Serum Tissue Polypeptide Specific Antigen (TPS) in Loco-regional Failure and Distant Metastasis of Cervical Carcinoma

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Abstract

Tissue polypeptide specific antigen (TPS) was measured by the ELISA Technique in the sera of 51 patients with locoregional failure and metastasis of squamous cell carcinoma of the cervix in order to evaluate the serum level of TPS in known cases of metastasis and recurrence. There were 32 cases of local residual or recurrent disease and 19 cases of distant metastasis, including lymph nodes (paraaortic and supraclavicular lymph node) and visceral metastasis. The range of TPS levels in the locoregional failure group were 38.2 - 355.2 μ/l with a mean of 312.5 and 35.7 - 4822 μ/l with a mean of 833.36 μ/l in the metastatic group. With the cut-off value of 90 μ/l, the rates of TPS elevation were 27 in 32 cases (84.37%) of the loco-regional failure group and 16 in 19 cases (84.21%) of the metastatic group. Among the metastatic group, the mean of TPS level in visceral metastasis was much higher than the group of lymph node metastasis (1518.4 μ/l *vs* 215.1 μ/l). TPS level might be used as the follow-up guide for prediction of locoregional failure and metastasis in squamous cell carcinoma of the cervix after the completion of the treatment. In patients with a significantly high level of serum TPS, the distant metastases or local recurrence should be searched for. However, a prospective study of TPS levels in cervical cancer patients after completion of treatment should be done in order to evaluate the sensitivity and specificity of this tumor marker.

Key word : TPS, Cervical Cancer

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One of the major problems in cancer treatment is the monitoring of the patient during the follow-up period. Delineation of the tumor spreading and early detection of tumor recurrence or progression are the major problems. Apart from conventional evaluation such as CT and MRI which are limited by the cost and also the sensitivity in small lesions, tumor markers were studied and supposed to be helpful tools in judging the effectiveness of therapy as well as a guide in management of the patient[1-8]. Among these, squamous cell carcinoma antigen (SCC) has been introduced in gynaecologic practice to predict tumor recurrence or progression of disease in cases of squamous cell carcinoma of the cervix with 50 -70 per cent positive values, but some studies failed to demonstrate significant prognostic value[2,9-15].

Tissue polypeptide specific antigen (TPS) is a marker measuring a specific epitope structure on human cytokeratin 18 and can help to predict prognosis and response to treatment in different carcinomas[16], as serum TPS concentrations reflect tumor cell activity rather than tumor burden.

The TPS assay measures soluble fragments of cytokeratin 18, an acid cytokeratin protein of the cytoskeleton of epithelial cells[17]. As it reflects tumor cell activity, rather than tumor burden, it can provide additional information when assessing prognosis and response to treatment in different carcinomas. As higher concentrations of cytokeratin 18 are associated with malignant epithelial cells, TPS could be expected to be useful in the management of cervical cancer patients[18,19].

The current study was undertaken to evaluate TPS values in clinically proven metastasis and locoregional failure of cervical patients.

MATERIAL AND METHOD

From September 1995 to July 1996, 19 cervical cancer patients with metastatic disease and 32 patients with loco-regional failure were seen at the Department of Radiation Oncology, Siriraj Hospital. The mean age was 50 years old (range 28-78). Among the 19 patients with metastatic lesions, 10 lymph node metastasis (paraaortic with or without supraclavicular lymph nodes, 8 were lung, liver or bone and 1 patient with a combination of subcutaneous tissue, bone and lymph node metastasis. Thirty-two patients had loco-regional failure, 25 patients has residual disease and 7 patients had recurrence.

Blood samplings were obtained on the day the residual disease, recurrence or metastasis were diagnosed, in order to show the level of serum TPS in the patients with uncontrolled disease.

TPS was measured using TPS^{TM} ELISA (BEKI Diagnostic AB, Stockholm, Sweden). All samples were run in duplicate. The upper normal level of TPS^{TM} in serum was defined as 90 μ/l according to a previous evaluation in our clinic[20].

