CASE REPORT

Hypereosinophilia in a Young Patient: Occam's Razor or Hickam's Dictum?

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Abstract Hypereosinophilia is an uncommon clinical problem encountered in hematology practice. While most of such cases are secondary or reactive, a significant fraction of cases are due to clonal myeloproliferative disorders. We report a young patient who presented with marked hypereosinophilia and was investigated extensively for its cause. Finally a common tropical infection was responsible for such marked eosinophilia fulfilling the principle of Occam's razor. The case emphasizes the need to search for treatable reactive causes even in presence of marked hypereosinophilia in a tropical country.

Keywords Marked hypereosinophilia · Giardiasis · Occam's razor · Myeloproliferative disorder

Introduction

Hypereosinophilia is an uncommon condition and has large list of differential diagnosis. The common conditions that can cause hypereosinophilia are helminthic infestations, environmental allergens and drug reactions. We present here a young patient who presented with hypereosinophilia and proved the principle of Occam's razor.

Case Summary

A 32-year-old male, presented with intermittent high grade fever with rigor and chills of 3 months duration. The patient

also had history of nocturnal cough but no expectoration. He denied history of any breathlessness, abdominal pain or distension and appetite or weight loss. He smoked cigarettes for past 2 years and his smoking score was 4 pack-years. General physical examination was unremarkable. Respiratory system examination revealed bilateral polyphonic wheeze. There was no hepatosplenomegaly. Cardiovascular and neurological examination was normal. With this presentation, a possibility of chronic infection e.g. pulmonary tuberculosis was kept. A chest X-ray was unremarkable and Mantoux test was negative. Complete blood count showed hemoglobin of 162 g/L, white cell count of $51.8 \times 10^9/L$ and differential count showed 81 % eosinophils. Platelet counts were $156 \times 10^9/L$. On direct questioning, patient denied any history of itching on the skin, swelling of feet or scrotum, past history of bronchial asthma or promiscuous sexual activity. There was no peripheral neuropathy on examination. Patient was investigated for causes of hypereosinophilia.

Peripheral smear examination after diethyl carbamazine citrate (DEC) stimulation and antigen test for microfilaria were negative. In view of respiratory symptoms with eosinophilia, a possibility of allergic bronchopulmonary aspergillosis was considered; serum Ig-E was more than 10,000 U/mL but aspergillus skin test was negative. Chest X-ray was normal and spirometry showed mild restriction (FVC = 78 % predicted, FEV1 = 73 % predicted, FEV1/FVC = 0.77). Contrast enhanced computed tomography scan of chest revealed patchy areas of consolidation with ground glass opacities and air bronchogram in both lungs predominantly in the lower lobes. Tuberculin skin test was non-reactive. Anti-nuclear antibody and anti-neutrophil cytoplasmic antibody (ANCA) were negative. 2-D echo showed left ventricular ejection fraction of 62 % and no evidence of diastolic dysfunction. Finally a bone marrow

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examination was done to rule out myeloproliferative disorder (MPD). Bone marrow trephine biopsy showed mildly hypercellular marrow spaces with an excess of eosinophils (43 %) and no evidence of MPD.

Meanwhile stool examination showed numerous cysts of *Giardia duodenalis*. Considering the rare association of giardiasis with hypereosinophilia, patient was administered oral metronidazole 15 mg/kg body weight/day in three divided doses (06.02.2013) for 7 days. After starting metronidazole, the leukocyte count fell drastically with reduction in absolute eosinophil count (Table 1). A repeat stool examination done 7 days later did not show any cysts of *Giardia*. The patient became afebrile and his cough improved dramatically. Patient was discharged and on follow up visit after 1 month his TLC and AEC had normalized.

Discussion

Hypereosinophilia is defined as an absolute eosinophil count of $>1.5 \times 10^9/L$ as this level is thought to correlate with risk of tissue infiltration by eosinophils and end organ damage. Common causes of eosinophilia are ‘reactive’ to a stimulus inducing interleukin-5 (IL-5) release. These include helminthic parasitic infestations (filarial worms, intestinal helminthes, *Toxocara* spp), drugs and environmental allergens. Reactive eosinophilia can also occur with asthma but eosinophilia with asthma should prompt consideration of allergic bronchopulmonary aspergillosis and eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome). Sinister causes include adenocarcinomas, Hodgkin disease,

some T cell lymphomas and acute myeloid and lymphoblastic leukemias [1]. When reactive causes are not found patient is thought to have hypereosinophilic syndrome (HES). This heterogeneous group of disorders include two distinct subsets- clonal proliferation of myeloid cells associated in most cases with presence of FIP1L1-PDGRFA transcript called M-HES, and some cases of polyclonal hypereosinophilia due to deregulation of T-lymphocytes named L-HES. In majority of HES, exact cause is not known and is grouped under idiopathic HES [2, 3]. Idiopathic HES may be associated with arteriovenous thrombosis and eosinophilic vasculitis [4].

