A challenging case of eosinophilia, the era of personalized medicine has the key

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Outline

- Case presentation
- Eosinophil
- Causes of eosinophilia
- Myeloid neoplasms with eosinophilia and abnormalities of *PDGFRA*
- Conclusion remarks

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The Case

- 28 year old lady
- Referred from Prince Rashid Hospital
- -Recurrent oral ulcerations

  -Recurrent genital ulcerations

  -Uveitis

Physical examination

- Pale
- Normotensive Temp 37.5C
- H&N :Normal
- Chest :clear
- Heart: tachycardia
  N S1,S2
- Abdomen : splenomegaly
- MSK :RT elbow and left Knee effusion

Lab Data

CBC:

WBC 44,000

PCV 21

PLAT 140,000

Blood film:

Normochromic Normocytic anemia

Eosinophilia

Diagnosis

Behcet syndrome with uveitis and arthropathy

With eosinophilia ??

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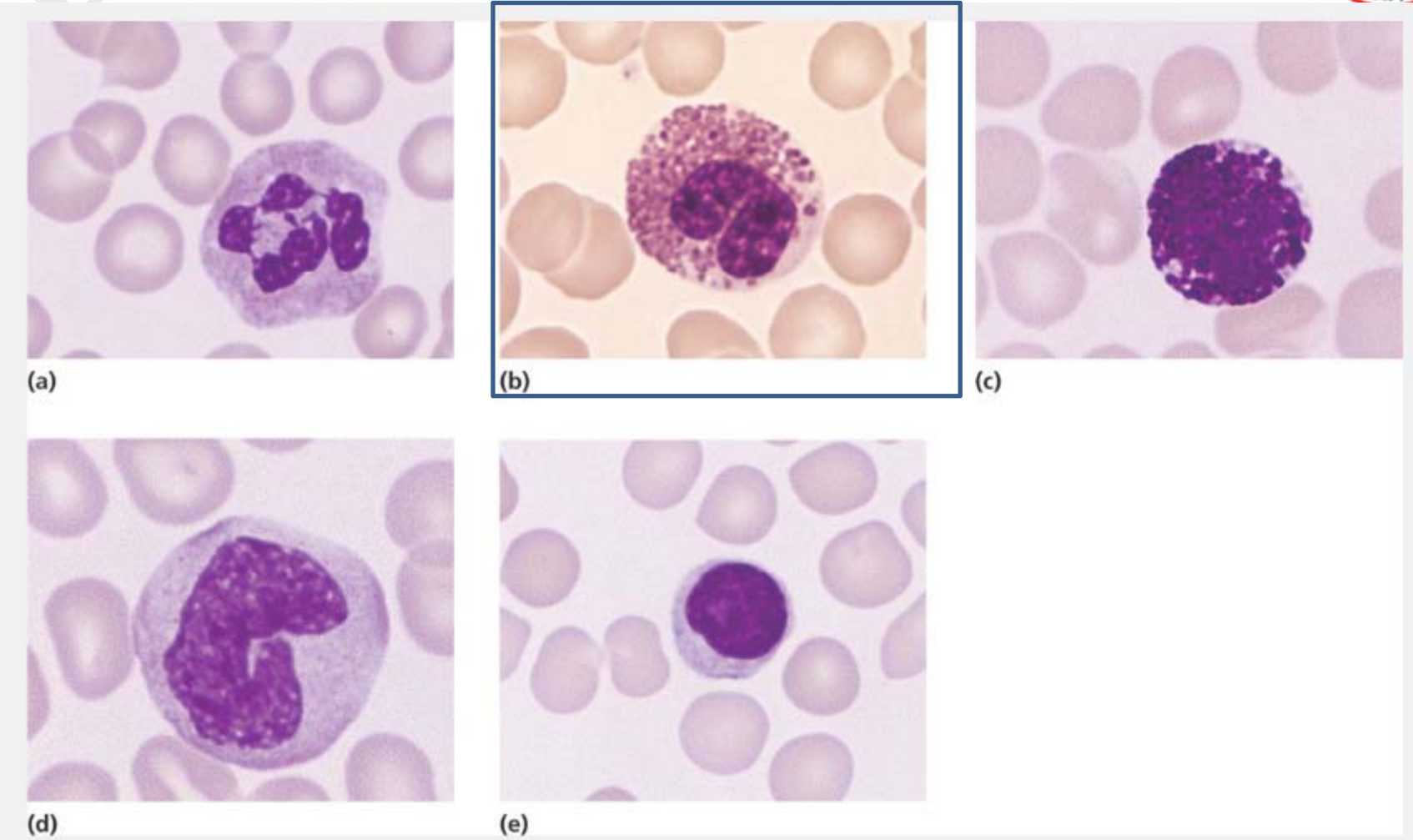
Eosinophil



