Clinical Application of Serum Tumor Associated Material (TAM) from Non-small Cell Lung Cancer Patients

Cheng-Guang Li¹, Xin-En Huang¹*, Lin Xu²*, Ying Li¹, Yan-Yan Lu¹

Abstract

Objective: To explore the associations of serum tumor associated material (TAM) with other common tumor markers like carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), carbohydrate antigen 19-9 (CA19-9) and its clinical application in non-small cell lung cancer (NSCLC) patients. Methods: A total of 87 patients were enrolled into this study, all with histologically or cytologically confirmed NSCLC. With the method of chemical colorimetry, the level of TAM was determined and compared, while chemiluminescence was used to measure the levels of common tumor markers. Results: The level of TAM decreased after chemotherapy compared with before chemotherapy when CT or MRI scans showed disease control. Furthermore, it increased when disease progressed and there was no statistically significant difference in monitoring of TAM and common tumor markers (P>0.05). Conclusions: Detecting TAM in NSCLC patients has a higher sensitivity and specificity, so it can be used as an indicator for clinical monitoring of lung cancer chemotherapy.

Keywords: Tumor associated material - tumor marker - lung cancer - NSCLC

Introduction

Altered glycosylation patterns are a hallmark of tumor phenotype. This phenomenon was first described by Meezan et al in 1969 with the demonstration that healthy fibroblasts have smaller membrane glycoproteins than their transformed counterparts (Meezan et al., 1969). This finding was later corroborated with histological evidence that lectins show differential binding to healthy compared with malignant tissue (Turner, 1992; Saussez et al., 1998). More recently, cancer-associated cell-surface glycans have been directly characterized using specific monoclonal antibodies and mass spectrometry (Shriver et al., 2004), further illuminating the molecular changes that occur upon malignant transformation (Matsushita et al., 1990; Pancino et al., 1991).

We now know that changes in glycosylation include both the under- and overexpression of naturally-occurring glycans, as well as neoexpression of glycans normally restricted to embryonic tissues. These structures most often arise from changes in the expression levels of glycosyltransferases in the Golgi compartment of cancerous cells. Changes in glycosyltransferase levels can lead to modifications in the core structure of N-linked and O-linked glycans. One of the most common changes is an increase in the size and branching of N-linked glycans. This increased branching is often attributed to increased activity of N-acetylglucosaminyltransferase V (GlcNAc-TV, also known as or MGAT5; the enzyme that leads to β1, 6GlcNAc branching) (Dennis et al., 1987).

The increased branching creates additional sites for terminal sialic acid residues, which, in conjunction with a corresponding upregulation of sialyltransferases, ultimately leads to an increase in global sialylation (Kim et al., 1997).

In addition to changes in the core structures of glycans, altered terminal structures are also associated with malignancy. Glycosyltransferases (for example, sialyltransferases and fucosyltransferases) involved in linking terminating residues on glycans tend to be overexpressed in tumour tissue. The increase in activity of these glycosyltransferases in turn leads to the overexpression of certain terminal glycans. Examples of terminal glycan epitopes commonly found on transformed cells include sialyl Lewis x (sLex), sialyl Tn (sTn), Globo H, Lewis y (Ley) and polysialic acid (prostate-specific antigen, PSA) (Gabius, 1988; Sell, 1990; Taylor-Papadimitriou et al., 1994; Hakomori et al., 1997). Many of these epitopes are observed in malignant tissues throughout the body, including the brain, breast, colon and prostate (Orntoft et al., 1999).

Another common feature of tumors is the overproduction of certain glycoproteins and glycolipids. For example, epithelial tumors often overproduce mucin glycoproteins, which are characterized by dense clusters of O-linked glycans. Mucins are used as diagnostic markers of cancer and can also function as scaffolds for most of the above-listed cancer-associated epitopes.
The aim of this study was to explore the application of Serum tumor associated material (TAM) testing kit, QINGDAO BO-XING Biotechnology Co., Ltd provides criteria: TAM detection value≥95U/ml demonstrates positive, <95U/ml negative. (Serum tumor associated material (TAM) testing kit, QINGDAO BO-XING Biotechnology Co., Ltd).

Materials and Methods

To be included in the study, patients who were hospital inpatients had to have histologically or cytologically confirmed NSCLC, and blood collected before and after treatment, as described elsewhere (Zhou et al., 2009; Yan et al., 2010).

