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CASE REPORT
ΕΝΔΙΑΦΕΡΟΥΣΑ ΠΕΡΙΠΤΩΣΗ

Is high Ki-67 proliferation index in grade II oligodendroglioma an important marker for adjuvant therapy?

Treatment decisions for oligodendrogliomas are usually made according to clinical variables. With the development of determination of genetic and epigenetic pathways, new approaches to treatment have been introduced. In this case report, the treatment approach was evaluated in a patient with high grade II oligodendroglioma whose Ki-67 proliferation index was investigated. There is a need for studies investigating the contribution of the Ki-67 proliferation index to treatment decisions, as an addition to 1p/19q combined deletion, and IDH1, IDH2 mutations in grade II oligodendrogliomas.

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Είναι ο δείκτης υψηλού πολλαπλασιασμού Ki-67 επίσης σημαντικός στην ενισχυτική θεραπεία του ολιγοδενδρογλοιώματος βαθμού ΙΙ;

Περίληψη στο τέλος του άρθρου

Key words

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Oligodendroglioma is a rare primary glial tumor originating from oligodendrocytes. The median age at presentation is 41 years. The most common presenting symptom is seizure. Frontal and temporal lobe involvement is more common. It has malignant transformation potential and the overall survival is close to 10 years. According to the World Health Organization (WHO) grading system, oligodendrogliomas are mainly divided into WHO grade II and WHO grade III (anaplastic) according to the degree of differentiation, cellular atypia, and tumor vessel changes.[1–3] Since 2016, WHO has included in the classification system mutations in isocitrate dehydrogenase 1 (IDH1), isocitrate dehydrogenase 2 (IDH2), tumor protein 53 (*TP53*) genes, and 1p/19q codeletion. The WHO classification system plays an important role in treatment planning.[2–4] In this case report, the treatment approach was evaluated in a patient diagnosed with high grade II oligodendroglioma whose Ki-67 proliferation index was high.

CASE PRESENTATION

A 57-year-old female patient consulted a doctor for vision problems. Cranial magnetic resonance imaging (MRI) revealed a 2.5×1.5 cm mass in the right temporal lobe with a cystic, necrotic and mild constrictive appearance (fig. 1). Gross total mass excision was performed. On histopathological examination of the tumor, glial fibril acidic protein (GFAP) was negative, oligodendrocyte transcription factor 2 (OLIG2) positive, α-thalassemia X-linked mental retardation syndrome (ATRX) diffuse nuclear staining, P53 mutation negative, and the neurofilament axonal staining positive 67 (Ki-67) proliferation index was 18%. Molecular analysis for IDH1/IDH2 mutations was negative and for the 1p19q codeletion was positive. Following evaluation of the morphological, immunohistochemical and molecular findings, WHO grade 2 oligodendroglioma was diagnosed. No residual or recurrence was detected on cranial MRI. The patient had a high risk factor, according to her age, above 40 years, and Ki-67 index. The patient was referred for oncological treatment. The indications and side effects of adjuvant therapy were discussed. The patient agreed to stay on follow-up, and she was monitored for three months.

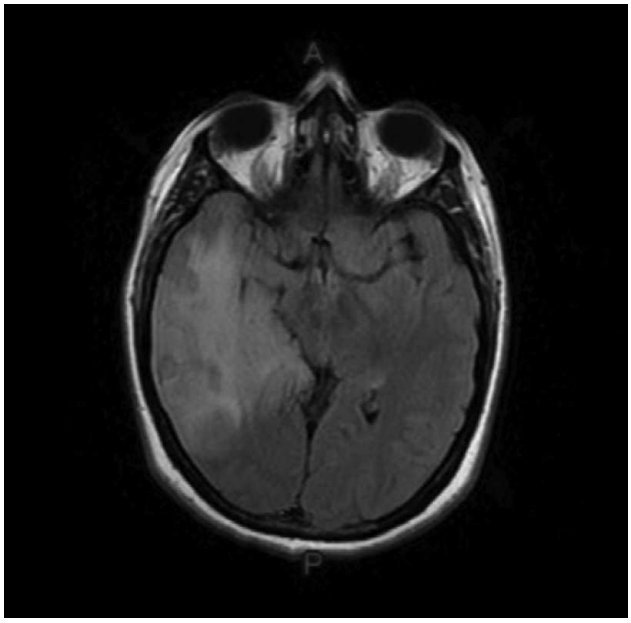

Figure 1. Cranial magnetic resonance imaging (MRI) in a 59-year-old female, showing grade II oligodendroglioma in the right temporal lobe.

