E-cadherin as a Predictive Marker of Brain Metastasis in Non-small Cell Lung Cancer and its Regulation by Pioglitazone in a Preclinical Model

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Introduction

It remains unclear whether patients with non-small cell lung cancer (NSCLC) develop brain metastasis during or following the standard therapy. The authors sought to identify biological markers that predict brain metastasis, and investigate the way to modulate the expression of the marker.

Methods

A case-control study of patients who were newly diagnosed with NSCLC and who had developed brain metastasis during follow-up was conducted between 2004 and 2009. These patients were compared with a control group of patients who had NSCLC, but no evidence of brain metastasis. Immunohistochemical analyses were performed for the expression of Ki-67, p53, Bcl-2, Bax, vascular endothelial growth factor, epidermal growth factor receptor, caspase-3, and E-cadherin.

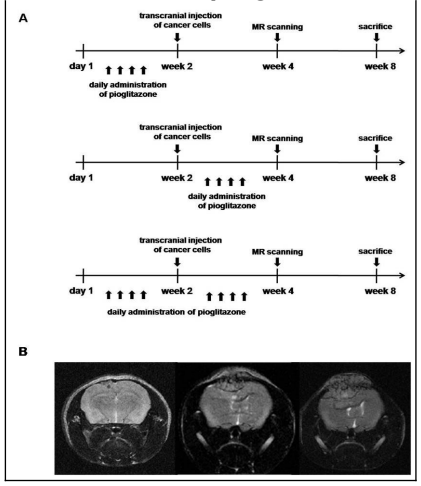
Results

A significantly increased risk of developing brain metastasis was associated with the presence of primary tumors with low E-cadherin expression in patients with NSCLC. Moreover, we investigated the effects of pioglitazone, a peroxisome proliferator-activated receptor ?-activating drug, in tumor-bearing mouse models. We found that E-cadherin expression was proportional to pioglitazone exposure time. Interestingly, pioglitazone pretreatment before cancer cell inoculation prevented loss of E-cadherin expression and decreased the expression of MMP9 and fibronectin, as compared to that in the control group.

Conclusions

E-cadherin expression could be a predictor of brain metastasis in patients with NSCLC. Preventive treatment with pioglitazone may be useful in modulating E-cadherin expression.

a Therapeutic schedule. b Serial magnetic resonance imaging (MRI) in the control group. A small tumor burden was noted in the cortex of the right hemisphere 4 weeks after the intracranial inoculation of 1 106 NCI-H358 cells (left). The tumor progre



Learning Objectives

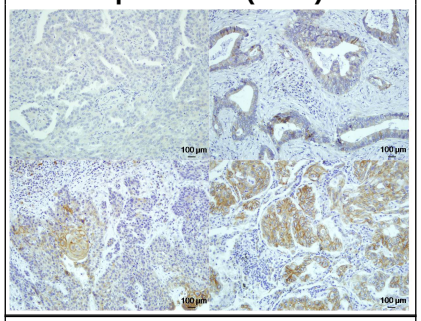
In this study, the candidate marker of brain metastasis was assayed in a tumor-bearing mouse model treated with PPAR?-activating agent, pioglitazone to evaluate the possibility as the preventive or therapeutic target of brain metastasis.

References

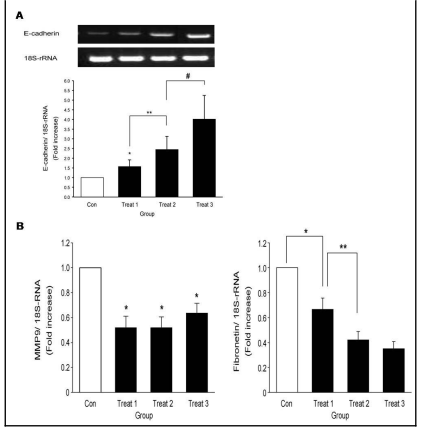
E-cadherin as a predictive marker of brain metastasis in non-small-cell lung cancer, and its regulation by pioglitazone in a preclinical model.

J Neurooncol. 2012 Sep;109(2):219-27.

E-cadherin Immunohistochemical Staining of Primary Lung Cancer Specimens (×100)



a Reverse transcription polymerase chain reaction (RT-PCR) results for E-cadherin. E-cadherin expression was mediated by pioglitazone treatment. Expression was higher in the pioglitazone-treated group after cell inoculation (Treat 2) than that before



A. Real-time polymerase chain reaction (PCR) results for E-cadherin. B. Real-time polymerase chain reaction (PCR) results for MMP9 and fibronectin.