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High rate of deletion of chromosomes 1p and 19q in insular oligodendroglial tumors

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Abstract

It has been reported recently that oligodendroglial tumors arising in the insula rarely harbor co-deletions of chromosomes 1p and 19q, a molecular signature which is associated with a good prognosis and increased responsiveness to radiation and chemotherapy compared with tumors in which 1p and/or 19q is intact. In the context of this claim, we analyzed a series of insular oligodendroglial tumors in order to determine the frequency of 1p/19q co-deletion in tumors arising in this region. We identified 14 insular cases operated on after 2003 in which testing for losses of 1p and 19q was performed. Of these cases, co-deletion of 1p and 19q occurred in eight (57%). Four (50%) of eight oligodendrogliomas and four (67%) of six oligoastrocytomas demonstrated 1p/19q co-deletions. Seven of the eight tumors with co-deletion of 1p/19q were WHO grade II gliomas. There were no statistical differences between tumors with 1p/19q co-deletion compared to those with 1p and/or 19q intact in terms of age, preoperative KPS, presenting symptoms, left versus right lateralization, tumor location (purely insular versus extension into frontal or temporal lobe), preoperative tumor size. There was a preponderance of females in the co-deletion group, and a greater average extent of resection. In contradistinction to previous reports, loss of 1p/19q occurs commonly in insular oligodendroglial tumors. With respect to 1p/19q, insular gliomas do not appear to be distinct from gliomas arising elsewhere in the brain.

Keywords

1p/19q co-deletion; Insula; Glioma; Oligodendroglioma

Introduction

The insula is increasingly recognized as a common location for the development of gliomas, particularly low grade gliomas [1]. The distinct cytoarchitectural organization of insular archicortex, along with differences in the development and differentiation of insular glial cells

compared with neocortical areas has led some investigators to hypothesize that insular gliomas are genetically distinct from gliomas in other brain areas.

Gliomas display a variety of molecular alterations, and there is substantial interest in determining which of these alterations have diagnostic and/or prognostic significance. The combined co-deletion of chromosome arms 1p and 19q, found commonly in oligodendrogliomas, but rarely in astrocytomas [2,3], has garnered attention as one such molecular signature with prognostic and predictive value. Recent studies, including Phase III trials of anaplastic (WHO grade III) oligodendrogliomas, have shown that tumors with co-deletion of 1p and 19q are associated with a better outcome and increased responsiveness to chemotherapy compared with tumors in which 1p and 19q are intact [4-8].

In this context, Goze et al. recently reported that co-deletion of chromosomes 1p and 19q occurs infrequently, if at all, in oligodendrogliomas arising in the insula. In their series of twelve insular WHO grade II gliomas, including eleven pure oligodendrogliomas and one mixed oligoastrocytoma, no tumor harbored co-deletion of both 1p and 19q, and only one case had a deletion of 1p [9]. Given the favorable prognosis associated with loss of 1p/19q, Goze et al. concluded that the infrequent loss of 1p and 19q in their cases supported the notion that insular gliomas carry an unfavorable prognosis compared with low grade gliomas in other brain areas [10]. This conclusion contrasted the recent report of Sanai et al who suggested that insular gliomas follow a more indolent course than gliomas in other brain areas [11], although analyses of 1p/19q were not undertaken. Therefore, we analyzed our series of insular gliomas [12,13] in order to determine the frequency of 1p/19q co-deletion in oligodendroglial tumors. In contrast to Goze et al., we report that co-deletion of 1p/19q occurred in 57% of 14 insular oligodendroglial tumors tested for this genetic marker.

