Squamous cell carcinoma antigen as an adjunct tumour marker in primary carcinoma of the lung

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Abstract

Aims—To determine (1) the detection rate of primary carcinoma of the lung by serological assay of CEA (carcinoembryonic antigen); and (2) whether addition of seroassay of squamous cell carcinoma related antigen before treatment improves detection sensitivity.

Methods—A prospective study spanning 27 months was conducted at the University Hospital, Kuala Lumpur. Serum CEA (Abbott IMx) and serum squamous cell carcinoma antigen (Abbott IMx) from patients clinically suspected of having primary carcinoma of the lung, were assayed using the microparticle enzyme immunoassay method.

Results—Thirty seven cases of histologically confirmed primary lung carcinoma were studied. Of these, 17 were squamous cell carcinomas, 10 adenocarcinomas, nine small cell carcinomas, and one large cell carcinoma. The patients' ages ranged from 34–82 years. The male:female ratio was 3.6:1. Squamous cell carcinoma antigen was raised above the cutoff value of 1.5 ng/ml in 94.1% of squamous cell carcinomas, 20.0% of adenocarcinomas, and 11.1% of small cell carcinomas. By comparison, CEA was raised above the cutoff value of 3.0 ng/ml in 70.6% of squamous cell carcinomas, 77.8% of small cell carcinomas, and 100% of adenocarcinomas. CEA and squamous cell carcinoma antigen were not raised in the patient with large cell carcinoma and in 14 healthy volunteers. None of 15 patients with a variety of benign lung diseases showed a rise of CEA, while two patients—a 25 year old Indian woman with pneumonia and a 64 year old Malay man with bronchial asthma—had raised squamous cell carcinoma antigen values above the cutoff. Serum CEA and squamous cell carcinoma antigen values did not seem to correlate with stage or degree of differentiation of the tumours.

Conclusions—The findings suggest that CEA is a good general marker for carcinoma, particularly adenocarcinoma. In contrast, squamous cell carcinoma antigen is more specific for squamous carcinoma.

Derived from TA-4 antigen, squamous cell carcinoma (SCC) related antigen has been successfully used as a marker for carcinoma of the uterine cervix.^{1,2} First described in 1977 by Kato and Torigoe, TA-4 antigen, a glycoprotein with a molecular weight of 48 000 daltons, was purified from squamous cell carcinoma of the uterine cervix.³ Although most commonly associated with cervical squamous cell carcinoma, a rise in serum SCC antigen has also been noted in glandular epithelial malignancies of the cervix⁴ and other epithelial malignancies, including carcinomas of the head and neck, oesophagus and lung.⁵⁻⁷ Furthermore, in the cervix the concentration of SCC antigen has been noted to correlate with tumour bulk, stage, and extent of disease.^{1,8}

Carcinoembryonic antigen (CEA) is one of the most commonly used serological markers for primary carcinoma of the lung.⁹ Various rates of detection, ranging from 50% to 80%, have been reported.¹⁰⁻¹² A prospective study was begun at University Hospital, Kuala Lumpur, to assess (1) the detection rate of primary carcinoma of the lung using the conventional CEA seroassay and (2) whether assaying serum SCC antigen before treatment in addition to CEA improves diagnostic sensitivity.

Methods

Patients were selected from those seen at the medical unit between August 1991 and October 1993. All patients clinically suspected of having primary carcinoma of the lung were assayed for SCC antigen (Abbott IMx) and CEA (Abbott IMx) using the microparticle enzyme immunoassay method before treatment. Of these, only histologically confirmed cases were considered for the study. Cases with recurrent carcinoma were not considered. Histological sections of all biopsy specimens were reviewed and classified according to the WHO histological classification system (1981). Histochemical and immunoperoxidase stains were carried out whenever necessary. Only histologically reconfirmed cases were finally included in the study. The tumours were graded as well, moderately, or poorly differentiated, and staged by the New International Staging System for Lung Cancer.¹³ Fifteen consecutive cases of clinically diagnosed benign lung lesions seen at the medical unit during the same period and 14 healthy volunteers were

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also seroassayed for CEA and SCC antigen. Arbitrary cutoff values of 1.5 ng/ml and 3.0 ng/ml were adopted for SCC antigen and CEA, respectively.

Results

Eighty two cases of suspected primary lung carcinoma were seroassayed for SCC antigen and CEA during the study period. Thirty seven histologically re-confirmed cases were included in the study: 27 Chinese, seven Malay, and three Indian people (age range 34–82; mean 60.4 years). The number of men totalled 29. Of the 37 cases, 17 were squamous cell carcinomas, 10 adenocarcinomas, nine small cell carcinomas and one large cell carcinoma. At the cutoff value of 1.5 ng/ml, the SCC antigen concentration before treatment was raised in 16 (94.1%) squamous cell carcinomas, two (20.0%) adenocarcinomas, and one (11.1%) small cell carcinoma. By comparison, 12 (70.6%) squamous cell carcinomas, seven (77.8%) small cell carcinomas, and all (100%) adenocarcinomas showed increased CEA beyond the cutoff of 3.0 ng/ml. Both SCC antigen and CEA were not raised in the case of large cell carcinoma. Taking into consideration all the histological types of primary lung carcinoma, the serum SCC antigen concentration before treatment was raised in 51.4% of cases and that of CEA in 78.4% (table). While CEA detected 29 of the 37 cases, four cases of squamous cell carcinoma exhibited increased SCC antigen without a raised CEA. By seroassaying SCC antigen in addition to CEA, detection sensitivity was therefore increased from 78.4% to 89.2%.

