Can oligodendrocyte transcriptional factor-2 (Olig2) be used as an alternative for 1p/19q co-deletions to distinguish oligodendrogliomas from other glial neoplasms?

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Abstract

Aim of the study: Oligodendrocyte transcriptional factor-2 (Olig2) is an essential marker for oligodendrocytes expression. We aimed to explore the expression of Olig2 in different glial neoplasms and to investigate if diffuse Olig2 expression can replace 1p19q co-deletion for the diagnosis of oligodendroglioma.

Material and methods: Olig2 was performed on 53 samples of different glial neoplasms using immunohistochemistry (IHC). 1p/19q deletions were investigated using fluorescence in situ hybridization (FISH).

Results: Olig2 labelling of different glial neoplasms revealed various expressions, in which 26 tumours showed diffuse expression (≥ 60%) and 23 tumours showed partial focal expression (< 50%). Four tumours showed no expression. Of the 26 tumours, 6 oligodendrogliomas had 1p19q co-deletion and the remaining 3 oligodendrogliomas showed no co-deletion. Three non-oligodendroglial tumours were found to have 19q deletion. The FISH of the remaining tumours (14/26) showed no aberrations. There was no significant difference in the final diagnosis by using 1p19q co-deletion test among glial neoplasms with diffuse Olig2 expression (p = 0.248).

Conclusions: Olig2 marker cannot be used as an alternative diagnostic method for 1p19q co-deletion to distinguish oligodendrogliomas from other glial neoplasms. Although some glial tumours showed diffuse Olig2 expression, 1p19q co-deletion testing is the best diagnostic method.

Key words: gliomas, oligodendroglioma, Olig2, FISH, 1p19q co-deletion.

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Introduction

The most common primary brain tumours are those with a glial cell origin, which cannot be fully classified by cellular morphology only [12]. The molecular analysis became crucial for glioma differentiation, grading and prognosis. Loss of heterozygosity (LOH) at specific chromosomes is critical for tumorigenesis and possible transformation of low-grade gliomas to higher grade gliomas [10]. One of these common genetic biomarkers is 1p19q co-deletion. This genetic alteration results from the combined deletion of entire 1p19q after unbalanced translocation between chromosomes 1 and 19 [t(1:19)(q10;p10)] [8]. Although there are currently no available molecular markers that reliably distinguish oligodendrogial tumours from astrocytomas, 1p19 co-deletion has been considered as one of the hallmark criteria for the diagnosis of oligodendroglia, based on the 2016 World Health Organization (WHO) Classification of Tumours of the Central Nervous System (CNS) [1,8,10]. Hence, recent clinical trials have approved the associations between 1p19q co-deletion and prolonged overall survival of patients treated with radiation with or without chemotherapy [3,4]. One of the limitations of FISH technique is that it can detect deletions at a particular locus but cannot assess the extent of these deletions (partial or full arm). This alteration recently was found in association with Isocitrate dehydrogenase-1 (IDH1) mutation; a common criterion to diagnose oligodendroglioma. However, IDH1 mutation can be seen in other subsets of astrocytomas [17].

Although partial loss of one or other chromosomes have been described in astrocytomas, such as LOH on 19q for anaplastic astrocytoma and secondary glioblastoma, the co-deletion has also been reported in some cases of astrocytoma [14,15]. Around 4-12% of primary glioblastomas were also proven to have 1p19q co-deletion [17]. Kaneshiro et al. found that 3% of 337 glioblastomas demonstrated evidence for 1p19q co-deletion [9]. This finding has never been discussed further in the literature. These tumours were astrocytic in nature and have shown features of classical glioblastoma [9]. It was unclear if these cases were primary glioblastoma or secondary glioblastoma upgraded from anaplastic oligodendroglioma. Another study done by Sim et al., who evaluated 80 glioblastomas, has explored 1p/19q co-deletion in only two tumours [16]. Despite these findings, FISH for 1p/19q co-deletions remains a widely employed methodology to evaluate gliomas with oligodendroglial components.

