Letter to the Editor

Recent advances, eosinophils, eosinophilia and hypereosinophilic syndrome

To the Editor,

I read with interest a recently published review titled "In the light of recent advances: eosinophils, eosinophilia and idiopathic hypereosinophilic syndrome" written by Yildiran and Ikinciogullari in the last issue of Turkish Journal of Hematology[1].

Eosinophils are derived from hematopoietic stem cells that are committed initially to the myeloid and subsequently to the basophil-eosinophil granulocyte lineage. The mature eosinophil, when examined by standard blood-staining techniques, displays a bilobed nucleus and an abundant cytoplasm filled with reddish-orange granules. The material in these granules includes cationic proteins (major basic protein, eosinophilic cationic protein, eosinophil-derived neurotoxin, eosinophil peroxidase), cytokines (interleukins, tumor necrosis factor), and lipid mediators (leukotriene C_4)[2]. Interleukin 5 is considered the major eosinophil growth and survival factor, whereas chemokines (eotaxin, platelet-activating factor, RANTES (regulated on activation, normal T expressed and secreted) and endothelial adhesion molecules (integrins, vascular cell adhesion molecules) contribute to eosinophil trafficking[3]. They are the primary mediators of eosinophil-associated toxicity to microbes (parasites, protozoa, bacteria, viruses) and human tissue (myocarditis, pneumonitis, dermatitis, neuropathy, vasculitis). Blood eosinophilia (absolute eosinophil count (≥ 600 cells/μL) is the usual initial clue for the presence of an eosinophilic disorder[4].

Firstly; this review may be inadequate for evaluating eosinophilia in adults. Because of some disorders in article had not clarified such as sarcoidosis, rheumatoid arthritis, angioimmunoblastic lymphadenopathy, angioimmunoblastic lymphoid hyperplasia, Sjogren syndrome, eosinophil myalgia and toxic oil syndrome. The history is the most important part of the evaluation for blood eosinophilia, and it should guide the extent and type of laboratory tests performed. Are there an international travel history and and recent medications? It should be replied. If there is no any drug use, a stool test should be performed in all cases to look for ova and larvae of intestinal worms. Then, depending on the travel history, the following tests and procedures should be performed: urine sediment tests (schistosoma), blood concentration tests (filaria), serology (strongyloides, filaria, trichinosis, visceral larva migrans, schistosomiasis), sputum examination (paragonimiasis, visceral larva migrans), chest radiography (paragonimiasis, ascariasis), computed tomography (echinococcus, cysticercosis), small bowel biopsy (isosporiasis, strongyloidosis), or muscle biopsy (trichinosis)[2]. All patients with suspected primary eosinophilia should undergo bone marrow examination with cytogenetics. The following PDGFRB rearrangements currently are detected by conventional cytogenetics: t(5;12)(q33;p13), t(5;10)(q33;q21), t(5;7)(q33;q11.2), t(5;14) (q33;q13), t(5;17)(q33;p11), and t(1;5) (q23;q33). Standard cytogenetic methods do not detect the usual PDGFRA rearrangement that is a result of an interstitial 4q12 deletion. This must be sought with either a fluorescence in situ hybridization (FISH)-based or a reverse transcriptase polymerase chain reaction-based laboratory technique[4].

As second point; management to idiopathic hypereosinophilic syndrome (IHES) is very important and some questions must be remembered for IHES according to Chusid et al.[5] 1: blood eosinophilia exceeding

1.500/mL for more than six consecutive months with signs and symptoms of hypereosinophilic disease; 2: absence of an underlying cause of hypereosinophilia despite extensive diagnostic evaluation; and 3: organ damage or dysfunction as a result of local release of the toxic contents of eosinophils. The diagnosis of the IHES is essential exclusion of secondary eosinophilias. The two broad groups of non-idiopathic eosinophilia are: 1. Clonal eosinophilic disorders, including eosinophil leukaemias, and 2. reactive eosinophilias. When these two broad groups are excluded and criteria 1 and 2 have been fulfilled, a diagnosis of HES can be made[6].

Finally; the clinical course of IHES may differ in adults from child. Because of pediatric cases with IHES has only a slight male predominance versus a male:female ratio of 9:1 in the adult and they have more commonly with fever, arthralgias, and rash versus fatigue, cough, and dyspnea in adult patients. Cardiovascular system involvement is mainly cause of morbidity and mortality, in adults. Pediatric HES has been associated with acute leukemia, especially acute lymphoblastic leukemia[6]. The abnormal fusion of the FIP1L1 and PDGFRA genes had identified in some adult patients with IHES while no pediatric case with the FIP1L1-PDGFRA fusion gene has been reported to date. Therefore treatment of IHES is different in adults and child. Therapy with imatinib mesylate is pharmacologically suitable for patients with the FIP1L1-PDGFRA gene while imatinib mesylate is usually no effective in pediatric IHES. Other treatment modalities except of imatinib mesylate should be preferred in cases with pediatric IHES[7,8].

According to these views; the causes of eosinophilia and clinical findings and pathogenesis and treatment of IHES in adults and children are different. Therefore, I believe that eosinophilia and IHES in adults and children should be evaluated distinctly.

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Response

We appreciate authors interest in our review article[1]. First, we would like to mention our contribution to the literature with a letter addressed to Katz et al.[2] regarding differences between adult and pediatric types of idiopathic hypereosinophilic syndrome (IHES). Based on their case report and review of the literature; their patient should have received imatinib therapy as the first choice. We pointed out that imatinib should be

the first choice when FIP1L1-PDGFRA fusion (F/P) is present or as a therapeutic trial in the presence of features of myeloproliferative disease. We believed that Katz et al. should have emphasized these points[3]. Secondly, there was no report in the literature, confirming adult versus pediatric IHES differentiation on a laboratory basis. Only recently, Rives et al. reported a child with F/P rearrangement[4].

Unfortunately, we cannot agree on other criticisms by the author. A careful review of our article would have answered his points. A focused history, related disorders, travel history and laboratory investigations are given in Table 2 of our review. Conventional and advanced cytogenetic analyses are stated in Table 3. Also, as appeared in Table 4, imatinib is the first choice when F/P is present, otherwise glucocorticoids and interferon alpha are the drugs of choice especially in lymphocytic variant at the present time. Despite the fact that the review by A. Tefferi[5], appeared on Pubmed database after we submitted the present review, our therapeutic options are in the same line with his management algorithm.

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