ISSN: 2395-6429

INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH

IJCMPR

Available Online at http://www.journalcmpr.com

DOI: http://dx.doi.org/10.24327/23956429.ijcmpr20170310

RESEARCH ARTICLE

ROLE OF EOSINOPHILS IN ALLERGIC MANIFESTATIONS

GPS Gill., Vikramjeet Singh Gill and RupinderBakshi

Consultant ENT, Patiala, Punjab, India Address for Correspondence A-32 Bank Colony Patiala

ARTICLE INFO

Article History:

Received 20th August, 2017
Received in revised form 13th September, 2017
Accepted 7th October, 2017
Published online 28th November, 2017

Key words:

Eosinophila, HES (Hypereosinophilic Syndrome)

ABSTRACT

Eosinophilia is not an uncommon finding in clinical practice andwhen found in association with other signs and symptoms, can serve as a very useful clue for differential diagnosis. Various underlying disorders and etiologies may cause eosinophilia. Common causes of eosinophilia include helminthic infections, atopic and allergic diseases and adverse drug reaction. This is a brief overview of the causes, practical approach to the diagnosis and treatment of patients with eosinophila.

INTRODUCTION

Eosinophilia is defined as an increase in the peripheral blood eosinophil count. The normal eosinophil count is up to 600/cmm, When the levels go beyond the normal the condition is called as eosinophilia. There is considerable diurnal variation in the eosinophil count which may be as much as 100% . The lowest counts are found in the morning (1000h to 1200h) a time at which endogenous steroids are the lowest and the highest in the midnight (0000h to 0400h). [1,2]

Eosinophils are bone marrow-derived leukocytes whose development and terminal differentiation are under the control of several cytokines (IL-3, GM-CSF and IL-5), with IL-5 being the cytokine that is primarily responsible for eosinophilopoiesis. Eosinophils and neutrophils share a common morphology but the eosinophils are a little larger than the neutrophils and measure 12-17 µm in diameter. They usually have two nuclear lobes and the cytoplasm has distinctive spherical orange granules. The underlying cytoplasm which is usually obscured by granules is pale pink. Eosinophils are predominantly tissue dwelling cells and express a specific chemo-attractant receptor and respond to a specific chemokine, eotaxin. They are moderately effective as a phagocyte for bacteria, yeast and protozoa but less effective than neutrophils.[1]

Eosinophils can kill a wide variety of helminthic worms especially in their larval stages, by depositing cationic proteins on the surface of the parasite.[3] Conventionally eosinophils have been considered as an end-stage cells involved in host protection against parasites. Numerous lines of evidence however have now changed this perspective by showing that eosinophils are pleiotropic multifunctional leukocytes involved in initiation and propagation of diverse inflammatory responses, as well as modulators of innate and adaptive immunity. The circulating life span of eosinophil is 6-12 hrs before it migrates to tissue but unlike the neutrophils it can recirculate and have a much longer life .[4]

Following terms are commonly used

- ***Absolute eosinophil count***-The absolute eosinophil count refers to the number of circulating eosinophils in the peripheral blood (in cells/microL). It is determined by multiplying the total white blood cell (WBC) count by the percentage of eosinophils. Some laboratories report this calculated number directly, while others require the clinician to make the calculation.
- ***Eosinophilia-*** Eosinophilia refers to an absolute eosinophil count in the peripheral blood of ≥500 eosinophils/microL; this is considered abnormal in most laboratories. The degree of eosinophilia can also be categorized as mild (500 to 1500 eosinophils/microL), moderate (1500 to 5000 eosinophils/microL),or severe (>5000 eosinophils/microL).
- ***Hypereosinophilia (HE)***-Hypereosinophiliais defined as an absolute eosinophil count ≥1500/microL> 6 months without evidence of any known cause. End-organ manifestations may be present, but are not

required for the HE designation. When the cause of the eosinophilia is unknown and clinical manifestations are absent, patients with hypereosinophilia are considered to have hypereosinophilia of unknown significance.