Table 1. Characteristics of the Patients

<table>
<thead>
<tr>
<th>NSCLC, non- small cell lung cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Age(yr)Median (Range)</td>
</tr>
<tr>
<td>Adjuvant therapy</td>
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<tr>
<td>Palliative therapy</td>
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</tbody>
</table>

Table 2. The Serum Tumor Associated Material(TAM) Level and Several Tumor Markers after Chemotherapy in Non-Small Cell Lung Cancer Patients

<table>
<thead>
<tr>
<th>Disease control (CR+PR+SD) Increase N(%)</th>
<th>Disease progression (PD) Decrease N(%)</th>
<th>OR (95%CI)</th>
<th>OR* (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAM</td>
<td>16(23.2)</td>
<td>53(76.8)</td>
<td>10(55.6)</td>
</tr>
<tr>
<td>CEA</td>
<td>31(44.9)</td>
<td>38(55.1)</td>
<td>9(50)</td>
</tr>
<tr>
<td>CA125</td>
<td>25(36.2)</td>
<td>44(63.8)</td>
<td>12(66.7)</td>
</tr>
<tr>
<td>CA19-9</td>
<td>30(43.5)</td>
<td>39(56.5)</td>
<td>11(61.1)</td>
</tr>
</tbody>
</table>

CEA, carcinoembryonic antigen; CA, carbohydrate antigen; TAM, serum tumor associated material; CR, complete response; PR, partial response; SD, stable disease (SD); PD, progressive disease (PD); **P=0.018, TAM after chemotherapy compared with before; *P=0.061, TAM compared with CEA; **P=0.351, TAM compared with CA125; ***P=0.089, TAM compared with CA199; OR, Odds Ratio; OR*, adjusted for age and sex; 95%CI, 95% Confidence Interval.
Statistical analysis
Continuous variables were summarized by descriptive statistics, categorical variables by frequency. Count data by Chi-square test; measurement data as mean ± standard deviation. P < 0.05 was considered statistically significant. The study data was analyzed through the STATA 8.0 software (Stata Corporation, 4905 Lakeway Drive College Station, Texas 77845 USA).

Results

From April 1st to July 31st 2011, 87 NSCLC patients were enrolled into this study, men 61, women 26, with age ranging from 33-79. All patients had histologically or cytologically confirmed NSCLC (Table 1). The level of TAM decreased after chemotherapy compared with before chemotherapy when CT or MRI scan showed disease controlled, in contrary, it increased when disease progressed (P<0.05), and there was no statistically significant difference in monitoring of TAM and common tumor markers (P>0.05) (Table 2).

Discussion

Serum tumor associated material (TAM) is a glycoprotein detection kit, substances such as glucosamine and L-hydroxyproline and other amino acids as the main detected objects. Sialic acid and other glycosaminoglycans substances are the main materials which constitute glycolipids and glycoproteins, closely relating with intercellular adhesion, contact, inhibition of cancerous cells, tumor metastasis and proliferation (Serum tumor associated material (TAM) testing kit, QINGDAO BOXING Biotechnology Co., Ltd).

About 85% of cancer patients with elevated serum sialic acid, serum salvia acid changes in the level of disease was positively correlated with cancer, continued to rise indicated a poor prognosis (Wu et al., 1983). In tumor recurrence or metastasis, the serum sialic acid content increased may be several weeks before the clinical diagnosis, which was significant for early detection and promptly treatment. The elevation level of hydroxyproline, bone and collagen catabolin, indicated of bone metastases, especially bone metastases of breast cancer. Liu et al., showed that the serum free hydroxyproline in patients with malignant bone tumors were significantly high; peptide with hydroxyproline can identify malignant and benign bone tumors (Liu et al., 1986). As the reagent for sialic acid and hydroxyproline and other tumor-related substances were detected at the same time, color overlay, and thus improve the detection sensitivity.

Furthermore, TAM removed most of the macromolecular protein complex (at 450nm can colour in the non-tumor-related material) that could affect the test results by sedimentation centrifuge, to make accurate of the test results. So that, it can detect more tumor marker in serum sample. Earlier authors showed that TAM was higher in malignant tumors than benign tumors and healthy tissues (Zou et al., 2004; Deng et al., 2010; Jiang et al., 2010). It had been reported that CEA, CA125, CA19-9 could monitor the treatment efficacy in NSCLC (Diez et al., 1996; Vinolas et al., 1998; Foa et al., 1999). So we compared TAM and these tumor makers in monitoring treatment efficacy in NSCLC. In our study the level of TAM decreased after chemotherapy compared with before chemotherapy when CT or MRI scan showed disease control. In contrast, it increased when disease progressed, and there was no statistically significant difference in monitoring of TAM and common tumor markers such as CEA, CA125, CA19-9 (P>0.05). Since the limitation of poor specificity of common tumor makers in efficacy monitoring, TAM had a good effect of monitoring non-small cell lung cancer treatment with common tumor markers, because of its accuracy.

However, the detection of glucosamine substances also composed of the body’s immune response protein, Zou et al. found that patients with autoimmune disease’s positive rate of up to 47.62%, significantly higher (Zou et al., 2004), so the identification of clinical applications should be noted.

In conclusion, serum tumor associated material (TAM) is a new serum tumor marker detecting technology, which is sensitive in monitoring NSCLC treatment, deserving of further clinical study.

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References