Hoffbrand, Victor, Paul Moss. Essential Haematology, 2nd Edition. John Wiley & Sons (STMS), 2/25/2011.

Causes of eosinophilia

Box 49-1 *Classification of Eosinophilia by Cause*

Reactive
- Allergy
  - Asthma
  - Atopic eczema
  - Urticaria
  - Allergic rhinitis
  - Allergic bronchopulmonary aspergillosis
  - Adverse drug reaction
- Skin disease
  - Pemphigus vulgaris
  - Bullous pemphigoid
  - Dermatitis herpetiformis
- Parasitic infection
  - Nematodes (e.g., ascariasis, hookworm infection, strongyloidiasis, filariasis)
  - Trematodes (e.g., fascioliasis, fasciolopsiasis, schistosomiasis)
  - Cestodes (e.g., cysticercosis, echinococcosis)
- Fungal infection
  - Coccidioidomycosis
- Neoplasia
  - Carcinoma
  - Sarcoma
  - Hodgkin's lymphoma
  - Non-Hodgkin's lymphoma
  - Acute lymphoblastic leukemia
  - Systemic mastocytosis*
- Vasculitis
  - Churg-Strauss syndrome
  - Systemic necrotizing vasculitis
- Endocrine disorder
  - Addison's disease
  - Hypopituitarism
- Administration of cytokines
  - Interleukin-3
  - Interleukin-5

Neoplastic
- Acute myeloid leukemia (occasionally)
- Lymphoid and myeloid neoplasms with *PDGFRA* rearrangement
- Myeloid neoplasms with *PDGFRB* rearrangement
- Lymphoid and myeloid neoplasms with *FGFR1* rearrangement
- Chronic eosinophilic leukemia, not otherwise specified
- Eosinophilic transformation of myeloproliferative neoplasms (e.g., chronic myelogenous leukemia, primary myelofibrosis)
- Systemic mastocytosis*

Unknown
- Idiopathic hypereosinophilic syndrome

Jaffe, Hematopathology . 1st edition, 2011

Eosinophilia Work UP

Table 49-1 **Investigations Indicated for Unexplained Persistent Hypereosinophilia**

Investigation	Possible Diagnostic Yield
Blood film	Lymphoblasts, myeloblasts, or lymphoma cells indicating hematologic neoplasm
Investigation of stool, urine, or blood for parasites; serology for parasitic infection	Parasitic infection
Immunoglobulin E and tests for allergy	Allergic disease
Bone marrow aspiration and trephine biopsy	Eosinophilic leukemia, Hodgkin's or non-Hodgkin's lymphoma, or systemic mastocytosis
Cytogenetic analysis of bone marrow aspirate	Eosinophilic leukemia
Molecular analysis of peripheral blood cells for *F1P1L1-PDGFRA* fusion gene	Eosinophilic leukemia
Molecular analysis of bone marrow cells for *KIT* mutation	Systemic mastocytosis
Serum tryptase	Eosinophilic leukemia or systemic mastocytosis
Immunophenotyping of peripheral blood T cells	Cytokine-driven eosinophilia
Computed tomography scan of chest and abdomen	Underlying lymphoma or other neoplasm

Modified from Fletcher S, Bain B. Eosinophilic leukaemia. *Br Med Bull.* 2007;81:115-127.

