Eosinophilia with an Uncommon Cause

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Abstract

Blood eosinophilia is an uncommon manifestation of solid tumors. The authors report a case of a previously healthy 78-year-old White male, admitted to our department with a two-week history of fatigue, weakness, anorexia, weight loss, fever, night sweating and hepatomegaly. The leukocyte count was 111700/mm3 with 58830/mm3 eosinophils. Abdominal ultrasound and computerized tomography scan showed a hepatic mass of 8x7 cm. Guided percutaneous needle biopsy of the liver showed metastasis of adenocarcinoma of unknown origin. Flexible colonoscopy showed a stenosing lesion of the mid-portion of the transverse colon and biopsy revealed a well-differentiated adenocarcinoma of the colon. A review of the literature found only two cases of colon cancer with more then 30000 eosinophils/mm3.

Key words: eosinophilia, neoplasms, parasitic diseases.

Introduction

Eosinophilia can be found in various pathologies, including allergic diseases, parasitic infestations, particularly helminth infections, connective tissue diseases, skin diseases such as dermatitis herpetiformis, pemphigus or mycosis fungoides, and Loeffler's syndrome.[1,2,3] Less frequently, eosinophilia may be associated with malignancies, particularly hematologic diseases. Blood hypereosinophilia is extremely rare in solid neoplasms.[4,5] This was the reason that led us to publish this clinical case.

Clinical case

F. J. P. C. M., aged 78, male, Caucasian, an artistic painter, without any known pathological history, was admitted in September 1993 with asthenia, adynamia, anorexia, unquantified weight loss, fever and night sweating, with two weeks of evolution. He had no complaints related to the cardiovascular, respiratory, digestive, osteoarticular or nervous systems. There was no relevant personal or family history. Objective examination positively identified a definite hard hepatomegaly, 4 cm below the costal arch, with no superficial venous collateral circulation or splenomegaly. There was no generalized lymph node enlargement.

Analytically, the following were observed at the time of admission: leukocytosis 111700/mm3, hypereosinophilia 58830/mm^3, prothrombin rate 56%, and lactic dehydrogenase, alkaline phosphatase and γ-GT levels were high (*Table I*).

Chest X-ray in posteroanterior and right profile views showed no changes. Echography and CT scan of the abdomen confirmed hepatomegaly, with a mass of 8x7x6 cm in diameter located in the right hepatic lobe (*Fig. 1*).

Given the clinical symptoms, the most likely diagnosis would be a liver abscess. Therefore, after targeted liver biopsy and collection of biological material for further analysis, therapy with ampicillin, metronidazole and netilmicin was begun. However, tests for eggs, cysts and parasites in the feces were negative. The histological and bacteriological tests of the material collected by CT-guided needle biopsy of the liver, as well as serology for Echinococcus, Fasciola hepatica, Schistosoma and Toxocara canis, were negative. The histological test of the collected material in the second liver biopsy, this time performed with a Menghini needle, showed metastatic adenocarcinoma of unknown origin. In view of these results, tumor marker assays were requested, the results of which were within the normal limits (*Table II*). A colonoscopy performed in the Polyvalent Intensive Care Unit (UCIP) showed a stenotic lesion in the middle 1/3 portion of the transverse colon, biopsy of which showed it to be well-differentiated adenocarcinoma.

There was no improvement in the clinical symp-

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TABLE I

Laboratorial tests on admission date

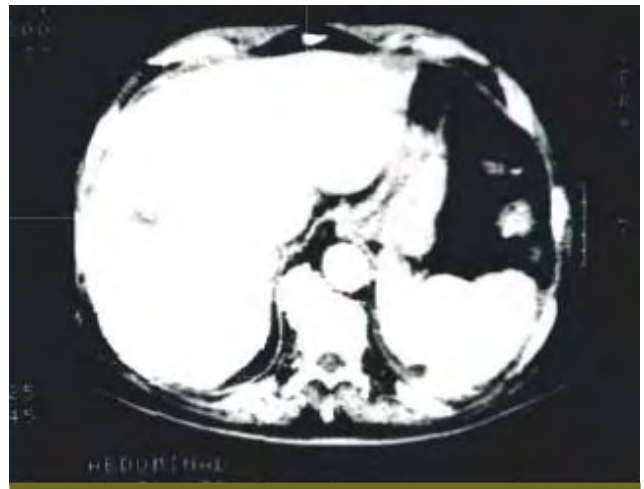
		Unit
Erythrocytes	4630000	mm3
Hemoglobin	13.8	mg/dl
Hematocrit	40.6	%
VGM	87.6	fL
Leukocytes	111700	mm^3
Neutrophils	46620	mm^3
Lymphocytes	4030	mm^3
Monocytes	2220	mm^3
Eosinophils	58830	mm^3
Platelets	246000	mm^3
Prothrombin rate	56%	%
VS	24 mm	1st hour
Alkaline Phosphatase	254	30-90 U/L
ALT	8	0-25 U/L
AST	18	0-29 U/L
γ-GT	207	5-38 U/L
LDH	495	160-320 U/L
CPK	26	15-130 U/L

toms with the therapy administered. On the contrary, on day 6 of hospitalization, the patient presented associated dyspnea at rest and worsening progressively orthopnoea. Eleven days after admission, the patient was transferred to the UCIP for mechanical ventilation and died a month later due to a heart failure.

Discussion

Eosinophils are polynuclear cells characterized by the presence of cytoplasm granulations that stain positively with eosin. Their main function is to act as secretory cells, although they can also act as macrophages.[1,6] Their number may be increased in a variety of situations (*Table III*) [2]. Usually, hypereosinophilia is defined as an increase in eosinophil count of more than 0.5 x 109/L.[1,2]

Allergic diseases are the most frequent cause of hypereosinophilia, especially where there is pulmonary involvement, or side effects due to the use of



CT scan of the abdomen showing a mass in the liver.