The cases of benign lung diseases seroassayed included five cases of pneumonia, one of pulmonary tuberculosis, two of bronchiectasis, one of bronchial asthma, one of eosinophilic pneumonitis, two of chronic obstructive airway disease, one of fibrosing alveolitis, one of inflammatory pseudotumour, and one of spontaneous pneumothorax. CEA was not increased in any of these. SCC antigen concentrations were below the cutoff in 13 of these cases but raised to 6.1 ng/ml in a 25 year old Indian woman with pneumonia, and marginally raised (1.6 ng/ml) in a 64 year old Malay man with bronchial asthma. Both serum CEA and SCC antigen were within normal limits in the 14 healthy controls.

Table Seropositivity for SCC antigen and CEA before biopsy in different histological types of primary lung carcinoma (n=37)

Histological type	SCC antigen No (%) positive	CEA No (%) positive
Squamous cell carcinoma (n=17)	16 (94.1)	12 (70.6)
Adenocarcinoma (n=10)	2 (20.0)	10 (100.0)
Small cell carcinoma (n=9)	1 (11.1)	7 (77.8)
Large cell carcinoma (n=1)	0 (0)	0 (0)
Total	19 (51.4)	29 (78.4)

A range of tumour differentiation and clinical stages were seen for each histological type of primary lung carcinoma. However, serum CEA and SCC antigen values correlated poorly with both degree of tumour differentiation and stage.

Discussion

The age range (34–82 years) and predominance of men among the cases noted here do not differ from other established studies. The male:female ratio of 3.6:1 is similar to that in the United Kingdom (4.36:1) and United States of America (4:1).¹⁴ In this study 73% of the patients were Chinese. By comparison, the Chinese constituted only 45.8% of all cases admitted to the medical unit during this period. There was a slight preponderance of Chinese patients, but the limited number of cases precludes meaningful statistical analysis. Whether primary carcinoma of the lung is more common in the Chinese is unclear and requires further study.

The detection rate of primary carcinoma of the lung by serological assay of CEA was 78.4%, similar to that seen in other studies.^{10–12} As has been observed by other workers,^{15,16} CEA was most efficient in the detection of adenocarcinomas, picking up all 10 cases. In contrast, CEA was raised in only 70.6% of squamous cell carcinomas and 77.8% of small cell carcinomas. Increased SCC antigen values were detected in 94.1% of squamous cell carcinomas while only 20.0% of adenocarcinomas and 11.1% of small cell carcinomas showed a similar rise. CEA seems to be a good marker for adenocarcinomas and SCC antigen for squamous cell carcinomas. Although most studies have shown that neurone specific enolase (NSE) is the ideal indicator of small cell carcinoma,^{17,18} CEA also seems to be reasonably effective, while SCC antigen is not.

Used as a single general tumour marker for primary lung carcinoma, irrespective of the histological type, serum SCC antigen managed to detect only 51.4% of cases. It seems to be inferior to CEA which detected 78.4% of the cases. However, the validity of this observation is debatable following the earlier observation that a rise in both CEA and SCC antigen is closely associated with histological type. None of the patients with benign pulmonary disease had increased serum CEA, while serum SCC antigen was raised in a patient with pneumonia and another with bronchial asthma. These findings are not unexpected as benign skin lesions and impaired renal function can result in raised SCC antigen.^{7,19} The reason for the rise in the two patients, whether due to the intrinsic lung disease or other independent conditions, is, however, not immediately apparent. Although not shown in this study, CEA is also known to rise in some benign lung conditions, false positive results being reported in as many as 10.7% of cases.⁹

Like Upham and Campbell,⁷ we too found that SCC antigen values correlated poorly

with both tumour stage and degree of differentiation. Similarly, CEA values did not correlate with either of the above parameters. This suggests that the serum concentrations of SCC antigen and CEA in primary lung carcinomas are influenced by factors not evaluated in this study. The possibility also remains that in lung cancers each case has its own baseline value of serological expression of these markers.

In conclusion, the findings of this study show that the sensitivity of CEA or SCC antigen is dependent on the histological type of lung cancer. CEA seems to be a more versatile general tumour marker that can detect squamous cell carcinomas, adenocarcinomas, and small cell carcinomas, although at varying degrees of sensitivity. None the less SCC antigen seems to be a better indicator for squamous malignancies. The seroassaying of SCC antigens in addition to CEA improved detection rate by 10.8%, from 78.4% to 89.2%. Therefore, for as long as squamous cell carcinoma continues to be a major histological type of primary lung cancer, we recommend seroassay of SCC antigen in addition to CEA to improve diagnostic accuracy. As a final note, it should be remembered that raised serum CEA and SCC antigen values should alert the physician to the possibility of malignancy but are not in themselves diagnostic. False positive results have always to be considered in the interpretation of results.

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