Materials and methods

Case identification

At The University of Texas MD Anderson Cancer Center routine testing for co-deletion of 1p and 19q of all oligodendrogliomas and oligoastrocytomas began in 2003. For this study we reviewed 31 consecutive cases of insular tumors resected by the senior author (FFL) after 2003 [12,13] and identified 14 cases of oligodendroglial tumors, all of which were tested for 1p/19q co-deletion as part of their routine work-up during diagnosis. The remaining 17 insular glioma cases were pure astrocytomas and were excluded from this study. The 14 identified cases were reviewed by a senior neuropathologist (KA) blinded to the original histopathological diagnosis. Based on this review there were eight oligodendrogliomas and six oligoastrocytomas.

Determination of loss of 1p and 19q

1p/19q co-deletion status was determined by real-time polymerase chain reaction (rtPCR) prior to 2006 ($n = 9$), using the molecular diagnostics laboratory at MD Anderson by quantitative microsatellite analysis as previously described [14]. The following markers were tested: D1S468, D1S214, D1S2736, D1S2783, D1S514, D1S228, D1S199, D1S2620, D1S2892, and D1S224 for chromosome 1. Chromosome 19 markers were: D19S424, D19S408, D19S596, D19S867, D19S418, and D19S926. Reference markers (from regions of the genome which are infrequently altered in glioma) were as follows: D2S385, D3S1554, D5S643, D8S1800, D12S1699, and D21S1904. Chromosomal loss was scored if the majority of each chromosome arm had a ratio of 0.6 or less, in order to assess for complete or near complete loss. After 2006 fluorescent in situ hybridization (FISH) probes became commercially available and after this time, FISH was routinely performed ($n = 5$), using probes from Vysis, Inc (SpectrumOrange labeled 1p probe, SpectrumGreen labeled 1q probe, SpectrumOrange labeled 19q probe, and

SpectrumGreen labeled 19q probe) as previously described [15]. Since these probes interrogate a large region of the chromosome they represent a surrogate for extensive region of loss.

Clinical characteristics

For the 14 patients whose tumors were tested for 1p/19q co-deletion, the database of the Department of Neurosurgery was queried to obtain clinical and radiographic data including age at presentation, gender, presenting symptoms, Karnofsky performance score (KPS), tumor location, extent of resection, immediate and long-term neurological outcome, time to progression (if any) and survival. Volu-metric analysis was carried out on preoperative and postoperative MRI images with MedVision 1.41™ software, as previously described [16]. For nonenhancing tumors hypointense regions on T1-weighted images and hyperintense regions on FLAIR images were used to determine preoperative tumor volumes and extent of resection. For tumors with contrast enhancement, volumes were based on the enhancing mass as seen on the T1-weighted images. In cases of subtotal resection, the operative report was consulted to determine if there were specific intraoperative findings that prompted abandonment of planned further resection.

Statistical analysis

Kaplan–Meier survival analysis was performed using SPSS 12.0 software and *P*-values determined using the log-rank method. Student's *t*-test was used to calculate *P*-values for comparison of means, and Fisher's exact test was used to calculate *P*-values for categorical frequencies.

Results

Overall characteristics of study population

Table 1 summarized the characteristics of the 14 patients with insular gliomas who were tested for 1p and 19q co-deletion as part of their routine diagnostic work-up. There were 11 females and 3 males, with a mean age of 41 years old (range 29–61 years old). Seizures were the presenting symptoms in twelve cases. Three of these patients also had headaches, two had memory loss, and three had speech dysfunction. Two otherwise asymptomatic patients presented with radiographic progression of previously known lesions. One patient had a KPS at first presentation of 60, while all the others had presenting KPS between 80 and 100.

There were eight pure oligodendrogliomas and six mixed oligoastrocytomas. Ten tumors (71.4%) were classified as WHO grade II gliomas. Four tumors (28.6%) were classified as WHO grade III gliomas.

