



A service of the U.S. National Library of Medicine and the National Institutes of Health

My NCBI [Sign In] [Register]

All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search PubMed for [Go] [Clear] [Advanced Search \(beta\)](#)

Limits Preview/Index History Clipboard Details

Display AbstractPlus Show 20 Sort By Send to

All: 1 Review: 0

1: [Cancer](#). 2008 Aug 20. [Epub ahead of print]

FULL TEXT AVAILABLE ONLINE Links

**Immunohistochemical markers associated with brain metastases in patients with nonsmall cell lung carcinoma.**

[Saad AG](#), [Yeap BY](#), [Thunnissen FB](#), [Pinkus GS](#), [Pinkus JL](#), [Loda M](#), [Sugarbaker DJ](#), [Johnson BE](#), [Chirieac LR](#).

Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts.

**BACKGROUND.:** To the authors' knowledge, there are no reliable markers able to identify patients with nonsmall cell lung cancer (NSCLC) that will develop metastases to the brain. The authors investigated associations between immunohistochemical markers and the development of brain metastases in patients with NSCLC. **METHODS.:** This was a hospital-based, case-control study of patients who were newly diagnosed with NSCLC between 1989 and 2003, developed brain metastases, and had pathology material available from both the primary NSCLC and the brain metastases. These patients were compared with a control group of patients who had NSCLC and no evidence of brain metastases. NSCLC was examined for expression levels of Ki-67, caspase-3, vascular endothelial growth factor A (VEGF-A), VEGF-C, E-cadherin, and epidermal growth factor receptor (EGFR) in 54 surgical pathology specimens using immunohistochemistry, and associations were evaluated between those markers and the development of brain metastases. **RESULTS.:** Brain metastases developed after a median of 12.5 months (range, 1.7-89.4 months) after the diagnosis of NSCLC. A significantly increased risk of developing brain metastases was associated with patients with NSCLC who had primary tumors with high Ki-67 levels (adjusted odds ratio [OR] of 12.2; 95% confidence interval [95% CI], 2.4-70.4 [P < .001]), low caspase-3 expression (adjusted OR of 43; 95% CI, 5.3 to >100 [P < .001]), high VEGF-C expression (adjusted OR of 14.6; 95% CI, 2.0 to >100 [P < .001]), and low E-cadherin (adjusted OR of 3.6; 95% CI, 0.9-16.4 [P = .05]). No significant risk was associated with VEGF-A or EGFR expression. High Ki-67 expression also was associated with a shorter overall survival (P = .04). **CONCLUSIONS.:** The results of the current study indicated that patients with NSCLC who had high Ki-67 expression, low caspase-3 expression, high VEGF-C expression, and low E-cadherin expression in their tumors may benefit from close surveillance because they may have an increased risk of developing brain metastases. Cancer 2008. (c) 2008 American Cancer Society.

PMID: 18720359 [PubMed - as supplied by publisher]

Display AbstractPlus Show 20 Sort By Send to

**Related Articles**

- ▶ Epidermal growth factor receptor, cyclooxygenase-2, and BAX expression in the primary non-small cell lung cancer and brain metastases. [Clin Cancer Res. 2003]
- ▶ Clinical significance of vascular endothelial growth factor C and vascular endothelial growth factor receptor 3 in patients with nonsmall cell lung ca [Cancer. 2003]
- ▶ Aberrant methylation of H-cadherin (CDH13) promoter is associated with tumor progression in primary nonsmall cell lung carcinoma. [Cancer. 2005]
- ▶ Association of Ki-67, p53, and bcl-2 expression of the primary non-small-cell lung cancer lesion with brain metastatic lesion. [Int J Radiat Oncol Biol Phys. 2002]
- ▶ Skip metastasis in nonsmall cell lung carcinoma: predictive markers and isolated tumor cells in N1 lymph nodes. [Cancer. 2004]

» See all Related Articles...

[Write to the Help Desk](#)

[NCBI](#) | [NLM](#) | [NIH](#)

[Department of Health & Human Services](#)

[Privacy Statement](#) | [Freedom of Information Act](#) | [Disclaimer](#)