The association of brain gliomas with 1p19q co-deletion and Olig2 expression has never been explored. Olig2, a member of the group of basic helix-loop-helix transcription factors, is essential for the development of neural progenitors and oligodendrocytes [12]. Several studies have detected prominent Olig2 expression in oligodendroglialomas and oligoastrocytomas [2,5-7,11,13]. Many neuropathologists use Olig2 marker as a diagnostic tool to diagnose oligodendroglial neoplasms (oligodendroglioma and oligoastrocytoma) when Olig2 is diffusely expressed in the tumours. However, this association is not proven yet and requires further investigations.

Lu et al. found that Olig2 was expressed in oligodendroglial tumours more than in astrocytic tumours [11]. Nevertheless, Olig2 cannot be used as a distinguishing marker between oligodendroglia and astrocytic neoplasms. The expression of Olig2 was proven to be weak in many glioblastomas except glioblastoma cases with oligodendroglial component (GBMO), which have shown prominent Olig2 expression in only oligodendroglial foci [7]. This also has been found in pilocytic astrocytoma cases where oligo nodules are seen [5]. Moreover, Olig2 expression is not merely restricted to oligodendroglial areas as it was typically expressed in some grade II astrocytomas.

In this study, we aim to explore the relationship between Olig2 expression and 1p19q deletion in different glial neoplasms and also to investigate if diffuse Olig2 expression can replace 1p19q co-deletion for the diagnosis of oligodendroglioma.

Material and methods

Patients selection

This study included 53 patients with different types of glial neoplasms from one medical institution in Saudi Arabia. The cases were diagnosed after complete surgical resection or tumour biopsy. The study was ethically approved by the National Biomedical Ethics Committee at King Abdulaziz University (HA-02-J-008) under general ethical approval. The clinical data retrieved from the hospital records included age, gender, tumour type and location, and recurrence interval (Table I). The histological diagnosis was made based on classification of the 2016 WHO [10].
Tumour samples

Archival formalin-fixed and paraffin-embedded (FFPE) tissue blocks of 53 tumours, diagnosed with different types of glial neoplasms, were utilized in this study. Haematoxylin and Eosin (H&E)-stained sections were re-examined by a certified neuropathologist (MK) to assure that the histopathological diagnosis has been made based on 2016 WHO classification of CNS tumours.

Methodology

Immunohistochemistry (IHC) for Olig2 and IDH1 antibodies

Protocol

4-μm FFPE tissue sections were used in the IHC process. The IHC assay was performed on two types of antibodies (a) anti-IDH1R132H (clone: H09, rabbit monoclonal antibody, Dianova) and (b) anti-Olig2 (EPR2673, rabbit monoclonal antibody, Cat#ab109186, Abcam). The procedure was performed with the ultraView DAB detection Kit on a BenchMark XT automated stainer from Ventana (Tucson, AZ, USA). A protocol was established so that the entire assay procedure consisted of deparaffinization with EZ Prep at 75°C, heat pre-treatment in Cell Conditioning medium (Ag unmasking) (CC1; Ventana) for 60 min and then primary incubation for 16 min at 37°C. The antibodies were optimized using different dilutions, range of 1 : 100-1 : 300. The slides were counterstained with Haematoxylin II for 16 minutes and bluing reagent was used for 16 min. After that, the slides were removed from the slide stainer and then immersed into successive alcohol buffers at different concentrations for 3 min.

Assessment

For Olig2, nuclear and perinuclear staining of tumour cells was considered a positive expression. After immunostaining, a single focal area of positive expression per patient sample was evaluated under light microscopy using high-power (40×) magnification. The positively stained cells and total cells, including positively and negatively stained cells, were counted manually using labelling index based on the following equation:

\[
\text{Labelling index (\%) = \frac{\text{(Olig2}^*\text{ stained tumour cells)}}{\text{(total cells) \times 100}}}.
\]