Five tumors were in the right insula, and nine tumors were in the left insula. Seven (50%) of the tumors were located solely within the insula (Fig. 1), whereas two tumors (14.3%) had frontal extension, three tumors (24.4%) had temporal extension, and two tumors (14.3%) had both frontal and temporal extension. Pre-operative volumetric data was available in 12 cases. The mean volume of FLAIR signal abnormality on the pre-operative MRI imaging was $70.9 \pm 45.3 \text{ cm}^3$ (range 16.8–146.9 cm^3). At the time of initial diagnosis, one anaplastic oligodendroglioma had significant contrast enhancement, while the remaining thirteen tumors were non-enhancing. For two tumors, post-operative volumetric data was not available.

Co-deletion of 1p and 19q

Co-deletion of 1p and 19q was present in eight (57%) of the 14 cases. In addition, there was one case of 1p deletion alone (19q intact) and one case of 19q deletion alone (1p intact). Both 1p and 19q were intact in the remaining four cases. A comparison of the histological, clinical

and tumor characteristics of the cases harboring co-deletion of 1p/19q with the cases where 1p and/or 19q was intact is shown in Table 2.

Regarding tumor type, four (50%) of the eight oligodendrogliomas and four (67%) of the six mixed oligoastrocytomas demonstrated 1p/19q co-deletions (Table 2). Seven of the eight tumors with co-deletion of 1p/19q were WHO grade II gliomas, while three of the six tumors with 1p and/or 19q intact were WHO grade II gliomas. Among WHO II gliomas, 7/10 (70%) had 1p/19q co-deletion, while in WHO III gliomas in our series, 1/4 (25%) had 1p/19q co-deletion.

There were no statistical differences between the groups with respect to age, preoperative KPS score, or presenting symptoms (Table 2). However, the only patient with a KPS of 60 was in the 1p/19q-intact group. Likewise, whereas all 8 patients whose tumors had co-deletion of 1p/19q presented with seizures, 4 of 6 patients whose tumors had 1p and/or 19q intact had seizures. Interestingly, all the patients in the co-deletion group were female, but only 3 of 6 patients (50%) in the intact group were female ($P = 0.06$, Fisher's exact test) (Table 2).

In terms of tumor characteristics, no major differences were observed in tumor lateralization as the ratio of left to right location was nearly the same in the two groups (Table 2). Importantly, tumors confined entirely to the insula were equally likely to harbor co-deletions of 1p/19q as they were to have 1p/19q intact (Fig. 1, Table 2). Specifically, of the seven tumors confined to the insula, four (57%) harbored 1p/19q co-deletions and three (43%) had 1p/19q intact ($P = 0.41$, Fisher's exact test). Likewise, among the seven tumors that extended into the frontal and/or temporal lobe, 4 were 1p/19q co-deleted and 3 were not. Lastly, there was no statistically significant difference in the preoperative tumor volumes between the two groups.

Surgical results

A comparison of surgical and long-term outcome between the 1p/19q-co-deletion group and the 1p/19q-intact group is shown in Table 3. A trend was observed towards greater average extent of resection in the 1p/19q co-deletion group ($90.1 \pm 6.8\%$, $N = 6$) versus the group in which 1p and/or 19q was intact ($70.3 \pm 26.9\%$, $P = 0.07$, $N = 6$). Likewise post-operative residual tumor volume, based on FLAIR MR images was 19.0 cm^3 ($N = 7$, range 0–49.72 cm^3) in the co-deletion group, and 39.2 cm^3 ($N = 6$, range 8.9–90.4 cm^3) in the intact group, and only 1 case in the co-deletion group had <85% resection, compared to 4 cases in the intact group. Of these five cases, tumor removal was halted in three cases after the development of new motor or speech disturbances during awake craniotomy, and in two cases resection was halted because the residual tumor was too intimately involved with important neurovascular structures.

Two patients with left insular tumors had post-operative deficits. One had mild contralateral weakness and speech deficit, while the second had speech deficit only. In both these cases, the deficits were transient and had fully resolved within 3 months. Both these patients had tumors with co-deletion of 1p and 19q. In all other cases, patients had unchanged or improved neurological status post-operatively.

