Plasma levels of carcinoembryonic antigen in bronchial carcinoma and chronic bronchitis

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Pauwels, R. and van der Straeten, M. (1975). *Thorax*, 30, 560–562. Plasma levels of carcinoembryonic antigen in bronchial carcinoma and chronic bronchitis. The plasma levels of carcinoembryonic antigen were increased in 80% of 49 patients with bronchial carcinoma and in 68% of 25 patients with an acute exacerbation of chronic bronchitis.

There was no statistically significant difference between the two groups. A single determination of the plasma carcinoembryonic antigen level has no prognostic value in patients with bronchial carcinoma.

Carcinoembryonic antigen (CEA) was first described by Gold and Freedman in 1965 (Gold and Freedman, 1965a; Gold and Freedman, 1965b; Gold and Freedman, 1965c). Originally it was thought to be an antigen specific for colonic carcinoma. Subsequently this antigen has been discovered in other gastrointestinal tumours, breast tumours, and bronchial carcinomas.

It appears also to be present at a very low level in normal tissue. The development of a radioimmunoassay method by Thomson and co-workers (Thomson *et al.*, 1969) and the subsequent modifications of this method made it possible to detect CEA in plasma (Chu, Reynoso, and Hansen, 1972). Normal persons rarely exceed a plasma level of 2.5 ng/ml, as measured by the method of Hansen (Hansen, Lance, and Krupey, 1971; Hansen *et al.*, 1974). Raised levels of CEA have been detected in various malignant diseases (Gerfo, Krupey, and Hansen, 1971; Chu and Reynoso, 1972; Laurence *et al.*, 1972; Reynoso *et al.*, 1972; Concannon, Dalbow, and Frich, 1973; Hansen *et al.*, 1974; Terry *et al.*, 1974) but also in non-malignant inflammatory conditions and in healthy smokers (Hansen *et al.*, 1971; Stevens and Mackay, 1973; Terry *et al.*, 1974).

Our study was started in order to determine the clinical value of plasma CEA levels in bronchial carcinoma and to see if we could in this way discriminate between patients with bronchial carcinoma and patients with other pulmonary disorders. Since most of the patients with bronchial carcinoma also had clinical evidence of chronic bronchitis it was logical to compare them

to a group of patients with chronic bronchitis. Furthermore, we decided to determine the CEA level in patients with chronic bronchitis during an acute infectious exacerbation since inflammation seems to be an important stimulus for CEA liberation in the blood or CEA production by tissue.

We also tried to correlate the initial CEA level to survival rate in patients with bronchial carcinoma.

MATERIAL AND METHODS

CEA levels were determined in the plasma of 49 patients with histologically proven bronchial carcinoma and in 25 patients with an acute infectious exacerbation of chronic bronchitis. Follow-up studies were carried out as far as possible. The CEA level was determined by the zirconium go radio immunoassay method of Hansen *et al.* (1971), and this was done at the medical research department of Hoffman La Roche, Basel.

Statistical analysis was performed using the Wilcoxon test and calculation of linear correlation.

RESULTS

The CEA plasma levels in the two groups are shown in Figure 1.

Accepting 2.5 ng/ml as the upper limit of normal (Hansen *et al.*, 1974) we found an increase of plasma CEA level in 80% of the patients with bronchial carcinoma and in 68% of the patients with an acute exacerbation of chronic bronchitis. There was no statistically significant difference between the two groups although some very high

FIG. 1. Plasma CEA levels in patients with bronchial carcinoma (left column) and in patients with an acute exacerbation of chronic bronchitis (right column).

values were found among the carcinoma patients.

When the patients with chronic bronchitis were tested again one to two weeks after the first determination, after the acute exacerbation had responded to treatment with antibiotics, sympathomimetics, methylxanthines, and corticosteroids, no significant lowering of the CEA level was observed (Fig. 2).

Sixteen of the carcinoma patients proved to be operable and subsequently 14 of them underwent lobectomy or pneumonectomy. The other 35 patients received only symptomatic treatment. No chemotherapy was given.

FIG. 2. Plasma CEA levels during and after treatment of an acute exacerbation of chronic bronchitis.

Follow-up of patients with bronchial carcinoma was continued over a period of one year; during this time 70% of these patients died. When comparing the initial CEA level of patients who died during this year with the level in patients who survived, no statistically significant difference could be found and patients who proved to be operable did not have different CEA levels from the other carcinoma patients (Fig. 3). Moreover, there was no significant correlation between the initial CEA level and the survival time in patients who died (Fig. 4).

FIG. 3. Initial plasma CEA levels in patients with bronchial carcinoma divided into three groups: those who died within one year, those who survived one year, and those who were operable.

FIG. 4. Correlation between initial plasma CEA level and survival time in the patients with bronchial carcinoma who died.

