

Eosinophilia and HIV

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Proud member of the MWAETC ECHO HIV family

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Disclosures

Sadly, no conflicts or disclosures to report

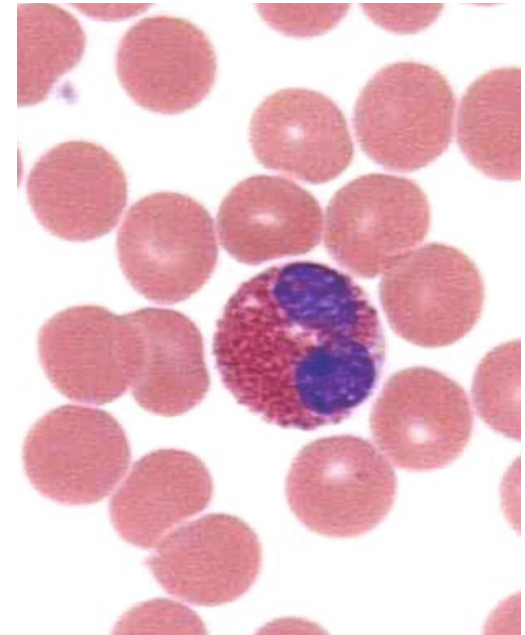
Eosinophilia and HIV

Outline

- The eosinophil
- Conditions associated with eosinophilia
- How does HIV modify this
- Proposed evaluation of eosinophilia in patients with HIV

Eosinophilia

- Within the granulocyte line, have a t1/2 in the blood of 8-18 hours
- Most eosinophils reside in tissues where they can persist for weeks
- Functions
 - Antigen presentation
 - Cytokine expression
 - Degranulation responses to helminths and parasites
 - Homeostatic immune responses
 - Granules contain: Major Basic Protein, Eosinophil Cationic Protein, Eosinophil peroxidase and Eosinophil Derived Neurotoxin
- Eosinophilia: An absolute eosinophil count > 450 – 500 cells/uL or a percent > 5%



Eosinophilia – Categories of Conditions

- Allergic sensitization (eosinophils typically < 1500 cell/uL)
- Parasites and other infections
- Autoimmune disease
- Primary hypereosinophilic syndromes
- Malignancies
- Immunodeficiency syndromes
- Miscellaneous conditions

Eosinophilia: causes

- Allergic Sensitization (eosinophils typically < 1500 cell/uL)
 - Allergic rhinitis and asthma
 - Atopic dermatitis
 - Chronic sinusitis – polypoid type with ASA sensitivity
 - Allergic bronchopulmonary aspergillosis (ABPA)
 - Chronic eosinophilic pneumonia (BAL $> 40\%$ eosinophils)
 - Drug allergy including DRESS (fever, hepatitis and adenopathy): most common: antibiotics, anticonvulsants, ARVs (nevirapine and efavirenz), allopurinol, NSAIDs

Eosinophilia: causes

Parasite and Infection Related: Helminths, Protozoa, Fungi and Viruses

- Tissue dwelling & skin burrowing: Yes. Luminal only (tape worms, protozoa) & intact cysts (hydatid cyst and neurocysticercosis): No

Nematodes	Filaria	Flukes	Protozoa	Fungi & Viruses
Angiostrongyliasis	Tropical pulmonary eosinophilia	Schistosomiasis	Isospora belli	Coccidioides
Ascariasis	Loiasis	Fasciola	Dientamoeba	Histoplasma (adrenal insuff)
Hookworm	Onchocerciasis	Clonorchis	Sarcocystis	Cryptococcus
Strongyloides		Paragonimiasis		Aspergillus (ABPA)
Trichinella				
Toxocara (VLM)				HTLV-1
Gnathostomiasis				HIV (TH1 → TH2)
Cysticercosis				
Echinococcus				

Eosinophilia: causes

- Autoimmune disease
 - Eosinophilic Granulomatosis with Polyangiitis (EGPA or Churg-Strauss)
 - Inflammatory bowel disease
 - Sarcoidosis
 - IgG4 disease
- Primary Hypereosinophilic Syndromes (affecting: lung, skin, heart, blood vessel, sinuses, kidney brain, intestine)
 - Idiopathic – Eos > 1500 with end-organ damage
 - Myeloproliferative – Eos > 1500, splenomegaly, heart disease, thrombosis, ~ chronic eosinophilic leukemia
 - Lymphocytic – skin > other, at risk for T-cell lymphoma
 - Episodic eosinophilia (Gleich syndrome) - cyclic fevers, hives, angioedema, pruritis, elevated eosinophils and IgM

Eosinophilia: causes

- Malignancy
 - Acute and chronic eosinophilic leukemia
 - Lymphoma (T-cell and Hodgkin's)
 - Chronic myelomonocytic leukemia

 - Adenocarcinoma of the GI tract
 - Lung cancer
 - SCCA (cervix, genitals, nasopharynx, bladder)
 - Thyroid

Eosinophilia: causes

- Immunodeficiency syndromes
 - Job's syndrome (autosomal dominant, Hyper IgE, severe eczema, abscesses and hypereosinophilia)
 - Wiskott-Aldrich syndrome (X-linked, eczema, thrombocytopenia, recurrent infections, hypereosinophilia)
 - Adenosine deaminase deficiency (recurrent infections, eczema and hypereosinophila)

