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The Pivotal Ischemic Mechanism in the Proliferation and Growth of Glioma – The Hypoxia Induced Glioma Derived Exosome and miRNA-199a-3p Increased Ischemic Injury of the Neurons by Inhibiting mTOR Pathway

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Introduction

The mechanism about the glioma remains unclear. Recent studies suggested that glioma would cause the hypoxic microenvironment in the areas of intra- and para-tumor. We hypothesize that glioma has the unique mechanism of aggravating the hypoxic injury of neural cells, which is related with the progression of glioma.

Methods

We observed if there was any hypoxic injury in the para-tumor area through the imaging and pathological examination. Also we carried out the in vitro molecular biological experiments using C6 glioma cell line and normal neuron cells.

Results

In this study we found the definite hypoxic injury of nerve cells in the para-glioma area, which suggested that glioma had the specific mechanism of aggravating the hypoxic injury of the neural cells around the tumor. In indirectly co-culture system, hypoxia would enlarge the ischemic injury of neurons, while the proliferation of C6 glioma cells increased a little bit after hypoxia. Moreover, hypoxia could activate HIF-1a of C6 glioma cells and promote the expression of miRNA-199a-3p in Hypoxia Induced Glioma Derived Exosome (HIGDE) released by C6 cells compared with None Hypoxia Induced Glioma Derived Exosome (NHIGDE). The induced miRNA-199a-3p in HIGDE could aggravate the OGD(Oxygen and Glucose Deprivation) ischemic injury directly in normal cultured neurons in vitro by inhibiting the transcription of mTOR and its down-streams, which suggest HIGDE derived from glioma cells had the definite ability of increase the ischemic injury of the normal neurons.

Conclusions

This study revealed the actual ischemic mechanism in the proliferation and growth of glioma. The in vitro experiments supported that HIGDE and miRNA-199a-3p may exacerbate the hypoxic injury of neurons and facilitate the proliferation of glioma in vivo, which may be an important insight and a potential therapeutic target against brain glioma.

Learning Objectives

By the conclusion of this session, participants should be able to: 1)Notice the link between ischemia and tumor growth. 2) Discuss the potential mechanism of hypoxia environment in para-tumor. 3) Identify the effects of HIGDE and miRNA-199a-3p.