Long term outcome

Mean follow-up from the time of first diagnosis was 45.8 months in the group with co-deletion of 1p/19q, and mean follow-up was 49.5 months in the group with 1p and/or 19q intact ($P = 0.40$) (Table 3).

All patients harboring insular tumors with 1p/19q co-deletion were alive at last follow-up, including 6 WHO grade II tumors and 2 WHO grade III tumors. In contrast, two of the six insular gliomas with intact 1p and/or 19q had died: 1 of 3 patients with WHO grade III tumors

and 1 of 3 patients with WHO grade II tumors. These patients died 29 and 70 months after diagnosis of the tumor. Median overall survival based on Kaplan-Meier analysis was not reached for both groups.

In terms of tumor progression, in the group of patients with insular tumors harboring co-deletion of 1p/19q, three patients progressed at 29.3, 78.8, and 132.1 months, respectively. In the group of patients with insular tumors in which 1p and/or 19q was intact, four patients progressed at 9.7, 11.6, 64.9 and 65.8 months, respectively. Median progression-free survival in the co-deletion group was 77.8 months (95% CI 5.2–150.4) and 64.9 (95% CI: 0–144.7) months in the intact group ($P = 0.11$).

Discussion

In this retrospective series of 14 insular oligodendroglial tumors, we found that eight (57%) harbored a co-deletion of chromosomes 1p and 19q. We report 1p/19q co-deletion in 50% of insular oligodendrogliomas, and 67% of insular mixed oligoastrocytomas.

These results are consistent with the rates of 40–70% reported in the literature for 1p/19q co-deletion of oligodendroglial neoplasms located throughout the brain [2–4,9]. However, they stand in stark contrast to the results reported by Goze et al., who found no cases of 1p/19q co-deletion in a series of 12 insular oligodendrogliomas [9], and who concluded that insular oligodendrogliomas have a unique molecular profile that gives them an inherently worse prognosis compared with gliomas in other parts of the brain. On the contrary, the frequent co-deletion of 1p/19q reported in our series suggests that insular oligodendroglial tumors are not molecularly distinct from oligodendrogliomas located in other parts of the brain, at least with regards to this one molecular signature.

To our knowledge Goze et al. were the first to analyze the rate of 1p/19q co-deletion specifically in insular gliomas. Therefore, our series represents only the second report specifically analyzing 1p/19q co-deletion in insular gliomas. However, preferential distribution of 1p/19q co-deletion in different brain area has been reported by others. Zlatescu et al. reported 1p/19q co-deletion occurred more frequently in anaplastic oligodendrogliomas located in the frontal, parietal, and occipital lobes compared with the temporal lobe, insula, and diencephalon [17]. Although this study included 5 insular tumors these cases were not analyzed separately, but were included with the temporal tumors. Other investigators have reported differing molecular profiles in oligodendroglial neoplasms found in the temporal lobe, compared with those found elsewhere, with the temporal tumors typically harboring intact 1p and 19q, like astrocytomas [18]. Other reports have shown higher frequencies of 1p/19q co-deletion in oligodendrogliomas found in the frontal lobes compared to parietal, temporal, and occipital locations [19,20]. Therefore, it remains unclear if tumors with 1p/19q co-deletion are distributed unevenly through the brain. In this context, the opposing results found by us and by Goze et al. may reflect the contradictory results reported for other brain regions and may be exaggerated by the small size of both studies. Clearly, larger series will be needed to decipher this issue.

