

Eosinophilia and Leukocytosis in a Patient with Lung Cancer

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Paraneoplastic eosinophilia is rarely described in association with solid tumors [1]. There are only a few cases describing peripheral eosinophilia in the context of lung cancer [2,3]. However, leukocytosis has been described in association with non-small cell lung carcinoma and was shown to have a poor outcome [4]. In this report, we present the case of a 54 year old male patient with paraneoplastic eosinophilia and tumor-related leukocytosis (TRL).

PATIENT DESCRIPTION

A 54 year old male was admitted to the internal medicine ward at Sheba Medical Center with a 3 week history of shortness of breath. He complained of night sweats and low grade fever accompanied by general weakness. Laboratory tests revealed

marked eosinophilia and leukocytosis [Table 1].

A chest radiograph demonstrated a large pleural effusion on the left side. The patient's history was remarkable for Raynaud syndrome that had been known for years but not treated. He had been a heavy smoker in the past and was still smoking approximately five cigarettes a day at the time of hospital admission. He was not taking any medications.

On the first day of hospitalization, the patient underwent thoracentesis. Cytology and bacteriology studies were negative for malignant cells and bacteria. Tests on the fluid supported an exudate. A cell count of the fluid showed marked eosinophilia. A computed tomography (CT) scan of the chest revealed a large pleural effusion on the left side, with multiple pleural nodules suspected to be malignant. The differential diagnosis was mesothelioma and carcinoma of the lung. Laboratory tests for rheumatologic disorders were all negative. There was no evidence of blast cells on a peripheral blood smear, and parasites were not found. A diagnostic thoracoscopy

with pleural biopsy was performed, which showed an undifferentiated pleomorphic tumor with focal immunoreactivity for thyroid transcription factor 1 and napsin A, favoring a diagnosis of adenocarcinoma of the lung.

The tumor cells stained positive for 90% programmed death-ligand 1 and the patient was referred to the oncology ward for treatment. At that point, he complained of a widespread rash on his chest, back and abdomen, as well as migratory arthralgia. His laboratory results showed 104 (K/ μ l) leukocytes and 41(K/ μ l) eosinophils.

The patient received steroids and allopurinol due to a diagnosis of a paraneoplastic syndrome with marked eosinophilia. He began chemotherapy with vinorelbine and cisplatin that later was replaced by cisplatin and pemetrexed. Subsequent to the beginning of treatment, the rash subsided substantially, and a dramatic decline in his leukocytosis and eosinophilia was noted [Table 1].

A few months after completing six courses of chemotherapy, the patient's white blood cell (WBC) and eosinophil

Table 1. Blood and pleural fluid counts

	Before initiating chemotherapy		Cisplatin + pemetrexed			Cisplatin + vinorelbine			Dabrafenib + trametinib			
	2016	2017	2017			2017			2017	2018		
Date	5 Dec.	12 Dec.	19 Jan.	20 Jan.	27 Feb.	4 June	13 June	27 June	8 Aug.	29 Aug.	14 Jan.	26 Jan.
WBC, K/ μ l	24	34	122	61	12	52	92	55	118	82	72	132
EOS, %	11	14	34	6	42	9	18	20	16	3	16	14
EOS abs, K/ μ l	3	4.8	42	4	5	4	16	11	18.5	2.5	12	19
EOS PE*, %	8	3										
EOS abs PE, K/ μ l	0.17	0.03										

*Eosinophilic pleural effusions is defined as a pleural effusion that contains at least 10% eosinophils

abs = absolute, EOS = eosinophilia, PE = pleural effusion, WBC = white blood cells

counts started rising, and he experienced recurrence of fever, arthralgia, and mild erythematous rash. A whole-body CT scan showed progression of his disease with new metastases in the liver and lymphangitic spread in the lungs. The chemotherapy treatment with vinorelbine and cisplatin was reinstated. However, after four courses of therapy, a CT scan demonstrated extensive progression of the disease.

A third line treatment with dabrafenib combined with trametinib initially achieved a good response; however, his disease continued to spread and a significant rise in his WBC and eosinophil counts was noted [Table 1]. The patient was readmitted to the internal medicine ward 5 months after he began his third-line treatment. At that point, he also presented with severe dyspnea. Due to his poor prognosis and general condition, he received only palliative care and died a short time later.