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Jaffe, Hematopathology . 1st edition, 2011

Eosinophilia Urgency

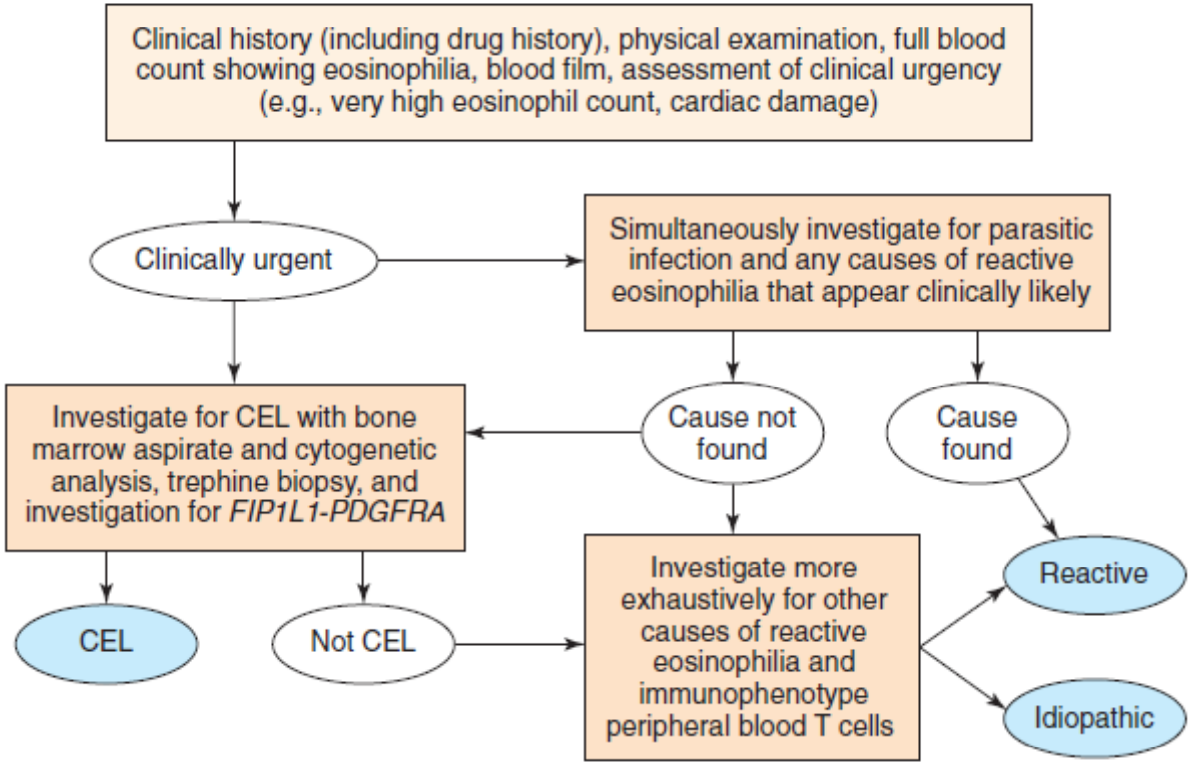

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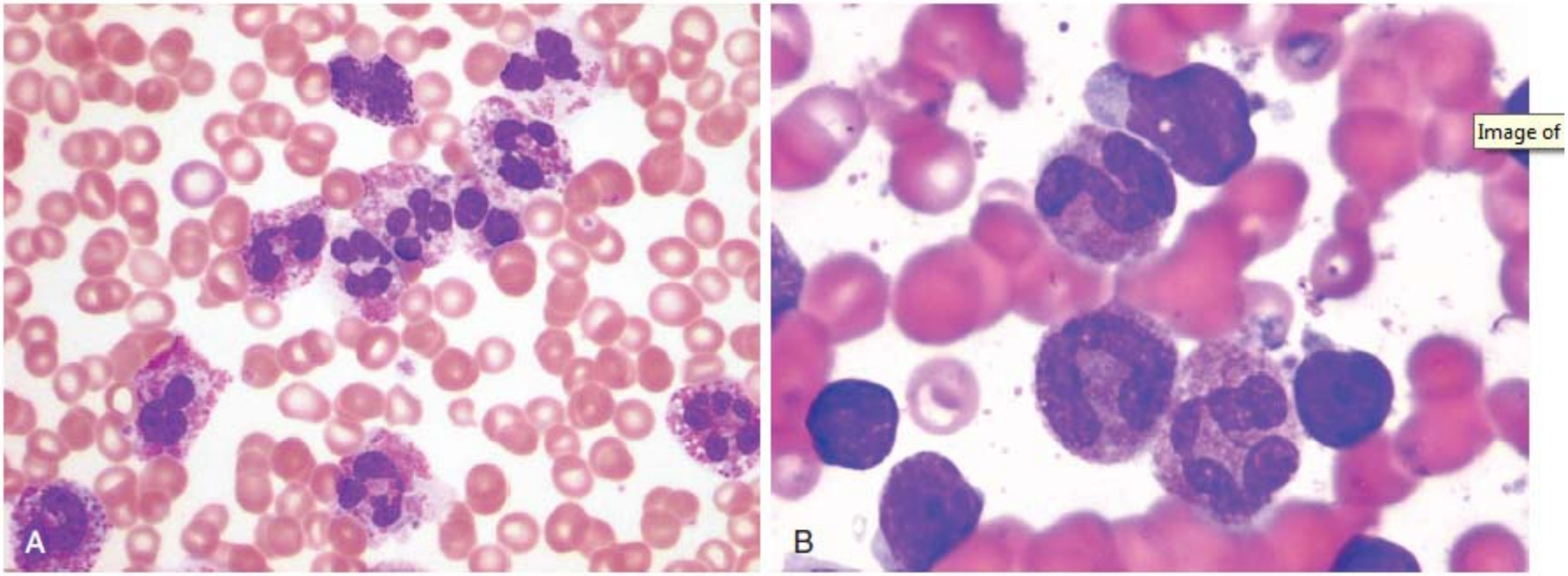
Figure 49-1. Flow chart of the suggested diagnostic process in a patient with hypereosinophilia when there is clinical urgency. CEL, chronic eosinophilic leukemia.

Jaffe, Hematopathology . 1st edition, 2011

Our Case



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Jaffe, Hematopathology . 1st edition, 2011

Myeloid neoplasms with eosinophilia and abnormalities of *PDGFRA*

Table 3.01 Diagnostic criteria of an MPN* with eosinophilia associated with *FIP1L1-PDGFRA*.

A myeloproliferative neoplasm with prominent eosinophilia

AND

Presence of a *FIP1L1-PDGFRA* fusion gene†

* Patients presenting with acute myeloid leukaemia or lymphoblastic leukaemia/lymphoma with eosinophilia and a *FIP1L1-PDGFRA* fusion gene are also assigned to this category.

† If appropriate molecular analysis is not available, this diagnosis should be suspected if there is a Ph-negative MPN with the haematological features of chronic eosinophilic leukaemia associated with splenomegaly, a marked elevation of serum vitamin B12, elevation of serum tryptase and increased bone marrow mast cells.

- WHO classification, 2008.