- ***Hypereosinophilic syndrome (HES)-*** Hypereosinophilic syndrome (HES) is used to describe a group of heterogeneous clinical syndromes; it does not necessarily imply a primary hematologic or neoplastic disorder.[1,2]

The causes of eosinophilla on the basis of severity are discussed below

Allergic diseases: In industrialized nations, allergic diseases constitute the most common cause of eosinophilla:-

1. ***Asthma:*** Most patients with asthma express eosinophilla at some time during their illness. Higher eosinophil counts are associated with intrinsic rather than extrinsic asthma, both in identifying possible allergens and confirming diagnosis.
2. ***Allergic rhinitis and hay fever:*** Though encountered more commonly in the west, they can give rise to fluctuating eosinophilla.
3. ***Drug allergy:*** The overall incidence of eosinophilla in patients receiving medications is less than 0.1%. Important drug induced reactions associated with eosinophilla are fever, rash, lymphadenopathy, hepatic, renal or cardiac dysfunction.

These drug reactions are symptomatic and need further investigations and prompt management. Some commonly used drugs responsible for drug allergy are: aspirin, penicillin, cephalosporin, nitrofurantoin, sulfonamide, iodides etc [Table-1].

Respiratory diseases: Eosinophilla may be associated with asthmatic respiratory symptoms, together with pulmonary infiltrates detectable on chest films. This syndrome presents a range of diagnostic possibilities, which have been classified as pulmonary eosinophilic syndromes [Table-2].

Parasitic diseases: Parasitic infections, as noted above, represent another common cause of hypereosinophilia that must be investigated in all cases. Although several parasitic disease can cause eosinophilia but the common ones are hookworm and round worm infestations.

Non parasitic diseases: Fungal infections, especially coccidiodomycosis and aspergillosis, may be accompanied by an eosinophilic response. Some cases of scarlet fever, brucellosis, myocardial diseases, cat scratch fever and chlamydial pneumonia also demonstrate eosinophilia. Mycobacterial infection and aspergillosis may be important causes in our country.

Skin diseases: Atopic dermatitis, eosinophilic cellulitis, pemphigoid, dermatitis herpetiformis, and psoriasis may be associated with eosinophilia. In addition, rare skin disorders (e.g vasculitis and granulomatous diseases may be characterized by eosinophilia or marked cutaneous eosinophilic infiltration.

Inflammatory and autoimmune diseases: Eosinophilic cellulitis, pemphigoid, dermatitis herpetiformis and psoriasis may be associated with eosinophilia. In addition, rare skin disorders e.g vasculitis and granulomatous diseases may be characterized by eosinophilia or marked cutaneous eosinophilic infiltration.

Malignant diseases*:* Eosinophilia in neoplasia is rarely severe except with lung cancer and hematologic diseases i.e Hodgkins disease, non Hodgkins lymphoma, acute leukemia. In lymphoid tumors, eosinophilia may even precede the diagnosis by one year [Table-3].

Hypereosinophilic syndrome: Some patients remain without diagnosis after all possible causes of eosinophilia have been investigated. In such cases a possibility of hypereosinophilic syndrome must be considered. The most dramatic hyper-eosinophilic syndromes (50,000- 1,00,000/cmm) are :- (a)Tropical pulmonary eosinophilia (b)Idiopathic hyper eosinophilic syndrome (c)Loeffler's syndrome (d)Loeffler's endocarditis(e)Eosinophilic leukemia.

Tropical pulmonary eosinophilia is a classic example of occult filiariasis and predominantly affects adult males. The syndrome is characterized by nocturnal, paroxysmal cough, hyper-eosinophilia (AEC 3,000-50,000/cmm) and elevated ESR. More than half such patients have constitutional symptoms e.g fever, weight loss, night sweats etc. cardiopulmonary disfunction is a major cause of morbidity and mortality in this syndrome. The levels of eosinophils are not related to the severity of symptoms. 15% of individuals with this ailment have extra pulmonary manifestations in the form of mild- moderate splenomegaly, lymphadenopathy and hepatomegaly. Chest X-ray shows diffuse miliary lesions or increase in bronchovascular marking and serology shows high titers of filarial antibodies. If untreated the condition may progress to chronic pulmonary fibrosis.