Table I. Demographic data of the 53 patients enrolled in this study. 26 cases were identified to have diffuse Olig2 expression through immunohistochemistry IHC

| Demographic data | Total cases (N = 53) | Cases with 1p19q (n = 26) |
|------------------|----------------------|---------------------------|
| Age              |                      |                           |
| Mean (SD)        | 28.8 (22.9)          | 36.1 (20.8)               |
| Gender, n (%)    |                      |                           |
| Female           | 21 (39.6)            | 12 (46.2)                 |
| Male             | 32 (60.4)            | 14 (53.8)                 |
| Tumour location, n (%) |            |                           |
| Frontal          | 13 (24.5)            | 12 (46.2)                 |
| Parietal         | 10 (18.9)            | 6 (23.1)                  |
| Temporal         | 10 (18.9)            | 6 (23.1)                  |
| Occipital        | 2 (3.8)              | 1 (3.8)                   |
| Lateral ventricle| 1 (1.9)              | 0 (0.0)                   |
| Posterior fossa  | 15 (28.3)            | 3 (11.5)                  |
| Brainstem        | 1 (1.9)              | 0 (0.0)                   |
| Thalamic         | 1 (1.9)              | 0 (0.0)                   |
| Histopathological diagnosis, n (%) |      |                           |
| Pilocytic astrocytoma | 3 (5.7) | 2 (7.7) |
| Pleomorphic xanthoastrocytoma | 2 (3.8) | 2 (7.7) |
| Diffuse astrocytoma | 5 (9.4) | 1 (3.8) |
| Oligodendroglioma | 9 (17.0)            | 9 (34.6)                  |
| Oligoastrocytoma | 1 (1.9)              | 1 (3.8)                   |
| Anaplastic astrocytoma | 5 (9.4) | 5 (19.2) |
| Glioblastoma     | 11 (18.9)            | 6 (23.1)                  |
| Ependymoma       | 17 (32.1)            | 0 (0.0)                   |
| Olig2 Labelling Index, n (%) |      |                           |
| Diffuse expression | 26 (49.1) | 26 (100) |
| Partial expression | 12 (22.6) |                             |
| Focal expression | 11 (20.8)            |                           |
| No expression    | 4 (7.5)              |                           |

The staining pattern was categorized as (i) diffusely expressed, (ii) partially expressed, (iii) focally expressed, and (iv) not expressed (Fig. 1A-C, 2A-D) based on the following scoring system:

| Expression | Labelling index (%)* |
|------------|----------------------|
| No expression | 0                    |
| Focal expression | > 0-19               |
| Partial expression | > 19-59             |
| Diffuse expression | ≥ 60                 |

*For statistical analysis, the scores were divided by 100.

Table I. Demographic data of the 53 patients enrolled in this study. 26 cases were identified to have diffuse Olig2 expression through immunohistochemistry IHC
Tumour cases \( (n = 26) \) with diffuse Olig2 expression have been tested for \( IDH1^{R132H} \) mutation. Sections in which > 10% of glial tumour cells positively stained were defined as \( IDH1^{mutant} \) (Fig. 2E, F).

**Fluorescent in situ hybridization (FISH) technique**

Fluorescent in situ hybridization (FISH) was used for the detection of deletions involving the human chromosomal region 1p36 as well as chromosomal...
region 19q13 on FFPE tissue slides of the 26 tumour cases that showed diffuse expression by Olig2.

Protocol

A 5-μm-thick FFPE tissue on positive charge slides was deparaffinised according to the instructions of the ZytoLight FISH-Tissue Implementation Kit (ZytoVision, Bremerhaven, Germany). This process was followed with digestion by pepsin to allow for probe hybridization. Then DNA was denatured by heating and the hybridization was performed using 10 μl of the probe onto each pretreated specimen. The used probe (ZytoLight SPEC 19q13/19p13 Dual Color Probe) appears with orange signals at 1p36 loci and the control locus 1q25 appears with red signals, the other probe target 19q13 locus with orange signals and the control locus 19p13 appears green. Target DNA and probes were codenatured at 74°C for 5 minutes and incubated at 37°C overnight in a humidified hybridization chamber (ThermoBrite, Abbott Molecular Inc.). Post-hybridization washing was performed to remove excess unbound probes. At the end, the slides were counterstained with DAPI (4′,6-diamidino-2-phenylindole) for cellular visualization.

Assessment

Enumeration of 1p/19q signals was conducted by two technologists independently. Scoring of 100 non-overlapping nuclei within the target areas (100 total tumour cell nuclei) for each probe set was performed using a Metasystem station (Zeiss MetaSystems, Thornwood, NY, USA) equipped with an appropriate excitation emission filter. Results were reported as the ratio of the total number of orange signals to green signals for each probe set (1p36:1q25 and 19q13.3:19p13 signals) (Fig. 3).