Diagnosis

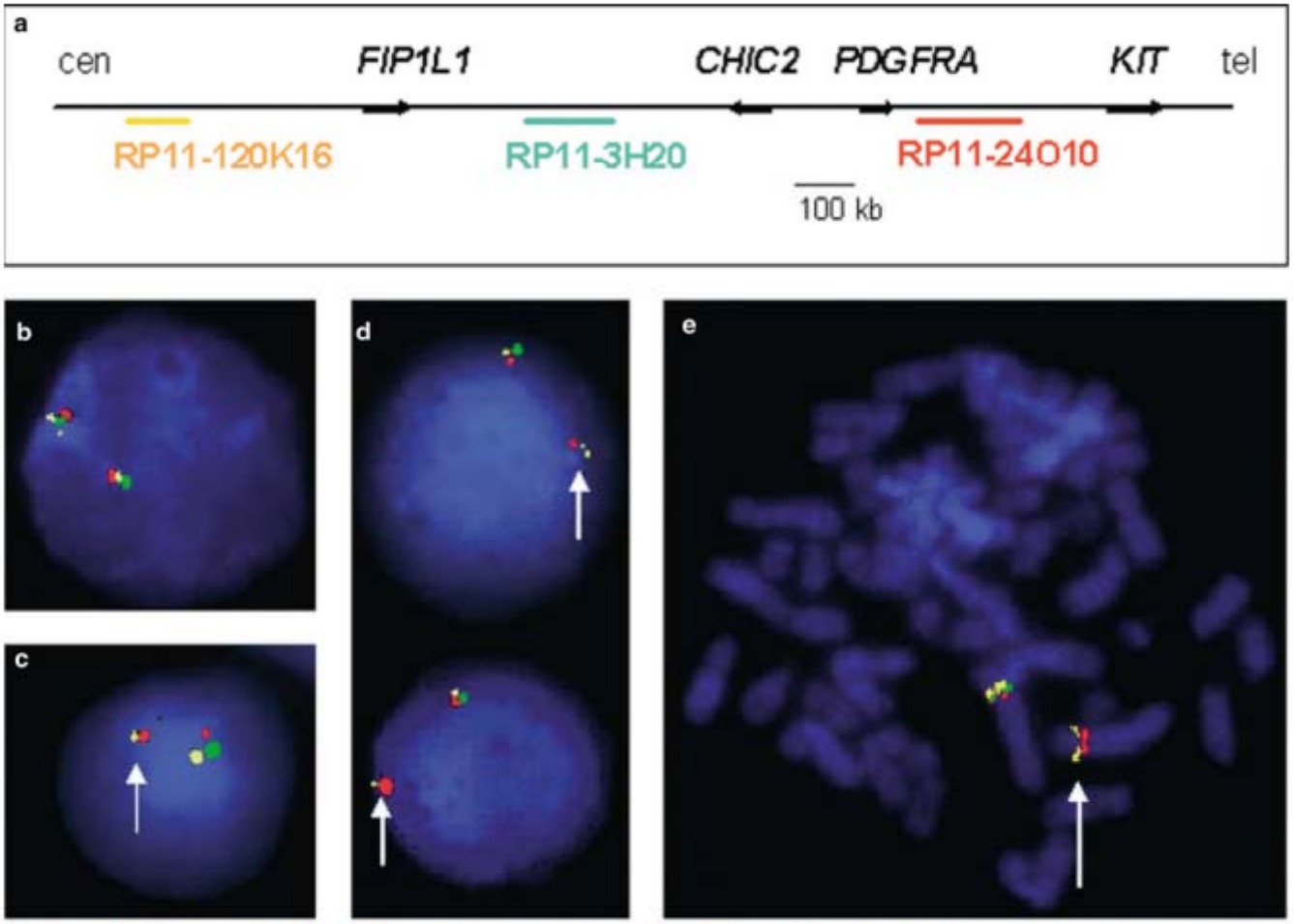

Figure 2 FISH detection of the 4q12 deletion associated with the *FIP1L1-PDGFRA* fusion. (a) A genomic map of the 4q12 region, with relevant genes and selected FISH probes is drawn to scale. Examples are shown of three-color FISH analysis performed on a control sample (b), patient 4 (c) and patient 8 (d and e), showing the loss of one 3H20 (green) signal in (c–e) (arrow). Arrow in (e) indicates a seemingly normal looking chromosome 4 with the cryptic del(4)(q12).

- *Leukemia* (2004) **18,** 734–742.

What is the deal

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Take home messages

- There are several causes of eosinophilia where clinicopathological correlation is of paramount importance to elucidate the etiology.
- Eosinophilia raises red flag in certain cases
- Personalized medicine could stratify and flip over the prognosis through genetic studies.

References

- 1. Leukemia. 2004 Apr;18(4):734-42
- 2. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Fourth Edition 2008
- 3. Hematol Oncol. 2010 Jun;28(2):93-7. doi: 10.1002/hon.919
- 4. Arch Pathol Lab Med. 2013 Feb;137(2):259-69. doi: 10.5858/arpa.2011-0597-RA