行政院國家科學委員會專題研究計畫成果報告

惡性肋膜積液中各種細胞之結合因子表現

Expression of Adhesion Molecules in Cells of Malignant Pleural Effusions

計畫編號：NSC 88-2314-B-002-0
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中文摘要

背景：癌細胞表面之各種結合因子與腫瘤細胞之侵襲性和轉移能力有密切之關係，轉移至肋膜積液中各種細胞上的結合因子表現未曾見諸文獻。
目的：為觀察惡性肋膜積液中各種良性細胞與惡性細胞表面之結合因子表現。
實驗設計：收集 15 **例經病理學和細胞學證實且有癌細胞存在的惡性肋膜積液，以細胞離心法製作抹片, 然後依** ABC peroxidase **法進行免疫染色，以顯微鏡計數各類細胞具結合分子表現之百分率。**
結果：癌細胞表面之結合因子以 CD44 (64%)**，**E-cadherin (60%)**為最常見；而中皮細胞則以** CD44 (72%)**和** VLA-4 (57%)**表現為最多，其餘其中白血球則以** CD44 (72%) **和** LFA-1 (71%)**為最多。**
討論：以往離體試驗發現具有 CD44 **和** E-cadherin **之癌細胞較具侵襲性和轉移能力，肋膜積液中癌細胞是否是原發腫瘤中較具侵襲性之細胞群？本研究發現人體內侵入肋膜腔內之癌細胞也以具有** CD44 **和** E-cadherin **表現之細胞為多數, 似乎印證以往之離體觀察。**
評論：本研究首次證明肋膜積液中各種癌細胞具有較高之CD44**和**E-cadherin**二種結合因子。各種細胞間之互動是否與結合因子表現有關？由於技術上之困難而無法充分清楚顯現而難以判斷。**

關鍵詞：惡性肋膜積液、結合因子、CD44**、**E-cadherin

ABSTRACT

Background: The expression of adhesion molecules on the surface of tumor cells has been found to be related to the invasiveness and metastasis of the neoplasm. The role of adhesion molecules on the cells of malignant pleural effusion has not been reported in the literature.
Purposes: To observe the expression of adhesion molecules on the cells in malignant pleural effusion.
Design: Fifteen histologically/cytologically verified malignant pleural effusions were enrolled in this study. The cells prepared with cytospin were stained with a pannel of adhesion molecules by ABC peroxidase method. The percentage of cells with expression of adhesion molecules were counted with a microscope.
Results: The most common adhesion molecules on the cancer cells are CD44 (64%) and E-cadherin (60%); on mesothelial cells are CD44 (72%) and VLA-4 (57%). Those on leukocytes are CD44 (72%) and LFA-1 (71%).
Discussion: Previous *in vitro* study revealed the cancer cells with expression of CD44 and E-cadherin were more invasive & metastatic. This study showed that the cancer cells in pleural effusion had high percentage of cells with CD44 and E-cadherin. This study confirmed the previous observation in different malignant

cells in vivo.

Comment: This is the first in vivo study that confirmed the malignant cells in pleural effusions expressied adhesion molecules of CD44 and E-cadherin. Due to technical difficulty, the role of adhesion molecule in the cell-to-cell interaction could not be clearly demonstrated.

Keywords: malignant pleural effusion, adhesion molecule, CD44, E-cadherin

INTRODUCTION

Adhesion molecules have been found to play a major role in the progress and metastasis of malignant neoplasms (1-3). The expression of adhesion molecules in cells of malignant pleural effusions may provide some clues for intrapleural metastasis of cancers. This study was designed to disclose the expression of adhesion molecules on the benign and malignant cells in the malignant pleural effusions.

MATERIALS AND METHODS

Fifteen histologically verified pleural effusions with presence of cancer cells were enrolled in this study. They included nine breast cancer, two lung cancer and four other cancers. Smears were prepared with cytospin centrifugation. After fixation with acetone, immunocytochemical stain with ABC peroxidase method was done with a pannel of adhesion molecules: ICAM-1, VCAM-1, E-cadherin, VLA-4, LFA-1, LFA-3, and CD44. The percentage of cells with positive immunostaing was counted with a microscope.

RESULTS

Table 1 shows the percentage of cells with expression of various adhesion molecules. The two most common expression of adhesion molecules on the cancer cells are E-cadherin and CD44. CD44 is the most common presence of adhesion molecule on all types of cells in the malignant pleural effusions.

The percentage of cells with expression of various adhesion molecules

	Cancer cells	Mesothelial cells	Leukocytes
E-cadherin	60%	20%	5%
CD44	64%	72%	72%
ICAM-1	39%	45%	3%
VCAM-1	41%	19%	0%
VLA-4	35%	57%	7%
LFA-1	5%	24%	71%
LFA-3	28%	31%	26%

DISCUSSION

The expression of adhesion molecules on the cells in malignant pleural effusions are very sophisticated. The cancer cells in the pleural effusion may be those with potentially higher invasiveness and stronger penetration capability. This study confirmed the previous *in vitro* studies on ovarian and pancreatic cancers that cancer cells with CD44 and/or E-cadherin showed higher invasiveness (4,5).

This is the first report confirmed the malignant cells in pleural effusions contained more CD44 and E-cadherin expression.

Kawaguchi S, et al. Reported that VLA-4 on tumor cells initiated an adhesion with VCAM-1 on endothelium (6). This study showed only 35% of cancer cells in effusions with VLA-4 molecule. This indicates VLA-4 may be not an important adhesion molecule

in the invasion of the mesothelium.

The direct observation of the role of adhesion molecules between cell-to-cell interaction in the malignant pleural effusion is technically difficult. The difficulties in identification of adhesion molecules at the cell-to-cell contact site may be caused by disruption of cell cohesion during smear preparation and weak immunostaing at the contact sites of cells.

Comment: This is the first in vivo study that confirmed the malignant cells in pleural effusions expressied adhesion molecules of CD44 and E-cadherin. Due to technical difficulty, the role of adhesion molecule in the cell-to-cell interaction could not be clearly demonstrated.

REFERENCES

1. Tuszynski GP, Wang TN, Berger D. Adhesive proteins and the hematogenous spread of cancer. Acta Haematologica 1997;97:29-39.
2. Kargi HA, Kuyucuoglu MF, Alakavuklar M, Akpinar O, Erk S. CD44 expression in metastatic and non-metastatic non-small cell lung cancers. Cancer Letters 1997;119:27-30.
3. Park HR, Yun I. Role of VLA-integrin receptor in invasion and metastasis of human fibrosarcoma cells. Cancer Letters 1996;106:227-233.
4. Cannistra SA, Kansas GS, Niloff J, DeFranzo B, Kim Y, Ottensmeier C. Binding of ovarian cancer cells to peritoneal mesothelium *in vitro* is partly mediated by CD44H[1]. Cancer Research 1993;53: 3830-3838.
5. Iwai K, Ishikura H, Kaji M, Sugiura H, Ishizu A, Takahashi C, Kato H, Tanabe T, Yoshiki T. Importance of E-selectin (ELAM-1) and sialyl Lewis[a] in the adhesion of pancreatic carcinoma cells to activated endothelium. Int J Cancer 1993;54:972-977.
6. Kawaguchi S, Kikuchi K, Ishii S, et al. VLA-4 molecules on tumor cells initiate an adhesive interaction with VCAM-1 molecules on endothelial cell surface. Jpn J Cancer Res 1992;83:1304-1316.