Statistical methods

Data are described as frequencies and percentages. Chi-square and Fisher’s exact were used to

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Fig. 3. FISH for 1p and 19q deletion using two probes in two different slides and normal control. The used probe (ZytoLight SPEC 19q13/19p13 Dual Color Probe) appears with orange signals at 1p36 loci and the control locus 1q25 appears with red signals, the other probe target 19q13 locus with orange signals and the control locus 19p13 appears green. “Green” signal is normal and “Red” signal is abnormal. A) 1p1q normal control, B) 19q19p normal control, C) 1p deletion, D) 19q deletion.
explore the association of between IDH1 mutation and the type of glial neoplasms. The McNemar χ² test was used to explore the diagnostic accuracy between oligodendrogial and non-oligodendrogial neoplasms using FISH technique or IHC. All statistical analyses were performed using the IBM SPSS1 ver. 24 statistical software programs (SPSS Inc., Chicago, IL, USA).

Results

This study included 53 patients diagnosed with different types of glial neoplasms (oligodendrogial and non-oligodendrogial tumours). The mean age was 28 years; 32 males (60.4%) and 21 females (39.6%). Patients aged less than 18 years were 19 cases. The type of glial neoplasms and their locations are summarized in Table I. Olig2 immuno-

| Table II. Demographic information of the 26 patients who showed diffuse Olig2 expression ≥ 60%. The differentiation includes histogenesis, IDH1 mutation, and 1p19q fluorescence in situ hybridization (FISH) testing |
|---------------------------------|-------------|--------|-------|----------|
| Histopathological diagnosis     | Grading     | Olig2 LI (%) | IDH1 status | FISH |
| Oligoastrocytoma                | Grade III   | 99      | IDH-wildtype | 19q deletion |
| Pleomorphic xanthoastrocytoma   | Grade II    | 97      | IDH-wildtype | Intact |
| Glioblastoma                    | Grade IV    | 96      | IDH-mutant   | Intact |
| Anaplastic astrocytoma          | Grade III   | 94      | IDH-wildtype | 19q deletion |
| Oligodendroglioma               | Grade III   | 94      | IDH-mutant   | 1p19q co-deletion |
| Oligodendroglioma               | Grade III   | 93      | IDH-mutant   | 1p19q co-deletion |
| Glioblastoma                    | Grade IV    | 93      | IDH-mutant   | Intact |
| Glioblastoma                    | Grade IV    | 92      | IDH-wildtype | Intact |
| Glioblastoma                    | Grade IV    | 92      | IDH-wildtype | Intact |
| Oligodendroglioma               | Grade III   | 91      | IDH-mutant   | 1p19q co-deletion |
| Oligodendroglioma               | Grade III   | 90      | IDH-mutant   | Intact |
| Oligodendroglioma               | Grade III   | 90      | IDH-mutant   | 1p19q co-deletion |
| Diffuse astrocytoma             | Grade II    | 87      | IDH-mutant   | Intact |
| Anaplastic astrocytoma          | Grade III   | 86      | IDH-wildtype | Intact |
| Pilocytic astrocytoma           | Grade I     | 85      | IDH-wildtype | Intact |
| Anaplastic astrocytoma          | Grade II    | 83      | IDH-mutant   | 19q deletion |
| Oligodendroglioma               | Grade III   | 83      | IDH-mutant   | Intact |
| Anaplastic astrocytoma          | Grade III   | 81      | IDH-mutant   | Intact |
| Pleomorphic Xanthoastrocytoma   | Grade III   | 80      | IDH-wildtype | Intact |
| Anaplastic astrocytoma          | Grade III   | 80      | IDH-wildtype | Intact |
| Glioblastoma                    | Grade IV    | 79      | IDH-wildtype | Intact |
| Pilocytic astrocytoma           | Grade I     | 77      | IDH-wildtype | Intact |
| Oligodendroglioma               | Grade I     | 65      | IDH-mutant   | 1p19q co-deletion |
| Glioblastoma                    | Grade IV    | 63      | IDH-mutant   | Intact |
| Oligodendroglioma               | Grade III   | 63      | IDH-mutant   | 1p19q co-deletion |
| Oligodendroglioma               | Grade III   | 60      | IDH-mutant   | Intact |