An important aspect of our study was that seven of the 14 cases were located entirely within the insular and 57% of these purely insular tumors harbored co-deletion of 1p/19q. Therefore, the different results reported by us and Goze et al. are not due to differences in the locations from which the tumor arose. In other words, it could be argued that tumors that arise either frontally or temporally have a rate of 1p/19q co-deletion reflective of gliomas of these more general brain locations and, therefore, studies that include tumors located in frontal and/or temporal lobes that secondarily extend into the insular may have a higher proportion of 1p/19q co-deletion compared with studies that include only bona fide insular tumors. The fact that 50% of our cases were purely insular tumors without extension into other brain regions makes

it unlikely that our results were skewed by the possibility that we included tumors that arose in the frontal or temporal lobes and then secondarily extended into the insular (Fig. 1). In addition, the seven cases with frontal and/or temporal extension in our series appeared to have originated in the insular because (1) the insular was the epicenter of the tumor in each case, and (2) the pattern of brain distortion was consistent with an insular origin. Specifically, frontal tumors with secondary insular extension typically compress the anterior insular, whereas insular tumors with secondary frontal extension do not. Similarly temporal tumors that secondarily extend into the insular often lift the inferior insular sulcus, whereas insular tumors with secondary temporal extension expand the inferior insula, pushing the inferior insular sulcus down. In the cases in this series, the pattern of growth was consistent with a primary insular tumor with secondary extension into the surrounding lobes. Lastly, there has been some speculation that frontal oligodendrogliomas more frequently harbor 1p/19q co-deletions than do temporal oligodendrogliomas [18,19]. However, we found no predilection for insular tumors with frontal extension to harbor co-deletions of 1p/19q co-deletion compared with insular tumors with temporal extension. In this context, the frequent loss of 1p and 19q observed in our insular gliomas cannot be explained by incorrect inclusion of tumors originating outside the insular.

The genetic mechanism that ultimately produces 1p/19q co-deletion in oligodendrogliomas is a translocation event, followed by preferential loss of the fusion chromosome [8]. This results in a whole-arm deletion of 1p and 19q that is typical of 1p/19q co-deleted oligodendrogliomas. The putative tumor-suppressor genes affected by 1p/19q co-deletion are currently believed to reside in regions 1p34-36 and 19q13 [20-22]. A reduction in the dose of the 1p gene *STATHMIN* is now suspected to play a role in increased sensitivity to chemotherapy [23]. Partial deletions of portions of 1p or 19q are not uncommon in astrocytomas, but do not carry the same degree of prognostic significance as complete loss of 1p/19q. It is certainly possible for partial deletions of 1p and 19q to occur as separate events within the same glioma, resulting in the appearance of a 1p/19q co-deletion that in actuality represents a different genetic event with a different impact, if any, on prognosis. The rtPCR and FISH techniques used in this study relied upon multiple probes designed to interrogate large regions of the chromosomes in order to detect extensive regions of loss and differentiate between complete and partial loss of the chromosome arm. Therefore, it is unlikely that our method detected only partial losses rather than complete chromosomal losses.

Our finding that co-deletion of 1p/19q is found in 50% of insular oligodendrogliomas may represent a more expected result than that of Goze et al. because it is consistent with the multiple anatomic and functional connections of the insular lobe. Specifically, the insula is a transition zone between allocortex and neocortex, and structurally possesses connections to frontal, temporal, and limbic areas [24]. As an interface, the insular cortex may be molecularly defined by the brain regions with which it anatomically and functionally integrates. Therefore, rather than being an area of unique molecular profile, it may instead be a combination of the regions and architectures that it acts to integrate and, therefore, may contain cells of diverse molecular profile. As such, within the insula there may be separate areas of frontal, temporal, or limbic origin, differentiation and molecular disposition. Consequently, our finding that insular gliomas include both 1p/19q-co-deletion tumors and 1p/19q-intact tumors is consistent with the notion that the insular is a molecularly heterogeneous region.

In our study there was a strong trend towards a female preponderance in cases with co-deletion of 1p/19q. All of the patients in the co-deletion group were female, whereas females comprised only 50% of the intact group ($P = 0.06$). To our knowledge, no study has shown a gender predilection for 1p/19q co-deletion [25]. However, there is a known female preponderance of anaplastic oligodendrogliomas [25], and female sex has been found to be a favorable prognostic factor for patients with oligodendrogliomas in general [6]. Interestingly, the patients in the

series reported by Goze et al were predominantly male (8 of 12) [9]. Although a correlation between female gender and co-deletion of 1p/19q in insular oligodendrogliomas remains an intriguing possibility, this finding could represent a statistical aberration due to the small size of our cohort.

