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(REVIEW ARTICLE)

Diagnosis and treatment of eosinophilia

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Abstract

Eosinophilia is frequently seen being the basis of various pathologies in the body. Eosinophilia is a condition when the blood count is raised to more than 500 per microliter; however it can vary from mild to severe. Idiopathic hypereosinophilic syndrome has been found to be a cause of moderate to severe eosinophilia. Improvement in treatment depends on the cause of the rise in count. This review will make the approach to diagnose the cause and treatment accordingly.

Keywords: Peripheral Blood film; Eosinophil count; Idiopathic

1. Introduction

Eosinophilia is a common finding in the patients coming for treatment in OPD [5, 6,7]. They come for treatment of diseases with various signs and symptoms. For management of such patients, the differential diagnosis of eosinophilia becomes critical [4]. Most laboratories have an accepted upper limit of normal for blood eosinophilia that varies somewhat, but is generally below 500 eosinophils per microliter of blood. The degree of eosinophilia associated with different conditions can be characterized as mild, (500–1500 eosinophils per microliter), moderate (1500–5000 eosinophils per microliter), or severe (greater than 5000 per microliter). The term hypereosinophilia refers to eosinophil levels above 1500. Most diseases are associated with levels between 500–1500. More significant hypereosinophilic syndromes and other significant causes can cause moderate or severe eosinophilia. Peripheral eosinophilia can be divided into categories of primary, secondary and idiopathic [4]. Primary eosinophilia usually occurs in the context of hematologic malignancies and myeloproliferative disorders, including acute or chronic myeloid leukemia, and a variety of other proliferative conditions with eosinophil counts usually greater than 5000/µl. Secondary eosinophilia is associated with many other conditions. Many infectious causes can cause secondary eosinophilia that can be of the moderate to severe level. In addition, a variety of diseases including most prominently allergic disorders, drug allergy, autoimmune diseases, endocrine disorders such as Addison's disease, and many different cancers can be associated with eosinophilia. Finally, idiopathic eosinophilia is associated with a diagnosis of the hypereosinophilic syndrome (HES), in which moderate to severe eosinophilia is associated with none of the primary or secondary causes of eosinophilia, and no other diagnosis of secondary eosinophilia can be discerned.

Table 1 Degrees of eosinophilia

Severity	Level (Eos/ul)	Differential Diagnosis
Mild	500–1000	allergic diseases, atopy, asthma, drug, allergy, bacterial and viral infections
Moderate	1500–1500	Parasitic infection, HES Churg-Strauss Syndrome, cancers, Sezary's Syndrome
Severe	>5000	HES, eosinophilic leukemia, myeloproliferative disorders, and cancer

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2. Disorders and Eosinophils

Numerous conditions can cause eosinophilia. It is called peripheral eosinophilia if the count is 500 per microliter, but it is subject to variations. Idiopathic hypereosinophilic syndrome is encountered in mild to severe pathologies. Understanding of basic knowledge is must. In this article we will study the details of various syndromes found in eosinophilia. Allergy is accompanied by eosinophilia invariably [1, 2, 3]. It is associated with a variable varieties of signs and symptoms. So differential diagnosis is must in all the pathologies [4].Most of the times the upper limit of normal count to various conditions, but is below 500 eosinophils/ml of blood. The different conditions can vary, mild, (500–1500 eosinophils/ml), moderate (1500–5000 eosinophils/ml), or severe (greater than 5000/ml). Hypereosinophilia is called if eosinophilic count is above 1500. The count varies between 500– 1500. Most of the times significant eosinophilia causes can cause moderate to severe eosinophilia. Peripheral eosinophilia can be divided into primary, secondary and idiopathic types [4]. Primary type is seen in hematologic malignancies and myeloproliferative disorders, chronic myeloid leukemia, and a variety of other proliferative conditions with eosinophil counts usually greater than 5000/µl. Secondary is seen in various other conditions. In cases of secondary eosinophilia count can be moderate to severe level. In case of allergic diseases, drug allergy, autoimmune diseases, endocrine disorders such as Addison's disease, and many lots of others are associated with eosinophilia. Hypereosinophilia syndrome (HES) is seen in which moderate to severe eosinophilia seen in primary to severe types, and no diagnosis of secondary eosinophilia can be decided. Often it relates to the eosinophilic to be stimulated from bone marrow precursors under the influence of cytokines and eosinophil hematopoietins. But they are only related to rise in levels of Interleukins IL-3, IL-5, and Granulocyte Macrophage Colony Stimulating Factor (GMCSF) [8]. And these cytokines activate bone marrow precursors, the eosinophils can be found in a variety of tissues in host defense or tissue returning to cell damage. This defines the response which is seen in hypereosinophilia[2,3] The most prominent are cases of allergic diseases like common ones as allergic rhinitis and conjunctivitis, asthma, eosinophilic esophagitis, eosinophilic gastroenteritis, and atopic dermatitis. Most of the times it is related to primary eosinophilic gastrointestinal disorders accompanied by IgE mediated allergic, and these eosinophilic diseases can be associated any type of eosinophilia. Autoimmune diseases can be seen under some circumstances [9]. These would include GI diseases such as primary billiary cirrhosis and lupoid hepatitis, systemic lupus, and a variety of vasculitides. In these chronic skin diseases including pemphigus and pemphigoid have been detected with eosinophilia [5,6]. By far the most common source of moderate to severe eosinophilia involves infectious diseases such as malaria, pseudomonas, borrelia infection including lyme disease and tissue infection with helminthic infestations including schistosomiasis Fungal infection can also be seen in eosinophilia. Although other syndromes with abnormal T cell responses can be seen with eosinophilia, including graft vs. host disease and some immunodeficiences such as hyper IgE syndrome, but eosinophilia contribution to the hyper IgE syndrome is not take into considered with varied major dysfunction. Drugs are associated with moderate or severe eosinophilia. The fatal cases are part of drug reactions which are associated with eosinophilia having systemic symptoms or Drug Rash with Systemic Eosinophilia (DRESS) syndrome. DRESS reactions can be are often with anti-convulsants, anti-epileptics, sulfonamides, allopurinol, nonsteroidal anti-inflammatory drugs, and a range of antibiotics. T cells seem to mechanism [5].

