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Aplastic Anaemia as a Paraneoplastic Syndrome in Lung Cancer

Pirjo Koistinen, Vuokko Kinnula and Timo Timonen

MALIGNANT lung tumours can be associated with haematological syndromes, such as leucocytosis, erythrocytosis and thrombocytosis [1]. Pancytopenia without bone marrow metastasis is rare [2, 3]. We report a patient with aplastic anaemia associated with epidermoid lung cancer.

A 62-year-old man was admitted because of progressive weakness and pancytopenia. His previous history included chronic bronchitis with 30 years of smoking. Rheumatoid arthritis had been diagnosed 10 years earlier. 6 months before admission he had been investigated elsewhere because of right-sided pleural effusion, which subsided spontaneously and was considered to be associated with his rheumatoid arthritis. His previous medication consisted of D-penicillamine for 24 months, which was discontinued 1 month before admission because of mild anaemia and leukopenia. On admission, the only findings were coarse bilateral basal inspiratory crackles. Haemoglobin (Hb) value was 88 g/l, white cell count 2×10^9/l with 11% neutrophils and platelet count 36×10^9/l. Bone marrow biopsy revealed severe marrow hypoplasia. Aplastic anaemia was diagnosed and treated with regular transfusion support with leucocyte-depleted, packed red cells and thrombocytes.

Over the next 6 months, chest radiography was used to observe the right upper lobe infiltrate. Fibreoptic bronchoscopy revealed tumour in the right upper lobe and histology confirmed a squamous cell carcinoma. No mediastinal lymph-node involvement nor any distant metastases were observed with computed tomography (CT) and skeletal scintigraphy. At thoracotomy a right upper lobectomy was done. After the thoracotomy the peripheral blood cell values spontaneously returned to normal. Bone marrow biopsy 3 months later revealed normal cellularity. After 10 months the patient became disoriented and brain CT revealed a solitary metastasis; mild pancytopenia also developed. 4 months after the removal of the brain metastasis, pancytopenia worsened, bone marrow hypoplasia recurred and the patient also had multiple liver metastases and hypercalcaemia. 15 months after the lung operation he died without any cytotoxic chemotherapy. At necropsy, metastases were found in mediastinal lymph nodes and liver, but not in lungs, brain or bone marrow.

Haematological abnormalities in lung cancer are common, but nearly always associated with metastasized disease. In our patient no signs of metastases were observed at thoracotomy. Although the pleural effusion may have been due to malignancy, it cleared spontaneously and repeated cytological examination of the fluid was normal. Rheumatoid arthritis can itself cause pleural effusions and the specimens of pleural fluid from our patient were similar to those seen in rheumatoid pleuritis.

Correspondence to: P. Koistinen, Ontario Cancer Institute, Rm 606, 500 Sherbourne Street, Toronto, Ontario, M4X 1K9, Canada.
P. Koistinen and T. Timonen are at the Department of Internal Medicine, Oulu University, Oulu and V. Kinnula is at the Department of Pulmonary Medicine, Helsinki University, Helsinki, Finland.

Our patient had been taking D-penicillamine for 2 years. When he stopped he already had mild cytopenia: Hb 115 g/l, white cell count 3.3×10^9/l, and platelet count 121×10^9/l. Over the following month aplastic anaemia developed fully. During the next 6 months, however, the peripheral blood count remained abnormal, as did the bone marrow cellularity. The return to normal and the recurrence of pancytopenia were associated with the removal and dissemination of the primary tumour, respectively. Hence, an effect of D-penicillamine on the bone marrow abnormality is highly improbable.

Paraneoplastic haematological syndromes include anaemia, leucocytosis, thrombocytosis, polycythaemia and bleeding disorders. Myelodysplasia in three lung cancer patients has been reported, but all these patients were inoperable and no total improvement of the bone marrow could be achieved [2]. One of the patients had adenocarcinoma and the other two squamous cell carcinoma of the lung. Two lung cancer patients with atypical bone marrow cluster formation have also been reported [4]. In addition, human squamous cell carcinoma of the lung can produce colony-stimulating factors provoking leucocytosis [5–7]. We did not do *in vitro* investigations in our case, but the recurrence of pancytopenia along with the tumour dissemination without bone marrow metastases suggested that the bone marrow abnormality was associated with the production of an inhibitor by the neoplastic cells.

1. Umsawasdi T, Valdivieso M. Paraneoplastic syndromes in lung cancer. *Semin Resp Med* 1982, **3**, 200–207.
2. Raz I, Shinar E, Poillack A. Pancytopenia with hypercellular bone marrow. A possible paraneoplastic syndrome in carcinoma of the lung: a report of three cases. *Am J Hematol* 1984, **16**, 403–408.
3. Focan C, Swale JL, Borles-Hermans G, Claessens JJ. Systemic sclerosis, aplastic anemia and amyloidosis associated with lung carcinoma. *Acta Clin Belg* 1985, **40**, 204–205.
4. McCarthy JH, Sullivan JR, Ungar B, Metcalf D. Two cases of carcinoma of the lung characterized by a bone marrow agar culture pattern resembling acute myeloid leukemia. *Blood* 1979, **54**, 530–533.
5. Asano S, Urabe A, Okabe T *et al.* Demonstration of granulopoietic factor(s) in the plasma of nude mice transplanted with a human lung cancer and in the tumor tissue. *Blood* 1977, **49**, 845–851.
6. Sato N, Asano S, Veyama Y *et al.* Granulopoiesis and colony-stimulating activity (CSA) produced by a human squamous cell carcinoma. *Cancer* 1979, **43**, 605–613.
7. Suda T, Miura Y, Mizoguchi H *et al.* A case of lung cancer associated with granulocytosis and production of colony-stimulating activity by the tumor. *Br J Cancer* 1980, **41**, 980–984.

Correction

Growth factor and electrolyte concentration in human breast cyst fluid.—In this article by H. Hamed and colleagues (Vol. 26, p. 479), Table 1 was omitted:

Table 1 Linear regression ($y = log_{10}ECF$ and x = electrolytes)

x	Slope $\times 10^3$	Intercept	r*
Na^+	− 4.2	2.79	−0.62
K^+	4.3	2.13	0.68
Cl^-	− 6.4	2.77	−0.68
Na^+/K^+	−42.2	2.65	−0.72

* All correlations $P < 0.001$.
No. of women studied was 41. Units were ng/ml for EGF and nmol/l for electrolytes.