RESULTS

In the locoregional failure group, the TPS level varied from 38.2 - 355.2 μ/l with a mean of 312.5 μ/l and in the metastatic group it varied from 35.7 - 4822 μ/l with a mean of 833.36 μ/l. Among the patients with metastatic disease, TPS level in 10 patients with lymph node metastasis were from 42.9 - 363.4 μ/l with a mean of 215.1 μ/l while 9 patients of visceral metastasis had a TPS range of 35.7 - 4822.0 μ/l with a mean of 1518.3 μ/l. (Table 1)

With the cut-off level of 90 μ/l, 27 of 32 (84.37%) in the metastatic group and 16 of 19 (84.21%) in the locoregional failure group showed positive results. (Table 2)

Table 1. TPS range and mean of each group.

Group	Number	TPS (range) (μ/l)	TPS (mean) (μ/l)
Metastatic group	19	35.7 - 4822.0	833.4
- Lymph node metastasis	10	42.5 - 363.4	215.1
- Visceral metastasis	9	35.7 - 4822.0	1518.3
Locoregional failure	32	32.8 - 355.2	312.5

Table 2. TPS level of each group, with the cut-off level of 90 μ/l.

Clinical	TPS level (μ/l)	Numbers
Distant metastatic group	> 90	16/19
	< 90	3/19
Locoregional failure	> 90	27/32
	< 90	5/32

DISCUSSION

The potential usefulness of tumor marker relates to screening, diagnosis, prognosis, choice of treatment, effect of treatment and follow-up. Most of the current used tumor markers are bulk markers, such as CEA, i.e. their serum levels reflect tumor mass. Some markers represent products of specific function of certain cell types in relation to their degree of differentiation. Those markers reflect the actual production with reference to mass, differentiation and localization (vasculation). The marker that reflects the actual biological activity of the tumor or proliferative marker would be more meaningful and important for evaluation of tumor response and prognosis. Tumor markers for cervical carcinoma such as SCC, TPA, CEA, CA125 and Cyfra 21-1 were reported corresponding to the tumor burden[21] : stage and tumor size in the pretreatment serum level. TPA and SCC were of prognostic significance in relation to stage, recurrence and poor survival[10]. Pretreatment SCC level has a significant independent effect on survival, even in node-negative patients[14].

Tissue polypeptide specific antigen (TPS) is the new tumor marker which is the specific epitope M3 of the Tissue polypeptide antigen (TPA) which has been isolated from various types of human cancer such as breast cancer, ovarian cancer, cervical cancer, lung cancer, gastrointestinal cancer and urologic cancer. It has been used as a prognostic parameter in several types of cancer since it is related to the proliferating activity of cancer cell and used for therapy monitoring and follow-up for recurrence or metastasis.

Our previous study on TPS levels in stage II and III cervical cancer showed the correlation with tumor stage[20]. Concerning the surveillance of cervical cancer patients, a proliferative marker such as TPS is interesting as to whether it can better reflect tumor activity and supplement SCC which mainly appears to reflect the burden. The result of this study revealed the high level of serum TPS in both locoregional recurrence and metastatic group with a positive rate of 84.21 and 84.37 per cent and with a mean of 312.5 and 833.4 μ/l respectively. In the metastatic group, when focused on the site of metastasis, the TPS level was markedly high in visceral metastasis rather than nodal metastasis with a mean of 1518.3 and 215.1 μ/l respectively. This finding could be correlated with the clinical feature of metastasis in that the visceral metastasis has a worse prognosis than nodal metastasis.

However, although this study showed the high serum level of TPS in locoregional recurrent and metastatic disease, especially for visceral metastasis in cervical cancer patients, the statistical significance could not be confirmed because the aim of this study was just to show the TPS level in known cases of frank disease. A further prospective study of serum TPS level before and after completion of treatment with definite interval will be done in order to evaluate whether the metastasis or loco-regional recurrence can be predicted or indicated by initial and follow-up TPS level or not. The result of such a study will then show the real sensitivity and specificity of the serum TPS in cervical cancer.

SUMMARY

TPS is one of the good tumor markers for squamous cell carcinoma of the cervix. It might be significant as a tumor marker for monitoring cervical cancer patients and might be useful in determining the prognosis and optimal treatment or other adjuvant therapy.

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