Reactive hypereosinophilia is a protective mechanism against intestinal nematode infestations and microfilarial infections. Parasites which invade tissues elicit a T-helper 2 mediated immune response with production of IL-5. It acts pleiotropically to cause eosinophilic inflammation. *Giardia duodenalis*, since it does not invade tissues, was previously considered as being unable to produce eosinophilia. However eosinophilia has been documented in giardiasis recently [5]. One study showed that patients with eosinophilia and intestinal giardiasis when compared to those with only eosinophilia and no intestinal parasitic infestation, had higher levels of IL-5 in serum and their peripheral blood mononuclear cells when stimulated with a mitogen, produced higher levels of IL-5 [6]. Excretory and secretory antigens of giardia in experimental animals induce a preferential TH-2 mediated response with IL-5 production, resulting in eosinophilia and intestinal mucosal eosinophilic infiltration [7].

The first report of an association of *G. duodenalis* infestation with marked and symptomatic hypereosinophilia

Table 1 Investigations

	28.1.2013	08.02.2013	12.02.2013	15.02.2013	16.03.2013
Hemoglobin (g/L)	162	13.5	14.7	13.8	14.3
Platelet count ($\times 10^9$ cells/L)	156	133	224	274	210
Total leukocyte count ($\times 10^9$ cells/L)	51.8	29.6	19.1	9.8	9.8
Polymorphs (%)	4	4	11	37	57
Lymphocytes (%)	14	5	10	17	32
Monocytes (%)	1	1	1	1	2
Eosinophils (%)	81	90	78	45	9
Absolute eosinophil count (AEC) ($\times 10^9$ cells/L)	41.96	26.64	14.90	4.41	0.88
MCV (fL)	90				
RDW	13.5	ESR (mm at 1 hour)	04	Serum vitamin B-12	315.4 pg/mL (187–1059)
			06.02.2013		13.02.2013
Stool microscopic examination					
<i>Giardia duodenalis</i> cysts		++			Absent

was of a boy who presented with acute gastroenteritis and hypereosinophilia [8]. Later, *Giardia* infection was documented to have produced marked hypereosinophilia in a patient with eosinophilic granulomatosis and polyangitis whose eosinophilia responded to oral metronidazole therapy. The authors postulated that hypereosinophilia was likely due to interactions between endogenous and exogenous eosinophilopoietic stimuli [9].

Marked leukocytosis with eosinophilia with systemic symptoms mimicking a MPD as seen in our patient has been reported twice. One involved a 9 year old male from Pakistan presenting with high fever and abdominal discomfort and the second an 88 year old female with shortness of breath, dysphagia and skin rash. Both these cases were initially mistaken for eosinophilic leukemia, but routine work up to rule out reactive etiologies revealed the association. Both were cured with oral metronidazole alone [10, 11].

Cases have also been reported where localized organ involvement by eosinophils in the form of eosinophilic pulmonary infiltrates, eosinophilic pleural effusion or synovitis resembling septic arthritis occurred in association with *G. duodenalis* infestation. These cases also improved with short courses of metronidazole, indicating a possible causative role [12–14]. Giardiasis may present with dermatological manifestations alone such as a lichen planus like eruption with eosinophilic inflammation in the dermis and erythema nodosum [15, 16].

In support of Occam's razor, reactive causes of hypereosinophilia must be considered foremost in tropical countries before considering other causes. *Giardia duodenalis* infestation is an easily remediable cause of symptomatic hypereosinophilia. Meticulous stool examination for *Giardia* cysts should be performed in all patients with suspected hypereosinophilic syndrome. If the stool examination is negative and the patient has abdominal symptoms, the physician may be justified in performing a gastroduodenoscopy to rule out giardiasis. Serological diagnosis may be useful in some cases as an adjunct to stool examination. This may be carried out in stool samples as well as blood.

Nitroimidazoles such as metronidazole and tinidazole are effective agents for eradicating giardia infestations. Recalcitrant cases may be managed with nitazoxanide. Appropriate control of environmental factors, hand hygiene and decontamination of food and water must be reinforced in all cases.

Conclusion

Hypereosinophilia is associated with several conditions. Before resorting to exotic investigations, common condi-

tions causing hypereosinophilia must be kept in mind applying Occam's razor. The diagnostic clue sometimes lies in doing a simple investigation like stool examination for parasites in patients presenting with hypereosinophilia and this can avoid unnecessary expensive investigations. Our case highlights the fact that so called simple or routine investigations should never be ignored while investigating for an uncommon condition.

Conflict of interests The authors have no conflicting interests to disclose.

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