The curious case of Eosinophilia in the night time

Tom Konikoff
6.6.17

Internal medicine “D”
Patient background

17 y/o female
Healthy
No meds
No drugs/ doesn't smoke
No known allergies
No relevant personal of family medical history
Fever

Productive cough

Dyspnea

Another hospital
Another hospital

11/2016

Leukocytosis
17K

Eosinophilia
1900

CRP
14 (N<5)
First episode

- Blood, Urine, sputum, fecal cultures - NEG
- Serology for EBV, CMV, Q-FEVER - NEG

- Eosinophilic pneumonia → Prednisone
- Clinical improvement, fever ↓, Eosinophil count ↓, CXR improves
- Discharge with steroid tapering down for 3 weeks
But 3 weeks later....

- No longer on steroids
- Throat pain, dyspnea
- Eosinophil count → 2400
- Bilateral alveolar infiltrates
Prednisone
30 mg
Second episode

- Eos count → 9000
- PLT → 33K
- Abdominal pain + light epigastric tenderness
- Maculopapular rash on limbs and abdomen
Left hepatic vein

Right hepatic vein

Left hepatic vein

Right hepatic vein
Due to susp. Budd-Chiari syn. transferred to Internal Medicine “D” Rabin Medical Center.

Eosinophilic disease with BUDD CHIARI SYNDROME
in PNIMIT D

- WBC 26K
- EOS 6.1K
- PLT 13K
- CRP 6
- Elevated liver enzymes (AST 348, ALT 602)
- INR (spont.) 1.57
Portal vein

Inferior Vena cava

Bypass (T.I.P.S)

Portal vein
Budd-Chiari syndrome secondary to Hypereosinophilic syndrome
CASE REPORT

Budd-Chiari Syndrome Associated with Hypereosinophilic Syndrome; A Case Report

Ai Inoue, Kojiro Michitaka, Shuichiro Shigematsu, Ichiro Konishi, Masatoshi Yasuda, Yoichi Hiasa, Hidetaka Matsu, Bunzo Matsuura, Norio Horii, Hiroaki Miyako, and Morikazu Onji

Successful Treatment of Eosinophilia-associated Budd-Chiari Syndrome in a Child

Heng-Kuei Lin, I-Chien Tsai, Jiaan-Der Wang, and Wen-Ya Lin

Hypereosinophilia, JAK2V617F, and Budd-Chiari Syndrome: Who is responsible for what?

Elena Mishchenko, Tamar Tadmor, Elad Schiff, Dina Attias, and Aaron Pollack

Budd-Chiari syndrome (BCS) is characterized by hepatic venous outflow obstruction, sometimes may be life threatening, with the development of fulminant hepatic failure. In cases of this kind, the most frequent underlying cause of BCS, myeloproliferative neoplasms (MPN), should always be excluded first, and molecular analysis of the Janus Kinase 2 (JAK2) mutation must always be performed. While the association of BCS with myeloproliferative neoplasms is well documented, hypereosinophilia has only been described in a few cases. Furthermore, JAK2 mutation in association with hypereosinophilia has been reported very rarely and its prevalence in this disorder still requires further investigation. To the best of our knowledge, cause of the above association occurring together with BCS has not been reported until now. Here, we describe a young woman presenting with hypereosinophilic, JAK2 mutation, and BCS. We also elaborate briefly on the biological mechanism and clinical features of this rare entity in our opinion. This case supports the formal inclusion of hypereosinophilic syndrome (HES) in the WHO MPN category and also raises the possible pathogenetic contribution of eosinophils, or their products, in MPN-associated thrombotic venous thrombosis.

A 22-year-old woman with a long history of previous diseases was bedridden and she was transferred to a larger referral center for transjugular intrahepatic portosystemic shunt, in preparation for possible liver transplantation. Sadly, the patient died on the following day before any procedures could be performed. The most prominent laboratory feature in the peripheral blood count of this patient is an eosinophilia associated with azotemia and normal platelet count in the presence of hepatomegaly and ascites. In case of this nature, the differential diagnosis of acquired eosinophilia must always be considered in its entirety. All laboratory work is necessarily performed to determine between the three major subcategories of eosinophilic secondary, clonal, and idiopathic. The causes of secondary eosinophilia include paroxysmal nocturnal hemoglobinuria, idiopathic myelofibrosis, autoimmune diseases, and others. 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Hematological Diseases & Budd-Chiari syn.