FIG. 1

drugs such as penicillin, chlorpromazine, gold salts or rifampicin. A well-established clinical history is, in most cases, diagnostic. In the laboratory test, the hypereosinophilia count was moderate (less than 109/L) and usually accompanied by total serum and/or specific high IgE[2]. In our case, there was no family and/or personal history of atopies; the chest X-ray in posteroanterior and profile views showed no infiltration, and total serum IgE was within the normal parameters.

Parasitic infestations are also a major cause of hypereosinophilia, particularly those associated with tissue invasion in opposition to intraluminal

TABLE II

Tumor markers

		Normal	Unit
Prostatic Acid Phosphatase	2.9	< 3.2	mg/L
Prostate-Specific Antigen	0.8	< 2.5	mg/L
β-HCG	< 2.0	< 5	mIU/ml
Carcino-Embrionary Antigen	1.87	0-4.9	ng/ml
α-Fetoprotein	2.92	1.7-11.8	ng/ml
CA- 19.9	< 2.0	< 37	IU/ml
CA- 125	23	< 35	IU/ml
CA- 15.3	12.7	7.3-19.3	IU/ml

TABLE III

Causes of eosinophilia

ALLERGIC:	**CONNECTIVE TISSUE DISEASES:**
Asthma	Rheumatoid arthritis
Rhinitis	Polyarteritis nodosa
Pulmonary Aspergillosis	Systemic necrotizing vasculitis
Reactions and drugs	Eosinophilic fasciitis
PARASITIC INFECTIONS:	**HEMATOLOGIC NEOPLASMS:**
Strongyloides	Lymphomas
Trichinellosis	Leukemia
Schistosomiasis	**SOLID TUMORS:**
Filariasis	Metastatic mucus-secreting neoplasms
Toxocariasis	**HYPEREOSINOPHILIC SYNDROMES:**
SKIN DISEASES:	Idiopathic hypereosinophilic syndrome
Allergic etiology (drugs, atopic dermatitis ...)	Eosinophilic leukemia
Pemphigus	Löffler's Syndrome

Adapted from Shurin SB. Pathologic states associated with activation of eosinophils.[6]

parasites that are usually accompanied by moderate eosinophilia.[2,6,7] Helminth infestations are, in most cases, secondary. The most significant examples are: Fasciola hepatica, Ascaris lumbricoides, Toxocara canis, Trichinella spiralis and Schistosomiasis. Although it is associated with less pronounced eosinophilia, hydatidosis should also be considered in the differential diagnosis of eosinophilia of parasitic etiology. The patients' history of travel to endemic areas, and their eating habits, are therefore particularly important.[2] In this case, despite the absence of suggestive epidemiology, the clinical symptoms associated with the images revealed by the echography and CT scan of the abdomen suggested a case of liver abscess, a hydatid cyst or, less likely, a secondary or primary neoplastic process of the liver. Subsequent results of the serologies requested for the most common parasites in Portugal, however, eliminated the hypothesis of a parasitic infestation. Also, liver biopsy showed metastatic adenocarcinoma of unknown origin.

Around 0.5% of neoplasms are accompanied by blood eosinophilia, particularly those of hematologic origin,[3,4,8] such as leukemia, lymphomas, and in particular, Hodgkin's disease, T-cell lymphomas and angioimmunoblastic lymphadenopathy.[2,9] Although these neoplasms often occur with massive eosinophilia and immature forms in the peripheral blood, the definitive diagnosis of these conditions is often difficult, even applying cytogenetic studies[2]. Cases of blood hypereosinophilia have been reported with some frequency in myeloproliferative disorders associated with chemotherapy, radiation or secondary to the use of interleukin-2.[3,9,10]

Blood hypereosinophilia associated with solid tumors are extremely rare and, in most cases, these are epithelial mucin-secreting tumors, the most frequent types being bronchial carcinoma and gastric, pancreatic, cervical and colon adenocarcinomas.[1,2,4] Its pathogenesis remains controversial, and various hypotheses are assumed for its origin, such as the release of a substance resulting from tumor necrosis, metastastization to bone marrow or the vagus reflex.[1,2,3] However, the most substantiated and accepted hypothesis in the literature is the production of an eosinophil colony stimulating factor [1,3,4,11]. Their presence is a sign of poor prognosis, probably reflecting the extension and/or spread of the primary tumor.[1,2,3,5] In a series published in 1972 by Viola, 83% of 46 patients with carcinomas associated with blood hypereosinophilia had metastasis in the nodes and/or liver.[12] The presence of peri-tumoral eosinophilia without blood eosinophilia would, however, be a good prognostic factor, especially in tumors of the rectum and colon.[1,2,5]

In our case, the patient had a massive hypereosinophilia and liver metastases. Colonoscopy identified the neoplasm in the early stage. In the literature consulted, only two cases of blood eosinophilia with values above 30000/mm^3 were associated with carcinomas of the colon.[5] As the tumor progresses, many patients develop endomyocardial fibrosis, a factor that contributes to the cause of death. Eosinophilic endomyocardial disease is observed in parasitic infections that occur with massive eosinophilia and affects about 30% of patients with tumors associated with hypereosinophilia.[13]In this case, the appearance of severe heart failure may be related to a case of en-

domyocardial fibrosis. Unfortunately, this hypothesis was not confirmed because the family refused to authorize an autopsy.

Despite its rarity, due to the need to consider solid tumors in the differential diagnosis of hypereosinophilic syndrome, the authors conclude that this case is very enlightening. ■

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