LI – labelling index, FISH – fluorescence in situ hybridization

| Table III. Fluorescence in situ hybridization (FISH) testing for the 26 tumour cases that showed diffuse Olig2 expression |
|------------------------------------------------------------------------------------------------------------------|
| FISH result                  | 1p19q cases (n = 26) |
| No deletion                  | 17 (65.4%)          |
| 19q deletion                 | 3 (11.5%)           |
| 1p19q co-deletion            | 6 (23.1%)           |
| 1p19q Co-deletion            |                     |
| No                           | 20 (76.9%)          |
| Yes                          | 6 (23.1%)           |

labelling of different glial neoplasms have revealed various staining expressions, in which 26 tumours have shown diffuse Olig2 expression (≥ 60%) while 23 tumours have shown partial or focal expression (< 50%). Four tumours have shown no Olig2 expres-
sion (Table I). Tumours that showed diffuse Olig2 expression of ≥ 60% were tested for IDH1 mutation and 1p19q co-deletion using FISH (Tables II, III).

Of the 26 tumours, 6 oligodendrogliomas had 1p19q co-deletion and the remaining three oligodendrogliomas showed unremarkable FISH results (Table II). However, all the 9 cases of oligodendrogliomas were IDH1mutant. Additionally, 3 tumours were found to have 19q deletion: 2 anaplastic astrocytomas and 1 oligoastrocytoma. The FISH of the remaining tumours (14/26) did not detect any chromosomal deletion or gain (Tables II, III). There was no significant difference in the final diagnosis among glial neoplasms with diffuse Olig2 expression by using FISH 1p19q co-deletion test (p = 0.248) (Table IV). It clarifies that diffuse expression of Olig2 cannot be solely used to distinguish oligodendroglioma from other glial neoplasms. Furthermore, IDH1 mutation cannot be also used as an additional marker to Olig2 expression to diagnose oligodendroglial neoplasms without 1p19q co-deletion (Table V). FISH for 1p19q co-deletion has revealed 100% diagnostic sensitivity, 85% specificity and 88.5% accuracy (Table VI).

**Discussion**

Since Olig2 is an essential marker for the development of neuronal progenitor, it is used to express oligodendrocytes in CNS. It has also been used for a long time as a marker to distinguish oligodendroglioma from astrocytoma. This diagnostic method is currently proven wrong. Several studies found that Olig2 is highly expressed in different types of glial neoplasms such as glioblastomas and astrocytomas [6]. Around 4-12% of glioblastomas were also proven to have 1p19q co-deletion [17]. A study done by Mizoguchi et al. detected rare cases of glioblastoma with 1p19q co-deletion and high Olig2 expression [13]. Although 1p19q co-deletion is the most common genetic alteration found in oligodendrogliomas, its association with IDH1 mutation was commonly

### Table IV. Relationship between glial neoplasms and 1p19q co-deletion in tumours with diffuse Olig2 expression (≥ 60%)

| FISH result          | Tumour with diffuse Olig2 expression ≥ 60% | Total | p-value |
|----------------------|------------------------------------------|-------|---------|
|                      | Oligodendroglioma | Non-oligodendroglioma |       |         |
| 1p19q codeletion      | 6             | 0                | 6     | 0.248*  |
| No 1p19q codeletion   | 3             | 17               | 20    |         |
| Total                | 9             | 17               | 26    |         |

*McNemar χ² test with continuity correction

### Table V. IDH1 mutation in glial neoplasm with diffuse Olig2 expression (≥ 60%)

| IDH status        | Oligodendroglioma | Non-oligodendroglioma | Total | p-value* |
|-------------------|-------------------|-----------------------|-------|----------|
| IDH1mutant        | 6 (100.0)         | 9 (45.0)              | 15    | 0.065    |
| IDH1wildtype      | 0 (0.0)           | 11 (55.0)             | 11    | 0.065    |