Idiopathic hyper-eosinophilic syndrome*:* It is a heterogeneous group of disorders characterized by prolonged idiopathic eosinophilia, tissue infiltration and organ system dysfunction. The bone marrow, heart, central nervous system, gastro intestinal tract, lungs, kidneys and skin may be involved to variable extent. Glucocorticoids, hydroxyurea and interferon-alpha have been used successfully for the treatment.

Eosinophilic gastroenteritis: It is characterized by infiltration of any part of the gastrointestinal tract. It affects both the sexes and usually presents in the 3rd to 5th decade. 20% of the patient may not have peripheral eosinophilia. When the disease involves predominantly the mucosa, patients may present with nausea, vomiting, malabsorption, and protein loosing enteropathy.

Eosinophilic leukemia: The diagnosis of Eosinophilic Leukemia is based on the presence of an increased number of immature eosinophils in blood and bone marrow. The clinical course is similar to others leukemia.[4,5]

Table 1 Parasitic Causes For Raised Eosinophil Count

- Strongyloidiasis: Strongyloidesstercoralis
- Liver fluke: Fasciola hepatica
- Hydatid disease: Echinococcusgranulosus.
- Filariasis: Wuchereriabancrofti, Onchocerciasis, Brugiamalayi, Loa loa.
- Schistosomiasis: S. hematobium, S. mansoni, S. japonicum

Table 2 Drug Induced Allergies and Raised Eosinophil Count

- Aspirin
- Gold compounds
- Allopurinol
- Nitrofurantoin
- Sulfa agents
- Non steroidalanti inflammatory agents
- Bleomycin
- Methotrexate
- Tolbutamide
- Semi synthetic penicillins

Table 3 Neoplastic Disorders That May Be Accompanied By Raised Eosinophil Count

- Myelodysplastic disorders
- Myeoproliferative disorders
- Malignant histiocytosis
- Systemic mast cell disease
- Carcinoma (lung, colon, pancreas, cervix)
- Plasma cell dyscrasias
- Lymphoma (Hodgkins, angioimmmunoblastic adenopathy with dysproteinemia)
- Leukemias (acute lymphoblastic, acute myelomonocytic, T-cell leukemia/lymphoma, chronic granulocytic eosinophilic leukemia)

Diagnostic Approach to A Case of Eosinophilia

History: A detailed history and physical examination of of the patient with reference to allergic symptoms such as rhinitis, skin, gastrointestinal, respiratory sypmtoms (cough, dyspnea, wheeze), history of any worm infestation and history of any drug intake. Use of supplements, herbal preparations, vitamins and steroids in the past is also to be obtained.

General and systemic examination*:* with special attention paid to skin, soft tissue, lungs, liver and spleen.

Investigations: The investigations include the following

(i) Complete blood count (CBC) and absolute eosinophil count (AEC).
(ii) Stool examination: For ova and parasites of Strongyloides, Hookworm, Fasciolopsisbuski and Clonorchissinensis. At times in cases of mild infestation multiple stool examinations may be required.
(iii) Serological tests: May be required for aircrew with tissue or blood-dwelling helminthic infections especially when the stool examination is negative. These include Trichinella, Echinococcus, Wuchereriabancrofti, Toxocaracanis and Schistosoma.
(iv) Urine sedimentation: For suspected Schistosoma haematobium and in the setting of chyluria due to Wuchereriabancrofti.
(v) Sputum analysis: For suspected pulmonary infection with Strongyloides or Paragonimus.
(vi) Studies to assess organ function: liver, renal & pulmonary function tests, urinalysis, chest radiograph, and electrocardiogram may be required in a few cases.
(vii) Cystoscopy: Aircrew, who frequent visit Africa and have eosinophilia with haematuria, should have their urine examined for the eggs of Schistosoma haematobium. At times to establish the diagnosis a cystoscopy may be required
(viii) If the constitutional symptoms are severe and eosinophilia is persistent, one must aggressively search for occult malignancy. In such cases at times bone marrow aspirates and biopsies may be required to assess fully the nature of the process. CT chest and abdomen to uncover lymphadenopathy or organ tumors and be suitably managed.[7]

