Detection and Sequencing of p53 Gene Mutations in Bronchial Biopsy Samples in Patients With Lung Cancer

To the Editor:

We read with interest the article by Mitsudomi et al1 who reported their experience detecting p53 gene mutations in bronchial biopsy samples from patients with lung carcinoma. They suggested point mutations could be screened in small biopsy snap-frozen samples obtained by fiberoptic bronchoscopy in preinvasive lesions detected by an imaging fluorescence endoscope device.

To evaluate a more cost-saving procedure, we screened lung cancer patients for the presence of anti-p53 seric antibodies with an original peptide enzyme-linked immunosorbent assay (ELISA) procedure described elsewhere.2 Such antibodies have been found in the sera of patients with various types of cancers.3,4 It has been shown that the presence of p53 antibodies in lung cancer patients is associated with p53 mutations.5 Sera were collected from patients at the time routine blood analyses were undertaken for diagnosis before any treatment. All sera were tested for p53 antibodies by immunoprecipitation and ELISA. In the ELISA, each serum was tested both on human p53 protein and also on an irrelevant antigen, with results expressed as the ratio of the value obtained with these two tests.6

Among 42 patients with lung carcinomas, 24 percent (10/42) exhibited seric antibodies to p53: 5/8 small cell lung carcinomas, 1/19 squamous cell lung carcinomas, 2/10 adenocarcinomas, and 2/5 large cell carcinomas. In the same period, we also evaluated 58 patients referred for nonmalignant pulmonary disorders. Of these, two subjects were found to have p53 serum antibodies: one patient with a chronic cough attributed to a documented esophageal reflux, and one patient considered to have a benign tracheal chondroma. They both, however, developed lung carcinoma, respectively, 4 and 12 months after screening and, therefore, must be considered as patients with occult malignancies at the time of the p53 antibodies screening.

Our results show that serologic analysis of immune response to p53 in lung cancer patients might be a useful and economic tool for screening p53 alterations, and it could detect preclinical lesions with early p53 alterations not detected by current procedures. Such detection in patients at risk for lung cancer or recurrence could lead to closer medical supervision and more aggressive procedures. Studies are on-going on this topic.

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REFERENCES

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Urinary 5-HIAA Unrelated to Cystic Fibrosis

To the Editor:

We read with interest the article by Sparrow et al,1 entitled “Relationship of Urinary Serotonin Excretion to Cigarette Smoking and Respiratory Symptoms” in Chest, April 1992. This prompted us to undertake a cross-sectional study of the relationship between urinary 5-hydroxyindoleacetic acid (5-HIAA) and disease severity in patients with cystic fibrosis.

We studied 19 patients with cystic fibrosis, ages 7 months to 21 years old. All patients were nonsmokers. All patients had a minimum of 10 mL of urine obtained during a clinic visit unassociated with a pulmonary exacerbation. 5-HIAA was measured by gas chromatography mass spectrometry, and the 5-HIAA concentration was determined as millimoles 5-HIAA per mole creatinine to correct for degree of urine dilution. The patients had the following determined: age; Brasfield chest x-ray film score, by a blinded observer; Schwanckman score, by a second blinded observer; cutaneous O2 saturation; nutritional status, expressed as percent of ideal body weight for height; and pulmonary function tests including FVC, FEV1, and FEF25-75 each expressed as percent of predicted.

Patients were found to have a mean 5-HIAA per creatinine concentration of 6.2 mmol/mol creatinine with a range of 0.5 to 59.2. All but one patient had a concentration ≤ 6.9. Brasfield scores ranged from 7 to 24 and Schwanckman scores from 55 to 98, and the two scores were significantly correlated with each other. There was no correlation between 5-HIAA concentration and any of the parameters listed above. There was no difference in levels between patients with mild and severe disease. The patient with the concentration of 59.2 mmol/mol creatinine was a 21-year-old with mild disease (Schwanckman score of 76).

We conclude that urinary concentrations of 5-HIAA are unrelated to the severity of the lung disease in cystic fibrosis.

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REFERENCE


The world of clinical medicine is filled with a wide array of organic diseases, and we as medical professionals are educated and are constantly honing our skills to diagnosis and overcome such illnesses. Yet, we are unprepared, to one degree or another, to deal with the minority of patients who, consciously or not, mislead us. As things stand now, turning the other cheek or denial, is probably a more common response to such a situation. Here lies the challenge for the next generation of medical educators.

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