*a Fisher’s exact test

### Table VI. The diagnostic accuracy of FISH 1p19q co-deletion superior to diffuse Olig2 expression (≥ 60%) in the diagnosis of oligodendroglioma

| Diagnostic decision | 95% Confidence interval |
|---------------------|-------------------------|
|                      | Estimate (%) | Lower (%) | Upper (%) |
| True prevalence      | 23.1         | 9.0       | 43.6      |
| Test sensitivity     | 100.0        | 54.1      | 100.0     |
| Test specificity     | 85.0         | 62.1      | 96.8      |
| Diagnostic accuracy  | 88.5         | 69.8      | 97.6      |
| Positive predictive value | 66.7     | 29.9      | 92.5      |
| Negative predictive value | 100.0   | 80.5      | 100       |
| Proportion of false positives | 15.0   | 3.2       | 37.9      |
| Proportion of false negative | 0.0       | 0.0       | 45.9      |
explored. This association has never been correlated with Olig2 expression in different glial neoplasms. Less than 50% of Olig2 expression in glial neoplasms are considered normal as the oligodendrocytes distribute normally in the neuropil and they may infiltrate into the tumours. Glial tumours with ≥ 60% Olig2 expression warrant what type of cellular lineage the tumour may have. Currently, some neuropathologists use Olig2 as a biomarker to distinguish oligodendroglioma from other glial tumours. In our study, we have diagnosed this diagnostic manner was wrong. We found that there was no significant difference in the final diagnosis among all glial neoplasms with diffuse Olig2 expression (≥ 60%) by using FISH test. This clarifies that diffuse Olig2 expression is not an optimum and standard method to distinguish oligodendroglioma from other tumours. However, FISH for 1p19q co-deletion remains the best diagnostic test for oligodendroglioma, regardless of Olig2 expression as it has shown 88.5% diagnostic accuracy. Although FISH can detect other chromosomal deletions at a particular locus it cannot assess the extent of these deletions (partial or full arm). In contrast, FISH can detect partial 1p and/or 19q LOH that are commonly found in astrocytic tumours.

Some glioblastomas have also demonstrated evidence for 1p19q co-deletion [9,16]. It was unclear if those cases were primary glioblastomas or secondary glioblastomas upgraded from anaplastic oligodendrogliomas. The expression of Olig2 was proven to be weak in these cases except glioblastomas with oligodendroglial component (GBMO), which showed prominent Olig2 expression in only oligodendroglial foci [5,7]. Despite these findings, FISH for 1p19q co-deletions remains a widely employed methodology in evaluating gliomas with oligodendroglial components. In our study, in 26 out of 34 tumours that showed diffuse Olig2 expression, the 1p19q co-deletion was only found in oligodendrogliomas. The remaining cases were not distinguished by using Olig2 expression.

Conclusions

Olig2 marker cannot be used as an alternative diagnostic method for 1p19q co-deletion to distinguish oligodendrogliomas from other glial neoplasms. Although some glial tumours have shown diffuse Olig2 expression, 1p19q co-deletion testing is crucial. Furthermore, IDH1 mutation is considered as an additional marker of 1p19q co-deletion to support the diagnosis of oligodendroglioma.

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Ethics approval

The study was ethically approved by the National Biomedical Ethics Committee at King Abdulaziz University (HA-02-J-008) under general ethical approval.

Availability of data and material

The data that support the findings of this study are available from the corresponding author (MK) upon request.

Disclosure

The authors report no conflict of interest.

References

1. Andrews C, Prayson R. 1p19q co-deleted fibrillary astrocytomas: not everything that is co-deleted is an oligodendroglioma. Ann Diagn Pathol 2020; 46: 151519.

2. Appolloni I, Calzolari E, Barilari M, Terrile M, Daga A, Malatesta P. Antagonistic modulation of gliomagenesis by Pax6 and Olig2 in PDGF-induced oligodendroglioma. Int J Cancer 2012; 131: E1078-1087.

3. Cairncross G, Berkey B, Shaw E, Jenkins R, Scheithauer B, Brachman D, Buckner J, Fink K, Souhami L, Lapeniere N, Mehta M, Curran W. Phase III trial of chemotherapy plus radiotherapy compared with radiotherapy alone for pure and mixed anaplastic oligodendroglioma: Intergroup Radiation Therapy Oncology Group Trial 9402. J Clin Oncol 2006; 24: 2707-2714.