3. Hypereosinophilic Syndrome

The hypereosinophilic syndrome (HES) is a fatal condition of moderate to severe eosinophilia [6,7,8,9]. The hypereosinophilic syndrome is associated with marked peripheral eosinophilia and involvement of multiple organs including the heart, GI tract, lungs, central nervous systems, and kidneys. Majority remains idiopathic, and rest are associated with aberrant Th2 lymphocyte activation. Rest is associated myeloproliferative disorders and even leukemia. HES associated with chromosomal abnormalities resulting in constitutive activation of FIP1L1receptor tyrosine kinase, is of critical importance because it is associated with response to kinase inhibitors such as imatinib. At the outset the preliminary effect is to repeat the eosinophil count is estimated two, and up to four weeks after initial observation in those whose eosinophilia is not easily explained. A continuous watch is done in the pathologies which are related with mild, moderate or severe eosinophilia. In some pathologies there is intense evaluation, even when chromosomal study is carried out. Treatment depends on etiology and level of eosinophilia. The level of modified underlying disorder is revealed. Autoimmune diseases are caused by primary autoimmune disorders. This is seen in cases of hold for immunodeficiency or infection. For patients with HES with the FIP1L1 genetic translocation treatment with imatinib should be initially considered. For very sick cases steroids are frequently given. Interferon alpha and other potential cytotoxic drugs such as hydroxyurea are necessary which is accompanied by severe hypereosinophilia. Finally, experimental treatment with anti-IL is carried out in asthma, as well as in the treatment of primary hypereosinophilia. This has resulted in significant success in terms of prevention of exacerbations of the underlying disease, as well as reduction in steroid dose required for the treatment of the primary and/or secondary cause of eosinophilia [4,5] .

Table 2 Biology of Eosinophilia

Origin	Bone Marrow derived myeloid cell development driven by cytokines IL-3, IL-5, and GMCSF
Tissue Distribution	Widespread, primarily epithelial and subepithelial tissues, responsive to chemokines for movement and adhesion
Functions	Host Defense and Tissue Remodeling
Factors/Product	Cationic Proteins – (MBP, ECP, EDN, EPO) Cytokines, Chemokines, PAF, Prostaglandins Leukotrienes

Table 3 Treatment of Eosinophilia

Treat underlying disorders as primary treatment
For HES
Steroids
Interferon alpha
Hydroxyurea
Imatinib
Anti-IL-5 (Mepolizumab, Reslizumab)
Anti-IL-5 receptor (MEDI-563)

4. Approach to Treatment

Many Stastical processes and various organizations with eosinophilia and hypereosinophilia have tried to analyze the disease. Initially chronic hypereosinophilia syndrome would have to repeat the eosinophil count within two, and to four weeks after initial finding in patients in whom eosinophilia is persistent and couldn't explain.. Attention needs to be paid to all of the diseases depicted above and their potential associations with mild, moderate or severe eosinophilia. Under certain conditions more intense evaluation, including chromosomal count, for the underlying disease needs to be intensely observed. Treatment depends on suspected etiology and level of eosinophilia.

5. Conclusion

The level depends on correct treatment of the underlying disease. If an autoimmune disease is found, appropriate treatment of basic autoimmune disease is carried out. This also includes immunodeficiency or infection. For patients with HES with the FIP1L1 genetic disease treatment with imatinib should be started. For those without the translocation, steroids are the mainstay of treatment. Interferon alphas as well as the cytotoxic drugs such as hydroxyurea are given in intense cases. In terminal cases treatment with anti-IL 5 is given along with secondary diseases including asthma, as treatment of primary hypereosinophilia. This has been extremely useful in terms of prevention of exacerbations of the underlying disease, as well as reduction in steroid dose required for the treatment of the primary and/or secondary cause of eosinophilia.(3,4).

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