In patients whose tumors harbored co-deletion of 1p/19q compared with those in which 1p and/or 19q remained intact, we found trends towards greater average extent of resection (90% vs. 70%, $P = 0.07$). Similar trends were observed in post-operative tumor volumes (19 vs. 39 cm³, respectively), and the proportion of tumors where [85% resection was achieved (83% vs. 33%, respectively) (Table 3). These results suggest the hypothesis that insular tumors with co-deletion of 1p and 19q may be more easily resected. Why this might be so was not specifically investigated in this study, but intra-operative reports suggested that tumors with co-deletion of 1p/19q were less likely to infiltrate functional brain regions and to violate anatomic resection planes. To our knowledge this is the first report suggesting that tumors with 1p/19q co-deletion are more easily resected than those tumors with 1p/19q intact. Indeed, this difference may impact the improved survival associated with lesions harboring 1p/19q co-deletions. Clearly larger studies analyzing the resectability of these tumor subtypes will be necessary to resolve this issue.

Given the established positive prognostic significance of 1p/19q co-deletion [4,5,7,8,26], it is not surprising that we found a trend towards improved progression-free survival and long term survival in patients with intact 1p and/or 19q. However, it is difficult to draw definitive conclusions because there was a greater proportion of higher grade tumors among the patients in which 1p and/or 19q were intact, and because the sample size was small. It has been suggested that insular gliomas have a poorer overall prognosis compared with gliomas in other brain regions [10], although other reports contradict this assertion [11]. Our data does not address whether the prognosis of patients with insular gliomas with 1p/19q co-deletion is similar to or worse than patients with gliomas with 1p/19q co-deletion located in other parts of the brain. Clearly, large series that control for age, tumor grade, extent of resection, and other prognostic variables will be needed to determine whether insular tumors, in general, and those with 1p/19 deletions, in particular, behave differently compared with tumors in other brain locations.

In conclusion, in contrast to the recent report of Goze et al., we show that loss of 1p/19q is not infrequent in insular oligodendroglial tumors. However, given the small size of both our series and that of Goze et al., further studies will be needed to further define the actual frequency of 1p/19q co-deletion in insular gliomas.

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Fig. 1.
Comparison of low grade gliomas involving only the insula. **a** Tumor with 1p/19q co-deletion.
b Tumor with 1p/19q intact

Table 1

Summary of patient and tumor characteristics for patients with insular oligodendroglial tumors tested for 1p/19q co-deletion status

<i>N</i>	14
Age, years	
Mean $\pm$ standard deviation	40 $\pm$ 9.8
Range	29–61
Male:Female	11:3
Pre-operative KPS	
Median	90
Range	60–100
Presenting symptoms	
Seizures (%)	12 (86%)
Speech deficit (%)	3 (21%)
Memory disturbance (%)	2 (14%)
Headache (%)	3 (21%)
Radiographic progression (%)	1 (7%)
Pathological diagnosis	
Oligodendroglioma	
WHO II	4
WHO III	4
Oligoastrocytoma	
WHO II	6
Total ratio WHO II:III	10:4
Right:Left	5:9
Location	
Insula only (%)	7 (50%)
Insula-Frontal (%)	2 (14%)
Insula-Temporal (%)	3 (21%)
Insula-Frontotemporal (%)	2 (14%)
Pre-operative FLAIR abnormality volume, cm ³	
Mean $\pm$ standard deviation	70.9 $\pm$ 45.3
Range	16.8–146.9
Post-operative FLAIR abnormality volume, cm ³	
Mean $\pm$ standard deviation	28.3 $\pm$ 26.9
Range	0–90.4

