Leukocytosis as a Paraneoplastic Phenomenon in Patients with Malignant Lung Tumors

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SUMMARY

Objective: leukocytosis as a paraneoplastic syndrome may occasionally occur in patients with lung carcinoma. The aim of the study was to assess the prevalence of leukocytosis in our sample of patients with lung carcinoma, to determine if leukocytosis is more common with a particular type of lung carcinoma, and whether leukocytosis caused inappropriate prescribing of antibiotics in patients with lung carcinoma. Methods: The study included 100 lung carcinoma patients treated at Department of Lung Diseases, General Hospital, during a three-year period (2003-2006). The methods of descriptive statistics were used on statistical analysis. Results: during a three-year period (2003-2006), 100 patients with lung carcinoma were treated at General Hospital, 23% of them with leukocytosis as a paraneoplastic phenomenon. Antibiotic therapy was prescribed in five of 23 (1,25%) patients. Conclusion: leukocytosis was most frequently associated with squamous cell carcinoma of the lung (43%), however, without statistical significance. Antibiotic therapy was prescribed in 1,25% of leukocytosis patients, suggesting that leukocytosis was correctly recognized as a araneoplastic phenomenon and was not unnecessarily treated with antibiotics.

Key words: leukocytosis, lung carcinoma

1. INTRODUCTION

Tumors can produce signs and symptoms distant from the tumor or its metastases, by a mechanism involving hormones, protein, cytokines, various growth hormones or antibodies, known as paraneoplastic syndrome. The paraneoplastic syndrome involving the hematopoietic system is a common phenomenon. A form of this syndrome is leukocytosis or granulocytosis (L≥12.0x10^9/L) without signs of infection or leukemia. Leukocytosis is most commonly observed in association with lymphoma and other solid tumors of the stomach, lung, pancreas and brain, and malignant melanoma (1). The basic mechanism of associated leukocytosis includes the formation of granulocyte growth factor (G-CSF), granulocyte-monocyte growth factor (GM-CSF), interleukin 3 (IL-3) and interleukin 1 (IL-1) in tumor cells (1, 2). G-CSF is a glycoprotein active in very low concentrations, which stimulates the proliferation and maturation of immature hematopoietic cells, and functional capacity of mature blood cells. However, growth factors generally also favor the growth of tumor cells. GM-CSF stimulates the growth of small-cell lung carcinoma (SCLC) (2).

Histologically, lung carcinomas are classified into four large groups: squamous cell carcinoma (SCC), adenocarcinoma (ADC), small cell lung carcinoma (SCLC), and large cell lung carcinoma (LCC).

The aim of the study was to assess the prevalence of leukocytosis in our sample of patients with lung carcinoma, to determine if leukocytosis is more common with a particular type of lung carcinoma, and whether leukocytosis caused inappropriate prescribing of antibiotics in patients with lung carcinoma.

2. PATIENTS AND METHODS

The study included 100 lung carcinoma patients treated at Department of Lung Diseases, General Hospital, during a three-year period (2003-2006). The diagnosis of lung carcinoma was made on the basis of clinical finding, radiologic finding of the lungs, computed tomography of the chest, and cytology or histopathology of the sputum or material obtained by bronchoscopy. 1..

In addition to leukocyte and granulocyte count, the following tests were obtained: C-reactive protein (CRP), sputum and urine microbiology, blood culture as indicated by clinical picture, and bone marrow cytology in some cases, which definitely ruled out infection or leukemia as the possible cause of leukocytosis.

There were 89 male and 11 female patients, age range 37-84 years. SCC was diagnosed in 45, lung ADC in 23, SCLC in 17, and undifferentiated carcinoma of the lungs or unavailable data in 13 patients (Table 1). The methods of descriptive statistics were used on statistical analysis.

Leukocytosis meant the number L ≥ 12x10^9/L, as a paraneoplastic syndroma ,when leukocytosis was found during the analysis, that is, diagnostic procedure. We

have carefully taken the consultation about drugs which the patients were taking. Those who were taking glucocorticoids have been excluded from the study, because it is very well known that glucocorticoids cause leukocytosis.

3. RESULTS

The study series included 100 patients, 89 male and only 11 female. Leukocytosis was recorded in 23 (23%) . The main clinical characteristics of these patients are shown in Table 2. Of these 23 patients, SCC was present in ten, adenocarcinoma of the lungs in six, SCLC in four, and undifferentiated lung carcinoma in three patients. CRP was elevated in six and within normal values in 17 patients. Five patients were prescribed antibiotic therapy.

Tumor type	n	Sex M:F	Age (yrs, median; range)		L ≥12.0x10^9/L
SCC	45	41:4	66	(47-84)	10
ADC	23	19:4	65	(37-79)	6
SCLC	17	16:1	63	(53-76)	4
Undifferentiated	13	11:2	67	(47-79)	3
Valid	2				
Total	100	89:11		37-89	23

SCC, squamous cell carcinoma; ADC, adenocarcinoma; SCLC, small cell lung carcinoma; Valid, no data; M, male; Female

Table 1. Clinical characteristics of patients with lung carcinoma

Tumor type	N	Age (yrs, median; range)	Sex M/F	Sputum antibiogram neg/pos	Blood culture neg/pos	Urine culture neg/pos	CRP N/ P	Antibiotic yes/no
SCC	10	60.5 (47-75)	9/1	10/0	10/0	10/0	9/1	1/9
ACC	6	66.5 (37-79)	5/1	4/2	6/0	6/0	3/3	2/4
SCLC	4	70.5 (56-76)	4/0	4/0	4/0	4/0	2/2	2/2
Undifferentiated	3	70 (47-73)	3/0	3/0	3/0	3/0	3/0	0/3
Total	23	37-79	21/2	23/0	23/0	17/6	5/18	5/18

SCC, squamous cell carcinoma; ADC, adenocarcinoma; SCLC, small cell lung carcinoma; M, male; F, female; CRP, C reactive protein

Table 2. Clinical characteristics of patients with leukocytosis

4. DISCUSSION

Leukocytosis of obscure etiology may occasionally be seen in patients with malignant tumors, most commonly in association with lung carcinoma, where it appears to be an unfavorable prognostic indicator (3). However, the true role of excessive leukocyte production and their implication in immune dysregulation and paraneoplastic syndrome remain unclear (5). In literature reports, the prevalence of leukocytosis in association with lung carcinoma ranges from 1.4% to 14.5% (3,6). In our series it was 23%. Some studies report on a statistically significant association of leukocytosis with non-small cell lung carcinoma, which was not confirmed in our study. In our patients, leukocytosis was most common in the subgroup of patients with squamous cell carcinoma of the lung, i.e. in ten of 23 (43%) patients; however, the difference did not reach statistical significance, perhaps due to the small patient sample. Antibiotic therapy was prescribed in five of 23 (1,25%) patients. These five patients had elevated C-reactive protein and two of them also had positive sputum finding, which must have influenced the decision on antibiotic therapy.

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