DISCUSSION

There is no definitive curative treatment for oligodendroglioma. Treatment includes surgery, radiotherapy (RT), chemotherapy (CT), and combined therapies. Radiotherapy is frequently used as an adjuvant in the treatment of oligodendroglioma, but CT is not commonly applied, and its optimal timing is still not clear. Due to the early and late side effects of RT, CT may be preferred over RT in the treatment of high-risk oligodendroglioma and it has been reported to have positive results. Generally, the scheme of temozolomide and procarbazine/lamustine/vincristine (PCV) is preferred. It is also used in adjuvant therapy in high-risk patients in combination therapies.[1–6]

The prognosis of oligodendrogliomas has not improved over the years despite the development of new diagnostic and therapeutic methods. As a result of molecular investigations, oligodendrogliomas in general have been found to show genetic variation. Among these genetic differences, mutations in IDH1, IDH2 and TP53 genes and 1p-/-19q codeletion were found to be important for tumor identification, classification, treatment and expected results.[1,3,4] Research is ongoing for new biomarkers including the Ki-67 index, which may be used in the management of oligodendrogliomas.[2,6]

The Ki-67 proliferation index is a proliferation marker of tumor cells that is frequently used to evaluate disease prognosis in all neoplasms. Increased Ki-67 proliferation was found to be closely related to prognosis in many tumors, including as breast and bladder cancers. The value of the Ki-67 proliferation index in predicting survival in oligodendroglioma has not yet been clearly established, as the number of studies in the literature on this subject is limited.[2,6,7] In one study, the Ki-67 proliferation index rate was 1% in pilocytic astrocytoma, 4.2% in grade II oligodendroglioma, 4.2% in grade II astrocytomas and oligodendrogliomas and 8.5% in glioblastoma multiforme. It was emphasized that in glioblastoma multiforme the Ki-67 level may be due to low tumor heterogeneity.[2] Another study reported that Ki-67 is lower and prognosis is better in oligodendriomas with 1p-/-19q codeletion.[4] In a study of 32 cases of WHO grade II oligodendroglioma, in those cases with a Ki-67 index >3%, the prognosis was worse. In a study with 89 cases of oligodendroglioma, the 5-year survival rate was higher in patients with Ki-67 index <5%.[7]

In the case presented here, the positive risk factors were small tumor size, tumor not exceeding the midline, absence of neurological deficit, good performance status, absence of IDH1/IDH2 mutation, 1p-/-19q codeletion, low grade glioma and total removal of the mass. The high risk factors were age above 40 years and a high Ki-67 index. Since the decision about adjuvant treatment was not clear, the possible side-effects were discussed with the patient, and monitoring was decided.

CONCLUSIONS

Treatment decisions for oligodendrogliomas are usually contingent on the clinical variables. With the development of determination of genetic and epigenetic pathways, a more promising approach to treatment has become available. As an addition to the use as markers of the combined deletion of 1p-/-19q, and IDH1, IDH2 mutation, studies are needed to investigate the contribution of the Ki-67 proliferation index to treatment decisions in patients with oligodendroglioma.

ΠΕΡΙΛΗΨΗ

Είναι ο δείκτης υψηλού πολλαπλασιασμού Ki-67 επίσης σημαντικός στην ενισχυτική θεραπεία του ολιγοδενδρογλοιώματος βαθμού II;

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Οι αποφάσεις για τη θεραπεία των ολιγοδενδρογλοιωμάτων εφαρμόζονται συνήθως σύμφωνα με διάφορες κλινικές μεταβλητές. Με τον προσδιορισμό των γενετικών και επιγενετικών οδών στην ανάπτυξη έχουν αρχίσει να δοκιμάζονται νέες προσεγγίσεις στη θεραπεία. Στην παρούσα περίπτωση η θεραπευτική προσέγγιση έγινε σε μια ασθενή που διαγνώστηκε με υψηλού βαθμού II ολιγοδενδρογλοίωμα, με αξιολόγηση του Ki-67. Υπάρχει ανάγκη εκπόνησης μελετών που διερευνούν τη συμβολή του δείκτη πολλαπλασιασμού Ki-67 για τον προσδιορισμό της θεραπείας ως εναλλακτική λύση για τη συνδυασμένη διαγραφή 1p/19q, τη μετάλλαξη IDH1, IDH2 σε ολιγοδενδρογλοιώματα βαθμού II.

Λέξεις ευρετηρίου: Δείκτης πολλαπλασιασμού Ki-67, Θεραπεία, Ολιγοδενδρογλοίωμα, Πρόγνωση

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