

Hypereosinophilic Syndrome (HES) a case series

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HYPEREOSINOPHILIC SYNDROME

HES is a group of disorders marked by the sustained over production of eosinophils ,in which eosinophilic infiltration and mediator release causes damage to multiple organs.

Weller,PF,Bubly,GJ.The Idiopathic hypereosinophilic syndrome.Blood
1994;83:2759

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This study was done on 8 patients of
adult age group diagnosed as having

hypereosinophilic syndrome.

OBJECTIVES

To observe the clinicohaematological features and variants of HES

DURATION

- Three years i.e; from Jan 2006-Dec 2008

INCLUSION CRITERIA

- This study includes 8 adult patients (>15 yrs)
- both genders
- AEC >1500/mm³ for more than 6 months

EXCLUSION CRITERIA

- Patients with other causes of eosinophilia were carefully excluded according to the findings in history, physical examination and investigations

SETTING

- Haematology department, Shaikh Zayed medical complex which is 750 bedded hospital affiliated with FPGMI.

DATA COLLECTION TECHNIQUE

- From all selected patients, presenting complaints in history ,findings in physical examination and investigations were recorded
- CBC was done on sysmax Kx-21
- Peripheral smear stained by giemsa for manual AEC
- Bone marrow biopsy was done.

DATA ANALYSIS

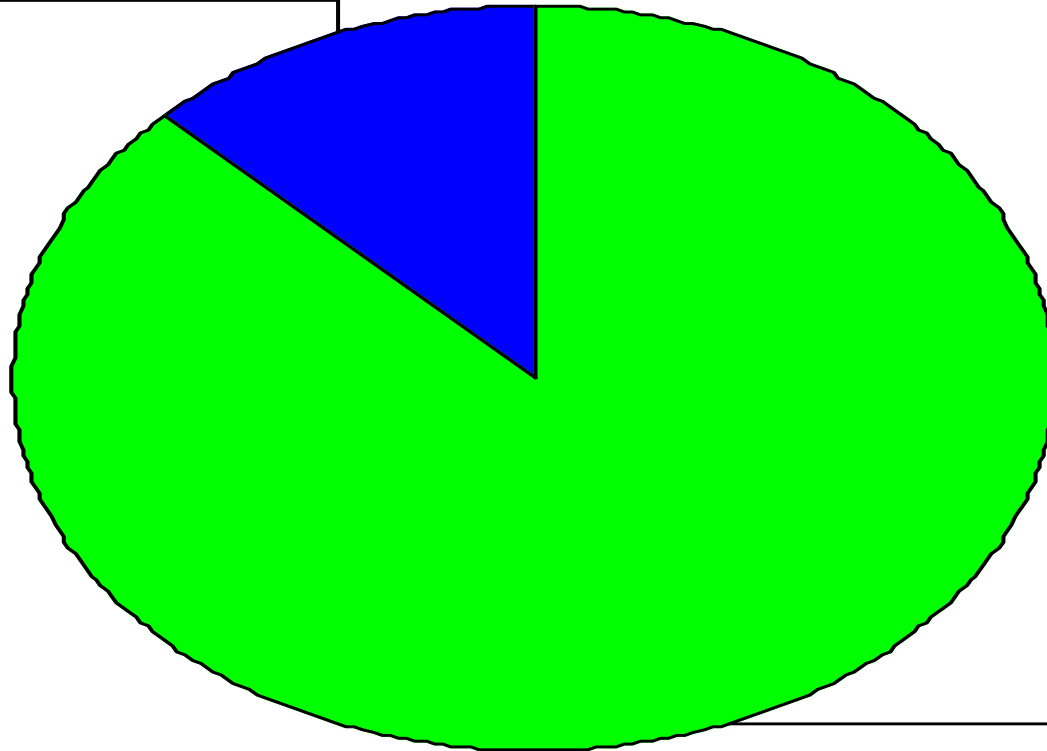
All selected data was entered into SPSS version 10.0 for analysis and results were expressed as **mean, median, standard deviation, frequencies and percentages.**

