BMET-19. CLINICOPATHOLOGICAL SIGNIFICANCE OF N-CADHERIN AND VEGF IN ADVANCED GASTRIC CANCER BRAIN METASTASIS AND THE EFFECTS OF METFORMIN IN PRECLINICAL MODELS
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BACKGROUND: Gastric cancer is the second most common cause of cancer-related death worldwide. Although brain metastasis is a rare complication of gastric cancer, no standard therapy for gastric cancer brain metastasis has been established. METHODS: A case-control study of patients newly diagnosed with gastric cancer who had developed brain metastasis during follow-up was conducted between 1997 and 2009. These patients were compared with a control group of patients who had advanced gastric cancer but no evidence of brain metastasis. Immunohistochemistry was used to analyze the expression of E-cadherin, N-cadherin, MSS1, claudin-3, claudin-4, Glut1, clusterin, ITGB4, vascular endothelial growth factor (VEGF), epidermal growth factor receptor (EGFR), and p53. RESULTS: No significant differences in biomarker expression were detected between the cases and controls. However, the expression of VEGF tended to be higher in the case group (33.3% vs. 0%, p = 0.055). Median survival was significantly correlated with vascular invasion (12 vs. 33 months, p = 0.008) and N-cadherin expression (36 vs. 12 months, p = 0.027). We also investigated the effects of metformin in tumor-bearing mouse models. VEGF expression was decreased and E-cadherin increased in the metformin-treated group compared with the control group. The expression of the mesenchymal marker MMP9 was decreased in the metformin-treated group. CONCLUSIONS: Brain metastasis of advanced gastric cancer was associated with the expression of VEGF. Metformin treatment might be useful for modulating the metastatic capacity of gastric cancers by reducing VEGF expression and blocking epithelial-to-mesenchymal transition.