COMMENT

Paraneoplastic eosinophilia is a rare phenomenon. Eosinophilia is usually associated with benign conditions such as allergic reactions, parasitic infections, vasculitis, and drug reactions [1,3]. In this report, we present a patient with eosinophilia and excessive

leukocytosis secondary to adenocarcinoma of the lung with aggressive progression. Leukocytosis associated with malignancy can be caused by an overlap infection or bone marrow metastases [4]. Some patients have been found with leukocytosis without evidence of any of the mentioned conditions and therefore were considered to have TRL. This condition is most likely caused by excessive production of hematopoietic cytokines such as granulocyte-colony stimulating factor, granulocyte-macrophage colony-stimulating factor, or interleukin 6.

A study by Kasuga et al. [4] found TRL to be associated with a shorter median survival time and poorer responses to chemotherapy and radiotherapy. The clinical meaning and pathogenesis of paraneoplastic eosinophilia remain unclear. The most common mechanism suggested by several studies is also associated with excessive production of cytokines with regard to TRL [3], which suggests paraneoplastic eosinophilia is an ominous prognostic sign as well. Previous studies supported this theory [3,5].

CONCLUSIONS

Our case study shows an aggressive disease that progressed over a relatively short period of time despite treatment. Interestingly, it seems that there was a correlation between

the progression of the disease and the rise in leukocyte and eosinophils counts. This finding implies that TRL and paraneoplastic eosinophilia are not only prognostic signs, but reflect the activity of the disease and the effectiveness of treatment. Further studies should be conducted to better understand this rare phenomenon.

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References

1. Samsozuk M. Eosinophils and human cancer. *Histol Histopathol* 1997; 12 (3): 807-12.
2. Lo CH, Jen YM, Tsai WC, Chung PY, Kao WY. Rapidly evolving asymptomatic eosinophilia in a patient with lung adenocarcinoma causes cognitive disturbances and respiratory insufficiency: case report. *Oncol Lett* 2013; 5 (2): 495-8.
3. Pandit R, Scholnik A, Wulfekuhler L, Dimitrov N. Non-small-cell lung cancer associated with excessive eosinophilia and secretion of interleukin-5 as a paraneoplastic syndrome. *Am J Hematol* 2007; 82 (3): 234-7.
4. Kasuga I, Makino S, Kiyokawa H, Katoh H, Ebihara Y, Ohysahiki K. Tumor-related leukocytosis is linked with poor prognosis in patients with lung carcinoma. *Cancer* 2001; 92 (9): 2399-405.
5. El-Osta H, El-Haddad P, Nabbout N. Lung carcinoma associated with excessive eosinophilia. *J Clin Oncol* 2008; 26 (20): 3456-7.

Capsule

The impact of systemic lupus erythematosus on the clinical phenotype of antiphospholipid antibody-positive patients

Although systemic lupus erythematosus (SLE) is the most common autoimmune disease associated with antiphospholipid antibodies (aPL), limited data exist regarding the impact of SLE on the clinical phenotype of aPL-positive patients. Unlu et al. compared the clinical, laboratory, and treatment characteristics of aPL-positive patients with SLE with those of aPL-positive patients without SLE. A secure web-based data capture system was used to store patient demographic characteristics and aPL-related clinical and laboratory characteristics. Inclusion criteria included positive aPL according to the updated Sapporo classification criteria. Antiphospholipid antibody-positive patients fulfilling the American College of Rheumatology criteria for the classification of SLE (aPL with SLE) and those with no other autoimmune diseases (aPL only) were included in the analysis. The study comprised 672 aPL-

positive patients from 24 international centers; 426 of these patients did not have other autoimmune disease, and 197 had SLE. The frequency of thrombocytopenia, hemolytic anemia, low complement levels, and IgA anti-β2-glycoprotein I (anti-β2GPI) antibodies was higher in the aPL-positive patients with SLE, whereas the frequency of cognitive dysfunction and IgG anti-β2GPI antibodies was higher in the aPL-only group. The frequency of arterial and venous thromboses (including recurrent) as well as pregnancy morbidity was similar in the two groups. The prevalence of cardiovascular disease risk factors at the time of entry into the registry entry did not differ between the two groups, with the exception of current smoking, which was more frequent in aPL-positive patients with SLE.

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