Karnofsky performance score (KPS) >90. Right side was invoved in 56% cases and preoperative tumor volume on T2 weighted MRI (in cm^3) > 50 cm^3 were observed in 88% cases. Median pre op. tumor volume was 89.72cm^3.

Post operative course and histopathological result

Post op clinical finding at 1 month, the commonest Neurological deficit was motor deficit observed in 32 % cases followed by Language deficit in 8%, and 8% was found in sensory deficit. Post op clinical finding at 6 months, motor and Language deficit were improved in 50% of affected cases. Commonest WHO grade tumor was grade-II 15(62.50%) followed by grade-IV 5(20.83%), grade-III 3(12.50%) and the grade-I tumor was 1(4.17%). Extent of resection (EOR) < 70% was seen in 21(87.50%) cases and EOR between 70-90% was in 4(16.67%) cases and EOR >90% was zero. Postoperative tumor volume was >30cm^3 in 19 (76%) cases and between 10-20 cm^3 in 4(16%) cases and <10cm^3 in 2(8%) cases. The median post op tumor volume was 60.9cm^3. One patient expired on 3 months after surgery due to unrelated causes. There is no intraoperative death in our series.

Discussion

Present study population included 25 patients in which 17(68%) male and 8 (32%) were female patients. In study by Sanai et al[4] male and female incidence was 42% and 62% whereas study by Praveen et al[1] showed 92% of male and 8% of female. The common presenting symptoms in our cases was headache (76%) followed by seizure (68%) motor deficit in 12%, sensory deficit in 4% , which is similar to study by praveen at al[18] having headache as most common symptom. However study by Sanai at al[4] and Duffau et al[16] showed seizure as the most common presentation.

In our study right sided tumours were more common as compared to left sided similar to study by Praveen et al[18.] In our study WHO grade II tumor was most common and constituted 62.50%, grade IV 20.83%, grade III 12.50% of patients whereas in series published by Sannai et al[4] , WHO grade II tumor was most common and constituted 60.1%, grade III 3o.4% and grade IV 8.7%.

In immediate post operative period, motor deficit developed in 8(32%) cases, speech disorder in 2(8%), sensory deficit in 2(8%) and vision in 1(4%) of the patients. At 6 months follow up motor deficit recorded in 4(16%) cases, vision deficit improved at 6 months follow up whereas language deficit continue in both the patients.

Hentschel and Lang[14] reported 11% transient motor deficit and 30% of transient speech deficit, whereas Sannai et al[4] recorded post operative deficit in only 14.4 % of cases , in our study 16% had transient post operative deficit supporting the idea of multimodal insular lobe which can also been supported by Skrap M et al[19].

Until recently EOR has often been estimated solely on the basis of intraoperative interpretation of the neurosurgeon resulting in the erroneous conclusion of the actual role of surgery. There are few studies on volumetric analysis of EOR and the studies show evidence supporting EOR as statically significant predictor of OS. In our study surgical removal of 70-90% of preoperative tumor volume was done in 16.67% of cases and less than 70% in 87.50% of cases. In cases with preoperative tumor volume more than 50cm^3, EOR was <70% in 90.48% of cases, though statistically, it was not significant, our data pointed out that EOR was less than 70% when preoperative tumor volume on MRI was more than 50cm^3.(FIG.1 and FIG. 2)

Similar result were also reported by Skrap M et al[19] in which EOR less than 70% when preoperative volume was more than 30cm^3.Thus suggesting that large preoperative tumour volume restricts EOR.

CONCLUSION

Insular glioma cases are difficult and challenging cases to operate and manage due to the inherent complexity and the adjacent vital structures around them and carry significant morbidity and complications.

In our study, we operated all cases under general anaesthesia and not been able to use intraoperative neuromonitoring and neuronavigation system but still, we are able to point out that large preoperative tumor volume restrict EOR and thus we can significantly increase the safe extent of resection with the use of above mentioned diagnostic tools. Under an experienced team and better anatomical knowledge helps us to bring out wider resection and better outcome. Though we cannot claim a substantial conclusion made from observations in 25 patients, however, our results provide early insights. Further, randomize studies required to evaluate these findings.