DISCUSSION

Raised CEA levels have previously been reported in 76% of patients with pulmonary carcinoma, in 67% of patients with pulmonary emphysema, in 33% of patients with bronchitis, in 46% of patients with pneumonia, and in 37% of patients with tuberculosis (Hansen *et al.*, 1974). Other studies reported similar findings (Vincent and Chu, 1973; Terry *et al.*, 1974). CEA has also been found in bronchial carcinoma tissue and even in normal lung tissue at a very low concentration (Pusztaszeri and Mach, 1973; Sizaret and Martin, 1973). Our work confirms the high percentage of elevated CEA levels in patients with bronchial carcinoma but CEA appears to be raised to a similar degree during an acute exacerbation of chronic bronchitis. Since patients with bronchial carcinoma often have chronic bronchitis and may also present with an acute pulmonary infection, there is doubt about the clinical value of a single CEA determination in the diagnosis of bronchial carcinoma.

Prognostic studies following CEA measurements in bronchial carcinoma have not previously been reported, and it would seem from our work that little can be expected from a single CEA determination. It is possible that repeated measurements of CEA levels during follow-up and treatment would have more prognostic significance.

REFERENCES

- Chu, T. M. and Reynoso, G. (1972). Evaluation of a new radioimmunoassay method for carcinoembryonic antigen in plasma, with use of zirconyl phosphate gel. *Clinical Chemistry*, **18**, 918.
- , —, and Hansen, H. J. (1972). Demonstration of carcinoembryonic antigen in normal human plasma. *Nature*, **238**, 152.
- Concannon, J. P., Dalbow, M. H., and Frich, J. C. (1973). Carcinoembryonic antigen (CEA) plasma levels in untreated cancer patients and patients with metastatic disease. *Radiology*, **108**, 191.
- Gerfo, P. L., Krupey, J., and Hansen, H. J. (1971). Demonstration of an antigen common to several varieties of neoplasia. Assay using zirconyl phosphate gel. *New England Journal of Medicine*, **285**, 138.
- Gold, P. and Freedman, S. O. (1965a). Demonstration of tumour-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. *Journal of Experimental Medicine*, **121**, 439.
- and — (1965b). Specific antigen similarity between malignant adult and normal fetal tissues of the human digestive system (abstract). *Journal of Clinical Investigation*, **44**, 1051.
- and — (1965c). Specific carcino-embryonic antigens of the human digestive system. *Journal of Experimental Medicine*, **122**, 467.
- Hansen, H. J., Lance, K. P., and Krupey, J. (1971). Demonstration of an ion sensitive antigen site on carcino-embryonic antigen using zirconyl phosphate gel. *Clinical Research*, **19**, 143.
- , Snyder, J. J., Miller, E., Vandevoorde, J. P., Miller, O. N., Hines L. R. and Burns J. J. (1974). Carcinoembryonic antigen (CEA) assay. A laboratory adjunct in the diagnosis and management of cancer. *Human Pathology*, **5**, 139.
- Laurence, D. J. R., Stevens, U., Bettelheim, R., Darcy, D., Leese, C., Turberville, C., Alexander, P., Johns, E. W., and Neville, A. M. (1972). Role of plasma carcinoembryonic antigen in diagnosis of gastrointestinal, mammary, and bronchial carcinoma. *British Medical Journal*, **3**, 605.
- Pusztaszeri, G. and Mach, J. P. (1973). Carcinoembryonic antigen (CEA) in non digestive carcinomas and normal tissues. *Immunochemistry*, **10**, 197.
- Reynoso, G., Chu, T. M., Holyoke, D., Cohen, E., Nemoto, T., Wang, J. J., Chuang, J., Guinane, P., and Murphy, J. P. (1972). Carcinoembryonic antigen in patients with different cancers. *Journal of the American Medical Association*, **220**, 361.
- Sizaret, P. and Martin, F. (1973). Carcinoembryonic antigen in extracts of pulmonary cancers. *Journal of the National Cancer Institute*, **50**, 807.
- Stevens, D. P. and Mackay, I. R. (1973). Increased carcinoembryonic antigen in heavy cigarette smokers. *Lancet*, **2**, 1238.
- Terry, W. D., Henkart, P. A., Coligan, J. E., and Todd, C. W. (1974). Carcinoembryonic antigen: characterization and clinical applications. *Transplantation Reviews*, **20**, 100.
- Thomson, D. M. P., Krupey, J., Freedman, S. O., and Gold, P. (1969). The radioimmunoassay of circulating carcinoembryonic antigen of the human digestive system. *Proceedings of the National Academy of Science of the United States of America*, **64**, 161.
- Vincent, R. G. and Chu, T. M. (1973). Carcinoembryonic antigen in patients with carcinoma of the lung. *Journal of Thoracic and Cardiovascular Surgery*, **66**, 320.

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