Eosinophilia: causes

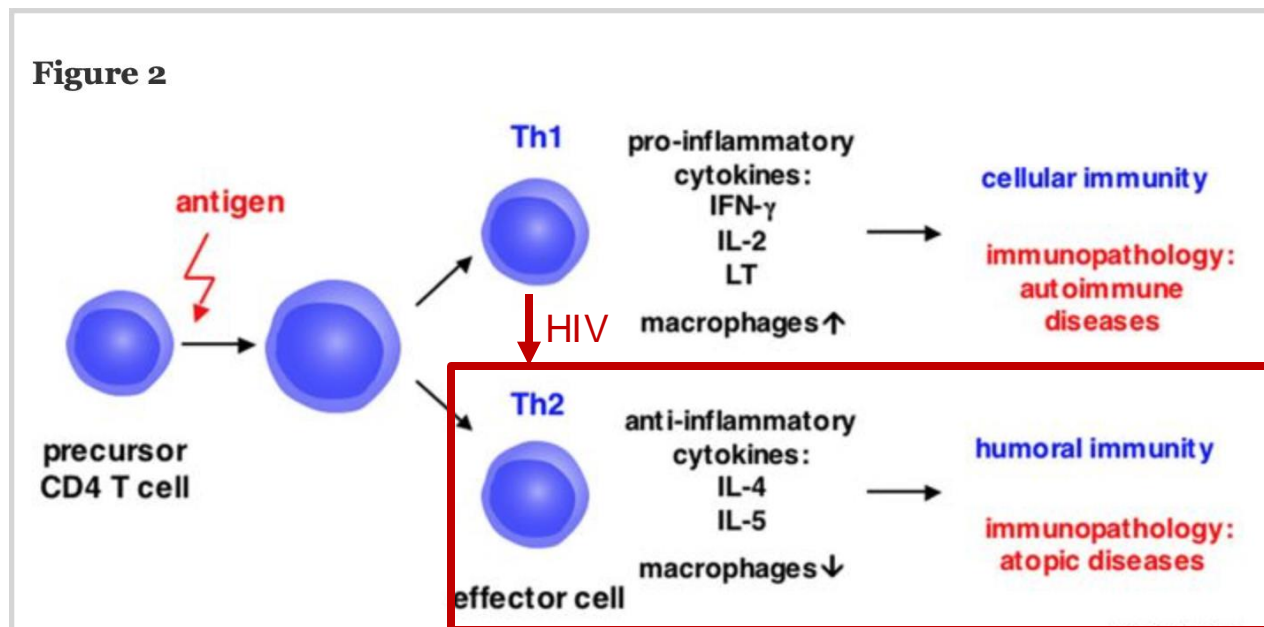
- Miscellaneous
 - SOT rejection
 - GVHD
 - Kimura disease (Asian males, head and neck masses) and epithelioid hemangioma (head and neck masses, especially around the ears)
 - Eosinophilia-myalgia syndrome (L-tryptophan) and toxic oil (aniline-denatured cooking oil from Seville, Spain 1981)
 - Adrenal insufficiency (an absence of corticosteroids)
 - Irritated serosal surfaces (PD catheters, chronic pleural effusions)
 - Cholesterol emboli

Eosinophilia in HIV infected persons

- Reported in up to 28% of persons infected with HIV (inclusive of those from parasite-endemic countries)
- Higher rates associated with
 - CD4 counts < 200 or < 50 (untreated HIV and disseminated infections)
 - Skin rash (eosinophilic pustular folliculitis (EPF), atopic dermatitis $>$ prurigo nodularis or papular pruritic eruption (PPE))
 - Foreign born: who are sero-positive for *Schistosoma* or *Strongyloides*
 - A history of living in the tropics for > 3 months
- Reports of *Strongyloides* hyperinfection syndrome as manifestation of IRIS after starting ART

Eosinophilia in HIV infected persons

- HIV itself may be the cause of eosinophilia
- HIV is associated with a shift of TH1 → TH2 CD4+ cells



- TH2 CD4+ cells make IL-4 (important in the production of IgE) and IL-5 (important in the production of eosinophils) = Allergic responses

Proposed Evaluation of Eosinophilia in HIV infected persons

Patient characteristic	What to do
All patients	Detailed H&P: country of origin, travel, medication (esp abx, anti-convulsants, some ARVs, NSAIDs). Discontinue offending medications. Don't forget about <i>Coccidioides</i> and <i>Aspergillus</i> (ABPA)
Untreated HIV	HIV related (TH1→TH2). Start ART (TH2→TH1)
CD4 < 50	Disseminated infection (MAC, TB, Histo) → consider adrenal insufficiency
Consider in all but especially foreign born or those with significant travel	Stool and urine studies (O&P), serology for <i>Schistosoma</i> and <i>Strongyloides</i> . Treat identified pathogens (<i>Schistosoma</i> – praziquantel, <i>Strongyloides</i> – ivermectin [screen for <i>Loa loa</i> first, if at risk])
Recently started ART	<i>Strongyloides</i> hyperinfection/IRIS.

Proposed Evaluation of Eosinophilia in HIV infected persons

Patient characteristic	What to do
End organ dysfunction	<u>Autoimmune</u> (EGPA, sarcoid, IBD, IgG4): get tissue Bx, ANCA and IgG4 level <u>Primary eosinophilic syndromes</u> : tissue biopsies
Still don't know?	Consider an <u>occult cancer</u> (leukemia, lymphoma (T-cell and HD), SCCA, lung, adenocarcinoma of GI, thyroid) <u>Rare causes</u> : toxins, cholesterol emboli, Kimura disease

Summary

- Eosinophilia in persons with HIV is more common in those with untreated disease and low CD4 counts.
- Investigations and treatment should be dictated by the patients' circumstances and any discovered pathogen or condition.
- Most patients with idiopathic, asymptomatic eosinophilia will resolve on ART suggesting the immunologic effects of untreated HIV were to blame.

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