Table.1- Summary of preoperative clinical & radiological features in studied cases

			Skrap et al[19]	Sanai et al[4]
No of patients =N=25	PARAMETERS	N (%)	No of patients- N= 66	No of patient- N=104
Age (in years)	<30 yr	10 (40%)	-	119
	30-60 yr	12 (48%)	-	58
	>60 yr	03 (12%)	-	13

Mean± SD(median)	36.24±11.75 (35) 18to 62	-	19 to 68	18 to 75
Sex	Male	17 (68%)	40	42(40.4%)
	Female	08 (32%)	26	62(59.6%)
	M:F	2.13:1	-	-
Clinical features	Headache	19 (76%)	2	7(6.7%)
	Seizures	17 (68%)	64	75(72.1%)
	Motor deficit	3 (12%)	1	0
	Sensory deficit	1 (4%)	0	13 (12.5%)
	Language deficit	0	3	5(4.8%)
KPS Score	90	4 (16%)	-	-
	>90	21(84%)	-	-
	Median KPS score	100	95	84
	98.40±3.74 (90 to 100)	-	80 to 100	-
Side of tumour	Right side	14 (56%)	22	58(55.7%)
	Left side	11 (44 %)	44	46(44.3%)
Preoperative tumor volume on T2 weighted MRI (in cm^3)	> 50	22 (88%)		-
	< 50	3 (12%)		-
	Median preoperative volume(cm^3)	89.72	108	-
	Mean ±SD (min to max)	95.70±39.99 (16.91to190.76)	6 to 250	-
Insular glioma according to Yasargil classification[2]	3A	1(4%)	2	-
	3B	2(8%)	8	-
	5A	12(48%)	37	-
	5B	10(40%)	9	-

Table.2- Summary of postoperative clinical findings, histopathological result and volumetric analysis of EOR in studied cases

		Skrap et al[19]	Sanai et al[4]
Postop. Clinical findings at 1month		**Immediate postop findings**	
Neurological deficit		22	-
Sensory deficit	2 (8%)	0	-
Motor deficit	8(32%)	11	-
Visual deficit	1(4%)	0	-
Language deficit	2(8%)	11	-
Post op. Clinical finding at 6 month			**Postop findings at 4.2 yrs**
Neurological deficit		4	-
Sensory deficit	2 (8%)	0	0
Motor deficit	4(16%)	2	5
Visual deficit	0	0	0
Language deficit	2(8%)	2	0
WHO grade tumour			
I	1(4.17%)	-	-
II	15(62.50%)	53	17(60.1%)
III	3(12.50%)	13	35(30.4%)
IV	5(20.83%)	-	10(8.7%)
EOR (EXTENT OF RESECTION)			
EOR >90%	0	22	24(23.1%)
EOR 70-90%	04(16.67%)	30	40(38.1%)[EOR 80-89%] 29(27.9%)[EOR 60-79%]
EOR <70%	21(87.50%)	14	11(10.6%)[EOR 0-59%]
Median postoperative tumor volume (cm^3)	60.93	13	-
Mean ±SD (min to max)	58.08±34.8 (4.99 to 119.87)	0 to 112	-

Table.3- Linear association between preoperative tumor volume and EOR

Preoptumor volume(cm^3)	EOR in preop tumor				Total
	<70%		>70%		
	No.	%	No.	%	No
<50	2	9.52	1	25	3
>50	19	90.48	3	75	22
Total	**21**	**100.00**	**4**	**100**	**25**
Chi-square	0.001 with 1 degree of freedom; P = 0.973NS				

FIG.1.

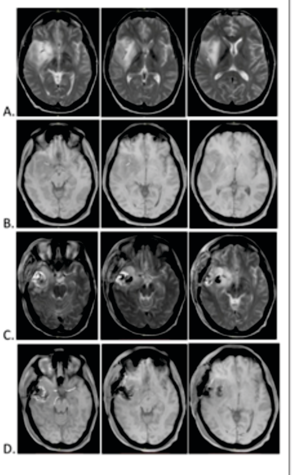

FIG.2.

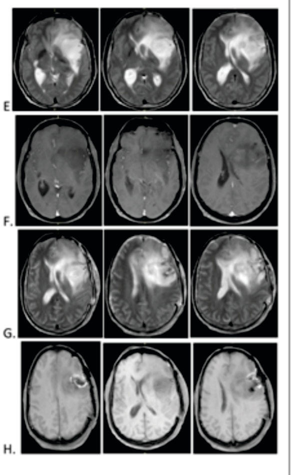

FIG.1. A case of right insular diffuse fibrillary astrocytoma. **(A).** preoperative axial T2-weighted MRI slices and **(B).** Preoperative axial T1- weighted MRI of right low-grade glioma with preoperative tumoral volume computed on postcontrast T1-weighted MRI was 50.9924cm^3 (axial slices). **(C).** Postoperative axial T2-weighted MRI slices and **(D).** Postoperative contrast axial T1- weighted MRI of right low-grade glioma with postoperative tumoral volume computed on postcontrast T1-weighted MRI was 7.1735cm^3 (axial slices). The tumoral volume was computed with OSIRIX software

FIG.2. A case of left insular diffuse astrocytoma **(E)** preoperative axial T2- weighted MRI and **(F)** preoperative axial T1- weighted MRI with pre operative tumor volume computed on post contrast T1 image was 88.4304cm^3.**(G)** Post operative axial T2 weighted MRI and **(H).** post operative contrast T1 –weighted MRi with post operative tumor volume computed on contrast T1- weighted MRI was 60.9347cm^3

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