- Hypercoagulable state (JAK2, factor V Leiden, Erythrocytosis)
- 49% of Budd-Chiari cases are due to myeloproliferative disorders
- May be presenting symptom
- Patients with Splanchnic vein thrombosis (including budd-chiari) and no underlying disorder identified → JAK2 testing

HES

Primary (neoplastic)  Secondary (reactive)  Idiopathic

Up to 6.3 per 100,000

>80%

Crane et al.,
Incidence of myeloproliferative hypereosinophilic syndrome in the United States and an estimate of all hypereosinophilic syndrome incidence.
Eosinophilia & Hypercoagulability (Budd-Chiari syndrome)

Coagulation abnormalities in patients with eosinophilia

L.J. Vázquez, A. Fernández Pavón, F. Arnalich, A. Gil, A. López Pastor, A. Peña and F.J. Barbado

Published in final edited form as: *Semin Hematol.* Author manuscript; available in PMC 2013 April 01.

Eosinophilia: Rare cause of arterial thrombosis and cardioembolic stroke in childhood

Sandeep Kumar Sharma, Suman Kumar, Tulika Seth, Pravas Mishra, Manoranjan Mahapatra

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Eosinophils and Disease Pathogenesis

Factor I (Fibrinogen)

Factor III (Tissue factor)

MBP, EPO

thrombomodulin

Platelets

Secondary causes of eosinophilia:

- **Infections** -> Endemic-worldwide vs. geographically limited
  - **Helminth**: strongyloidiasis, trichinellosis, schistosomiasis, filariasis, hookworm, toxocariasis
  - **Ectoparasite**: scabies, myiasis
  - **Protozoan**: isosporiasis, sarcocystis
  - **Fungal**: coccidioidomycosis, ABPA, histoplasmosis
  - **Viral**: HIV

- **Medications** -> NSAIDs, aspirin, penicillins, allopurinol, tryptophan
  - Eosinophilia-myalgia/toxic oil syndromes, DRESS, interstitial nephritis, eosinophilic hepatitis

- **Allergic diseases** -> Asthma, atopic dermatitis

- **Autoimmune/Idiopathic** -> Sarcoidosis, inflammatory bowel disease, connective tissue disorders

- **Neoplasia** -> Hodgkin lymphoma, solid tumors, T-cell lymphoma

- **Endocrine diseases** -> Addison’s disease

- **Miscellaneous** -> Atheroembolic disease, immunodeficiency (e.g. hyper-IgE syndrome, Omenn's syndrome, ALPS)
Seminars in Arthritis and Rheumatism

An outcome survey of 43 patients with Budd–Chiari syndrome due to Behçet’s syndrome followed up at a single, dedicated center

International Journal of Rheumatic Diseases

Original Article

Uncommon presentations of primary systemic necrotizing vasculitides: the Great Masquerades

European Journal of Dermatology

Recurrent cutaneous eosinophilic vasculitis

Rheumatology

A case of Budd-Chiari Syndrome presenting in a lady with newly diagnosed Churg-Strauss Syndrome
But what about the treatment?
Is an acute well-defined clot present?

- Yes

Contraindication for thrombolytic therapy?

- No
- Yes

Symptomatic?

- No
- Yes

Thrombolytic therapy successful?

- No
- Yes

Angiography/stenting successful?

- No
- Yes

Approach to Budd-Chiari in non-Cirrhotic patients

- TIPS
- Continue anticoagulation
Is an acute well-defined clot present?

Contraindication for thrombolytic therapy?

Thrombolytic therapy successful?

Symptomatic?

Angiography/ stenting successful?

TIPS

Approach to Budd-Chiari in non-Cirrhotic patients

AASLD practice Guidelines

But when is it best to TIPS?

- Primary intervention
- After Angioplasty
- Recurrent/Chronic Asymptomatic BCS
- Cirrhosis
“good long-term results”

Non comparison

High risk Patients

Primary TIPS over primary Angioplasty

“better patency and less mortality with primary TIPS“

Small size, retrospective → small paper
Primary Angioplasty  Vs.  Primary TIPS
Whatever you choose...always treat the underlying cause!

(in our case)

Idiopathic Hypereosinophilic Syndrome

 ✓ Steroids
 ✓ Hydrea
In summary

- Young healthy female
- Idiopathic Hypereosinophilic syndrome
- Secondary Budd-Chiari
- T.I.P.S (+ steroids and hydrea)
- Doing well (normal LFT)
• Budd-Chiari syn. may be the presenting symptom of many hematological disorders – not only Myeloproliferative

• Eosinophilia is a precipitating factor for splanchnic thrombotic events

• Early TIPS may be considered