4. Donahue B, Scott CB, Nelson JS, Rotman M, Murray K, Nelson DF, Banker FL, Earle JD, Fischbach JA, Asbell SQ, Gaspar LE, Markoe AM, Curran W. Influence of an oligodendroglial component on the survival of patients with anaplastic astrocytomas: a report of Radiation Therapy Oncology Group B3-02. Int J Radiat Oncol Biol Phys 1997; 38: 911-914.

5. Hartmann C, Johnk L, Kitange G, Wu Y, Ashworth LX, Jenkins RB, Louis DN. Transcript map of the 3.7-Mb D19S112-D19S246 candidate tumor suppressor region on the long arm of chromosome 19. Cancer Res 2002; 62: 4100-4108.

6. Hoang-Xuan K, Aguirre-Cruz L, Mokhtari K, Marie Y, Sanson M. OLG-1 and 2 gene expression and oligodendroglial tumours. Neuropathol Appl Neurobiol 2002; 28: 89-94.

7. Idbaih A, Marie Y, Pierron G, Brennetot C, Hoang-Xuan K, Kujas M, Mokhtari K, Sanson M, Lejeune J, Aurias A, Delattre O, Delattre JY.
Two types of chromosome 1p losses with opposite significance in gliomas. Ann Neurol 2005; 58: 483-487.

8. Jenkins RB, Blair H, Ballman KV, Giannini C, Arusell RM, Law M, Flynn H, Passe S, Felten S, Brown PD, Shaw EG, Buckner JC. A t(1:19)(q10;p10) mediates the combined deletions of 1p and 19q and predicts a better prognosis of patients with oligodendroglioma. Cancer Res 2006; 66: 9852-9861.

9. Kaneshiro D, Kobayashi T, Chao ST, Suh J, Prayson RA. Chromosome 1p and 19q deletions in glioblastoma multiforme. Appl Immunohistochem Mol Morphol 2009; 17: 512-516.

10. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 2016; 131: 803-820.

11. Lu QR, Park JK, Noll E, Chan JA, Alberta J, Yuk D, Alzamora MG, Louis DN, Stiles CD, Rowitch DH, Black PM. Oligodendrocyte lineage genes (OLIG) as molecular markers for human glial brain tumors. Proc Natl Acad Sci U S A 2001; 98: 10851-10856.

12. Lu QR, Yuk D, Alberta JA, Zhu Z, Pawlitzyk J, Chan J, McMahon AP, Stiles CD, Rowitch DH. Sonic hedgehog-regulated oligodendrocyte lineage genes encoding bHLH proteins in the mammalian central nervous system. Neuron 2000; 25: 317-329.

13. Mizoguchi M, Yoshimoto K, Ma X, Guan Y, Hata N, Amano T, Nakamizo A, Suzuki SQ, Iwaki T, Sasaki T. Molecular characteristics of glioblastoma with 1p/19q co-deletion. Brain Tumor Pathol 2012; 29: 148-153.

14. Nakamura M, Yang E, Fujisawa H, Yonekawa P, Kleihues P, Ohgaki H. Loss of heterozygosity on chromosome 19 in secondary glioblastomas. J Neuropathol Exp Neurol 2000; 59: 539-543.

15. Ohgaki H, Kleihues P. Genetic pathways to primary and secondary glioblastoma. Am J Pathol 2007; 170: 1445-1453.

16. Sim J, Nam DH, Kim Y, Lee IH, Choi JW, Sa JK, Suh YL. Comparison of 1p and 19q status of glioblastoma by whole exome sequencing, array-comparative genomic hybridization, and fluorescence in situ hybridization. Med Oncol 2018; 35: 60.

17. Yan H, Parsons DW, Jin G, McLendon R, Rasheed BA, Yuan W, Kos I, Batinic-Haberle I, Jones S, Riggins GJ, Friedman H, Friedman A, Reardon D, Herndon J, Kizilier KW, Velculescu VE, Vogelstein B, Bigner DD. IDH1 and IDH2 mutations in gliomas. N Engl J Med 2009; 360: 765-773.