Management of Eosinophilia

Primary eosinophila does not require any treatment, mostly the cases of secondary eosinophilia are treated on the basis of their underlying causes. Allergic manifestations are treated with corticosteroids. A group of physicians stick to the policy of using antihelminthic drugs on the basis cost effectiveness. Newer drugs are there to treat different manifestations caused by eosinophila [Table-4]. A follow up total leukocyte count with differential count after 1 to 3 months is indicated to ascertain that eosinophilia has resolved. But if the results of all investigations are negative and AEC> 1500/mm3 persists for more than 6 months, patient is diagnosed as having idiopathic hypereosinophilic syndrome. Antihelminthic drugs and eosinophil count may be repeated after 1 to 2 months to see the response.[9,10]

Table 4 Management of Eosinophilia

Manifestations In Eosinophilia	Choice of Treatment
Allergic manifestations	• Anthelminthic drugs and Corticosteroids
Primary eosinophilia without organ involvement	• No treatment only cardiac functions should be evaluated.
Systemic treatment of primary eosinophilia with organ involvement initially	• Corticosteroids, and interferon (IFN)-alpha for steroid-resistant disease. • For long-term maintenance regimens to control organ involvement, include Chlorambucil, Hydroxyurea, Vincristine, Cytarabine, Etoposide and Cyclosporine
In Hypereosinophilic syndrome(HES)	• Treatment with antibodies and antibody-based agents (eg, mepolizumab, alemtuzumab, brentuximab vedotin)
In refractory cases	• Tyrosine kinase inhibitors (eg, imatinib , and monoclonal antibodies are being studied. • Nonmyeloablative allogenic hematopoietic stem cell transplantation (HSCT) can also be considered

CONCLUSION

In conclusion, diagnosing and treating a patient with eosinophilia is great a challenge for the clinicians. Hypereosinophilia needs thorough investigations and meticulous treatment. Appropriate medicine depends on accurate diagnosis and the need for clinical urgency for introducing an eosinophil-lowering agent. Advances in understanding the pathogenesis of HES variants have resulted in improved outcome.

References

1. Rothenberg ME. Eosinophilia. *N Engl J Med* 1998;338:1592-1699
2. Spry CJ. Eosinophilia and allergic drugs. *ClinHematol*1980 ; 9: 521-34
3. Wardlaw AJ. Eosinophils in the 1990s: New prespective on their role in health and disease. *Postgrad Med J* 1994;70 (826):536-52.
4. Weller PF. The immunobiology of eosinophils. *N Engl J Med* 1991; 324(16): 1110-8
5. Teo CG, Singh M, Ting WC. Evaluation of the common conditions associated with eosinophilia. *J ClinPathol* 1985; 38 (3): 305-8.

6. Jameson MD, Segraves SD. Idiopathic hypereosinophilic syndrome. *Postgrad Med* 1988;84:93-101.
7. putterman C, Ben- Chetrit E, clinical problem solving: testing, testing, testing. *N Engi J Med* 1995; 333;1208-11.
8. Libman, MD, MacLean, JD, Gyorkos, TW. Screening for schistosomiasis, filariasis, and strongyloidiasis among expatriates returning from the tropics. *Clin Infect Dis* 1993;17:353
9. Muennig, P, Pallin, D, Sell, RL, Chan, MS. The cost effectiveness of strategies for the treatment of intestinal parasites in immigrants. *N Engl J Med* 1999;340:773.
10. MichaelannLiss, Emmanuel C Besa .Eosinophilia treatment and management. *Drugs & Diseases*. Updated Nov 21,2016.

****