

**Short Report****CLINICAL SIGNIFICANCE OF THE LYMPH NODE MICRO-METASTASIS IN PATIENTS WITH EARLY STAGE NON-SMALL-CELL LUNG CANCER**

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The postoperative 5-year survival rate is about 50-85% in the patient with the stage I non-small-cell lung cancer (NSCLC). It remains unclear how we should give these patients adjuvant radiotherapy and chemotherapy after operation. We performed a prospective study to assess the prognostic and treatment guiding significance of lymph nodes micrometastasis (LMM) in patients with completely resected NSCLC at stage I.

**MATERIALS AND METHODS**

We collected paraffin-embedded lymph nodes samples from 56 patients with stage I NSCLC who had been resected at our hospital and 301 hospital between September 1987 and September 1992. All patients had postoperative pathology diagnosis and had been followed-up more than 5 years. The cause of death of patients was all associated with lung cancer. The postoperative 5-years. The cause of death of patients was all associated with lung cancer. The postoperative 5-year survival rate of all patients was 55.4% (31/56). 252 lymph nodes from 56 patients' surgical samples were routinely cut to 4  $\mu$ m sections. 1 to 12 lymph nodes were included in each patient, the median number is 3. The immunocytochemical staining method, streptavidin-alkaline phosphates (SAP), was used to detect the micrometastasis in lymph nodes using the monoclonal antibody AE1/AE3 that is specific for cytokeratin antigens. The cytokeratin antigen is located in the cytoplasm of the cell. The positive cell is dyed to rose-red. If the

AE1/AE3 were deposited in lymph nodes and could be judged as tumor cell according to its tissue and cell formations, then the lymph nodes is judged as LMM<sup>+</sup>. Statistical analysis:  $\chi^2$  test was used to compare the general status of all patients and the survival rate in each group. The log-rank test was used to compare the survival time in each group.

**RESULTS**

Micrometastases were detected in 35.7% of all patients (20/56) and in 13.1% of lymph nodes (33/252). The postoperative 5-year survival rate in LMM<sup>+</sup> group is 35.0%(7/20), in LMM<sup>-</sup> group is 66.7%(24/36),  $\chi^2$  test,  $P < 0.05$ . Survival analysis by log-rank test,  $P < 0.05$ . In 45 patients with known disease-free survival time, the postoperative disease-free survival rate in LMM<sup>+</sup> group is 35.7%(5/14), and in LMM<sup>-</sup> group is 77.4%(24/31),  $\chi^2$  test,  $P < 0.01$ . Survival analysis by log-rank test,  $P < 0.01$ . The statistical analysis of survival between two groups showed that the presence of micrometastasis in lymph nodes for patients with stage I NSCLC had a close relationship with survival time and disease-free survival time.

**DISCUSSION**

The anti-cytokeratin monoclonal antibody could recognize the tumor cell, which come from epithelial tissue, and does not react with mesenchymal tissue. So it could be used to detect the micrometastasis in lymph nodes and bone marrow. AE1/AE3 is the ally anti-cytokeratin monoclonal antibody. It can react with many cytokeratin sub-types. Both sensitization and specificity was high. It can work on paraffin-embedded sections. Therefore it is the

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satisfactory monoclonal antibody to detect the micrometastasis in lymph nodes and bone marrow. Chen, et al. is the first author who reports the LMM of patients with NSCLC in 1992. But he did not report information of followed-up and survival. Thereafter several authors reported their study on micrometastasis in lymph nodes and/or bone marrow. They all considered that if the patient with NSCLC has LMM<sup>+</sup> and/or BMM<sup>+</sup> (bone marrow micrometastasis), their relapse rate was high and their disease-free time was short. Post-operative chemotherapy is suggested to eradicate micrometastasis that has been existed before operation. Postoperative adjuvant chemotherapy was not

necessary if there was no evidence of micrometastasis. Post-operative radiotherapy decreased the rate of local relapse or local lymph nodes metastasis. However, post-operative radiotherapy has no effect on the survival time of patients without local lymph nodes metastasis. LMM could not be detected with routine pathological method, and could be detected using immunocytochemical staining method. Our study showed that both the postoperative survival time and disease-free survival time in LMM<sup>+</sup> group were lower than that in LMM<sup>-</sup> group. The result suggested that the patients with LMM should accept adjuvant chemotherapy and/or adjuvant radiotherapy, while the patient without LMM should wait and see.