Table 2

Comparison of patient and tumor characteristics, 1p19q co-deletion present versus patients with 1p and/or 19q intact

	1p19q co-deletion	1p and/or 19q intact	<i>P</i>
<i>N</i>	8	6	
Age, years			
Mean $\pm$ standard deviation	41 $\pm$ 12	42 $\pm$ 7.1	0.39
Range	29–61	34–52	
Male:Female	0:8	3:3	0.06
Pre-Op Karnofsky performance score			
Median	90	90	0.41
Range	80–100	60–100	
Symptoms			
Seizures (%)	8 (100%)	4 (67%)	0.17
Speech deficit (%)	1 (13%)	2 (33%)	0.33
Memory disturbance (%)	2 (25%)	0 (0%)	0.31
Headache (%)	1 (13%)	2 (33%)	0.33
Radiographic progression (%)	0 (0%)	1 (17%)	0.43
Pathological diagnosis			
Oligodendroglioma			
WHO II	3	1	
WHO III	1	3	
Oligoastrocytoma			
WHO II	4	2	
Total ratio WHO II:III	7:1	3:3	0.18
Right:Left	3:5	2:4	
Location			
Insula only (%)	4 (50%)	3 (50%)	0.41
Insula-Frontal (%)	1 (13%)	1 (13%)	0.53
Insula-Temporal (%)	2 (25%)	1 (13%)	0.62
Insula-Frontotemporal (%)	1 (13%)	1 (17%)	0.53
Pre-op FLAIR abnormality volume, cm ³			
Mean $\pm$ standard deviation	66.4 $\pm$ 49.6	76.1 $\pm$ 43.8	0.36
Range	17.2–138.9	16.8–146.9	

Table 3

Comparison of surgical and long-term followup and outcome, 1p19q co-deletion present versus patients with 1p and/or 19q intact

	1p19q co-deletion	1p and/or 19q intact	<i>P</i>
<i>N</i>	8	6	
Extent resection (<i>N</i> = 12)			
<i>N</i>	6	6	
Mean ($\pm$ standard deviation)	90.1% $\pm$ 6.8%	70.3 $\pm$ 26.9%	0.07
Range	79.6–100%	27.5–97.3%	
>95% (%)	1 (16.7%)	2 (33.3%)	0.41
80–95% (%)	4 (66.7%)	0 (0%)	0.03
<80% (%)	1 (16.7%)	4 (66.7%)	0.11
Post-op FLAIR abnormality volume, cm ³			
Mean $\pm$ standard deviation	19.0 $\pm$ 19.1	39.2 $\pm$ 32.1	0.11
Range	0–49.7	8.9–90.4	
Surgical morbidity			
Immediate			
Speech deficit, L sided tumors (%)	2/5 (25%)	0/4 (0%)	0.28
Hemiparesis (%)	1/8 (13%)	0/6 (0%)	0.57
Any deficit (%)	2/8 (25%)	0/6 (0%)	0.31
30 day follow-up			
Speech deficit, L sided tumors (%)	0/5 (0%)	0/4 (0%)	1.000
Hemiparesis (%)	0/8 (0%)	0/6 (0%)	1.000
Any deficit (%)	0/8 (0%)	0/6 (0%)	1.000
Recurrence/Progression			
WHO II	3/7	3/3	0.17
WHO III	0/1	1/3	0.75
Whole group	3/8	4/6	0.25
Median PFS, months (95% CI)	77.8 (5.2–150.4)	64.9 (0–144.7)	0.11
Deaths			
WHO II	0/6	1/3	
WHO III	0/2	1/3	0.33
Whole group	0/8	2/6	0.60
Median OS, months (95% CI)	Not reached	Not reached	0.17
Follow-Up, months $\pm$ standard deviation	45.8 $\pm$ 46.7	49.5 $\pm$ 16.3	0.40

PFS progression free survival

OS overall survival