Eur J Cancer, Vol. 27, No. 12, p. 1711, 1991.
Printed in Great Britain
0277-5379/91 $3.00 + 0.00
Pergamon Press plc

Alveolar Macrophage Function Before and During Treatment with Cytotoxic Chemotherapy in Patients with Small Cell Lung Cancer

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IMMUNE FUNCTION is often depressed in patients with cancer. The ability to mount an effective immune response in the face of these immunosuppressive influences may be important in determining the outcome of the malignant process.

Chemiluminescence reflects phagocytic oxidising activity [1] and correlates with other methods of measuring phagocytic function [2–4] (Williams and Cole 1981, Schult *et al.* 1985).

We used a lucigenin-enhanced chemiluminescence assay to measure alveolar macrophage function in 17 patients with small cell lung cancer (SCLC) and 17 controls.

Patients with histologically proven SCLC (mean age 65 years) underwent bronchoscopy and bronchoalveolar lavage (BAL) at diagnosis. 17 smoking, matched subjects (mean age 54 years) undergoing diagnostic bronchoscopy who were subsequently found to have no significant pathology acted as controls.

Patients with SCLC underwent repeat BAL 6 weeks later, prior to the third of cycle of chemotherapy (cyclosphosphamide, doxorubicin, vincristine and etoposide). BAL was performed in a subsegment of the middle lobe or lingula, in the lung contralateral to the site of tumour. Warmed buffered saline was instilled and aspirated into a siliconised container.

The sample was filtered and centrifuged prior to resuspension in Medium 199 without phenol red at a concentration of one million cells per ml. Chemiluminescence was performed at 37°C using 1 ml cell suspension and 0.4 ml lucigenin (1 mmol). For stimulated assays, 0.2 ml of a 10% latex bead suspension was also added. Peak output was recorded as counts per minute (CPM) per 10^3 cells.

There was a wide variation in macrophage function within both groups. Control subjects had peak responses similar to patients with SCLC, but the 4 patients with extensive SCLC had lower mean responses than those with limited disease.

There was no association between chemiluminescence response and subsequent response to chemotherapy, except that 3 patients who died early from treatment-related causes had poor chemiluminescence responses. However, there was an association between alveolar macrophage function and survival time: $r = 0.62$ ($P<0.01$) for unstimulated studies, and $r = 0.67$ ($P<0.01$) for stimulated studies (Fig. 1).

Paired chemiluminescence data on 12 patients with SCLC who underwent BAL studies both prior to treatment and following two courses of chemotherapy showed a significant fall in the cell numbers recoverable during treatment (0.47 vs. 0.28×10^6 ml; $P<0.001$), but no change in the differential count or supernatant total protein concentration.

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Revised 12 Aug. 1991; accepted 22 Aug. 1991.

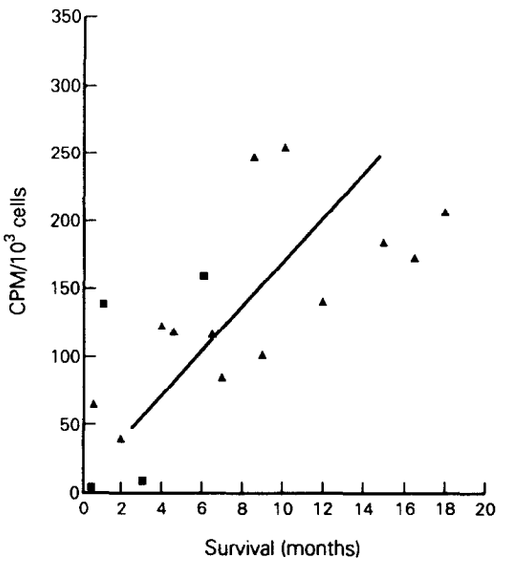

Fig. 1. Correlation between stimulated alveolar macrophage CL response and survival time in 17 patients with SCLC. ▲ = patients with limited disease, ■ = patients with extensive disease. $r = 0.67$, $P<0.01$, $n = 17$.

Chemiluminescence responses showed a non-significant fall in macrophage function during treatment in both unstimulated and stimulated assays.

The wide variation in individual responses limits the usefulness of comparing macrophage function in controls and patients with SCLC, but there was a clear association between alveolar macrophage function and survival time in the patients with SCLC.

Studies of alveolar macrophage function in lung cancer using other techniques have produced conflicting results [5]. Our results suggest that alveolar macrophage function may be depressed in patients with extensive disease SCLC.

3 patients who died within 1 month of starting treatment ("early death" group) all had very low chemiluminescence responses, suggesting that poor macrophage function at diagnosis may be predictive of early treatment-related death.

Rossi *et al.* reported a reduction in cell numbers recoverable from BAL following chemotherapy without any change in differential count in 8 patients with lung cancer [6], which is consistent with our results.

The finding of preserved function 3 weeks after the second pulse of treatment shows that any suppression of macrophage function is transient and reversible.

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