

Intisari

Latar belakang : Grading histopatologik astrositoma dapat diartikan sebagai perkiraan perilaku biologik astrositoma. Mitosis sangat penting dalam menentukan grading tumor. Matriks metalloproteinase 9 (MMP9) adalah endopeptidase yang mempunyai kemampuan mendegradasi protein-protein matriks ekstraseluler, yang diperlukan dalam proses invasi/infiltratif dan metastasis. *Phosphatidylinositol-3 kinase (PI3K)/ Protein kinase B* atau *Akt (PKB/AKT)/ mechanistic/mammalian target of rapamycin (mTOR)* adalah jaras sinyal yang berperan besar pada berbagai keganasan. Namun begitu hubungan aktivitas jaras sinyal PI3K/Akt/mTOR dengan proliferasi, invasi dan grading tumor masih belum jelas.

Tujuan : Penelitian ini bertujuan untuk mengkaji ekspresi PI3K, Akt, dan mTOR, sebagai komponen jaras sinyal PI3K/Akt/mTOR dalam hubungannya dengan tingkat proliferasi, infiltrasi, dan grading histopatologik astrositoma.

Metode penelitian : Penelitian observasional analitik dengan rancangan cross sectional study, dengan subyek blok parafin kasus yang ditegakkan diagnosis astrositoma maligna. Ekspresi mRNA PI3K, mRNA Akt, mRNA mTOR, mRNA Ki67, dan mRNA MMP9, diukur dengan qPCR. Hubungan antara ekspresi mRNA PI3K, mRNA Akt, mRNA mTOR dengan proliferasi, kemampuan invasi dan grading astrositoma dianalisis dengan uji korelasi Spearman dan analisis varian

Hasil : Didapatkan peningkatan ekspresi mRNA-PI3K dan peningkatan ringan ekspresi mRNA-Akt pada astrositoma dibandingkan jaringan normal, namun tidak didapat peningkatan ekspresi mRNA-mTOR.. Didapat hubungan yang bermakna antara ekspresi mRNA-Akt ($p=0.007$) dan mRNA-mTOR ($p=0.006$) ekspresi mRNA-Ki67. Tidak didapat hubungan yang bermakna antara ekspresi mRNA-PI3K ($p=0.360$), ekspresi mRNA-Akt ($p=0.670$) maupun ekspresi mRNA-mTOR ($p=0.980$) dengan grading histopatologik astrositoma.

Simpulan : Ekspresi mRNA-PI3K, mRNA-Akt, mRNA-mTOR dan mRNA-Ki67 tidak dapat digunakan untuk membedakan derajat histopatologik astrositoma. Tidak didapat korelasi antara mRNA-PI3K, mRNA-Akt dan mRNA-mTOR dengan grading histopatologik astrositoma.

Kata kunci : astrositoma; grading histopatologik; ekspresi mRNA-Akt; mRNA-mTOR

Abstract

Background: Histopathologic grade of astrocytomas can estimates the biological behavior of astrocytomas. Mitosis is very important to determine the grade of astrocytomas. Matrix metalloproteinase 9 (MMP9) is an endopeptidase that has ability to degrade extracellular matrix proteins to facilitate the process of tumor infiltration and metastasis. Phosphatidylinositol 3-kinases (PI3K) / protein kinase B or Akt (PKB / AKT) / mechanistic / mammalian targets of rapamycin (mTOR) is a signaling pathway that plays a major role in a variety of malignancies. But, the relationships of PI3K/ Akt / mTOR signaling pathway activity with proliferation, invasion and tumor grade is still unclear.

Objective: To examine the association of PI3K, Akt, and mTOR expression, as a component of the PI3K/ Akt/mTOR signaling pathway with the level of proliferation, infiltration, and the histopathologic grade of astrocytomas.

Methods: This was an analytic observational, cross sectional study. The subjects of the study were paraffin blocks of malignant astrocytoma cases. The expression of mRNA PI3K, mRNA Akt, mRNA mTOR, mRNA Ki67 and MMP9 mRNA were measured by qPCR. The association among the expression of mRNA PI3K, mRNA Akt, mRNA mTOR with proliferation, invasion and grade of astrocytomas were analyzed with correlation analysis and analysis of variant.

Results: Quantitative real-time PCR examination showed increase expression of mRNA-PI3K and mild increase of mRNA-Akt expression in astrocytomas compared to normal tissue, but not mRNA-mTOR. Statistic analysis showed significant correlation between the expression of mRNA-Akt ($p = 0.007$), mRNA-mTOR ($p=0.006$) and expression of mRNA-Ki67, as an indicator of the proliferation. Analysis of variance showed no significant correlation between the expression of mRNA-PI3K ($p = 0.360$), expression of mRNA-Akt ($p = 0.670$) as well as the expression of mRNA-mTOR ($p = 0.980$) and astrocytomas grade.

Conclusions: Expression of mRNA-PI3K, mRNA-Akt, mRNA-mTOR and mRNA-KI67 can not be used to distinguish histopathologic grade of astrocytomas. No correlation between mRNA-PI3K, mRNA-Akt and mRNA-mTOR and the histopathologic grade of astrocytomas.

Key words : astrocytoma, histopathologic grade; mRNA-Akt; mRNA-mTOR