RESULTS

- total 8 patients
- 7 patients were of **I-HES** variant.
- 1 patient was of **m-HES** variant.
- Males 87.5%
- females 12.5%
- Male to female ratio 7 : 1
- Different signs and symptoms are analysed
- Different laboratory parameters are analysed

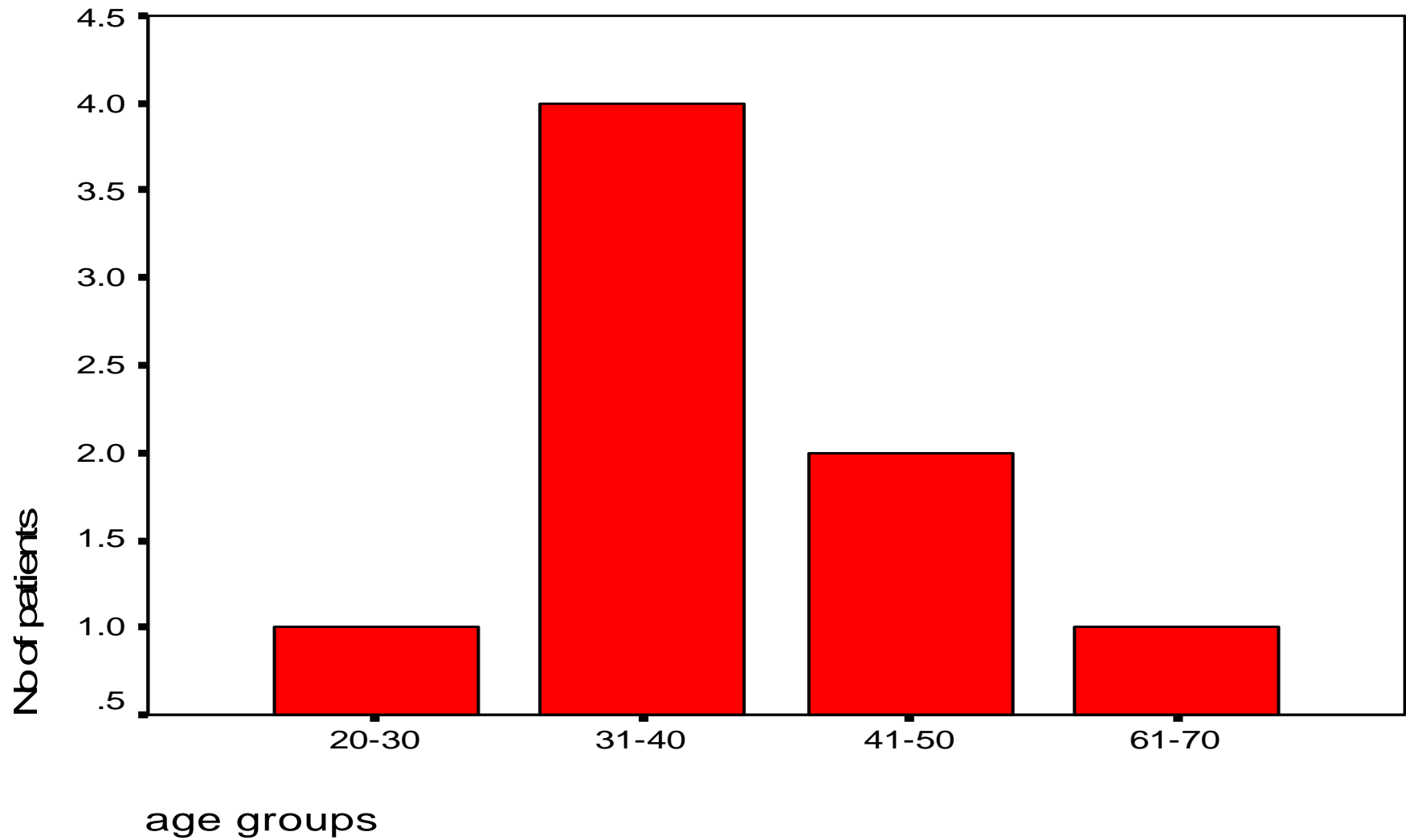
MALE :FEMALE ratio

female 13%

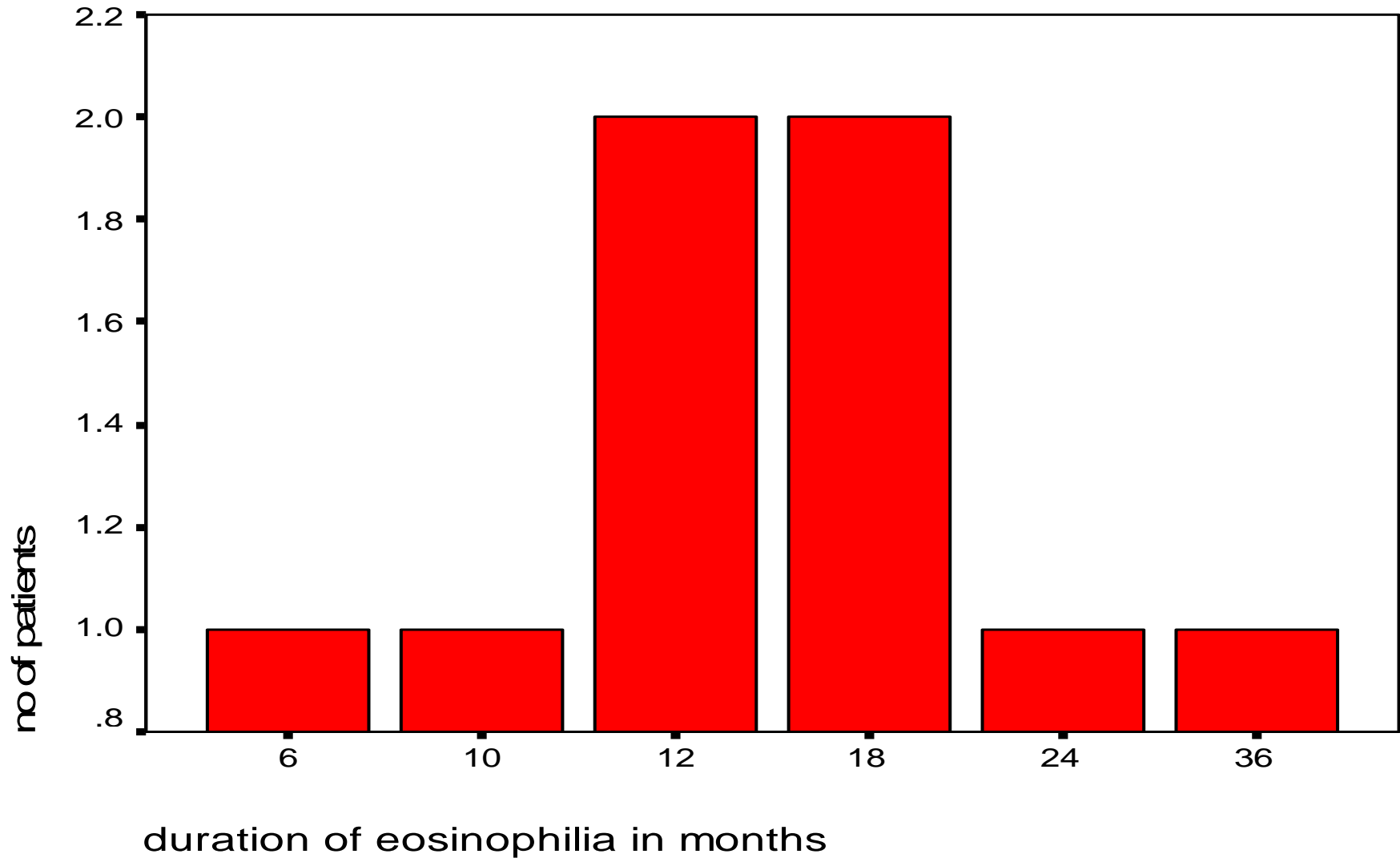


male 87%

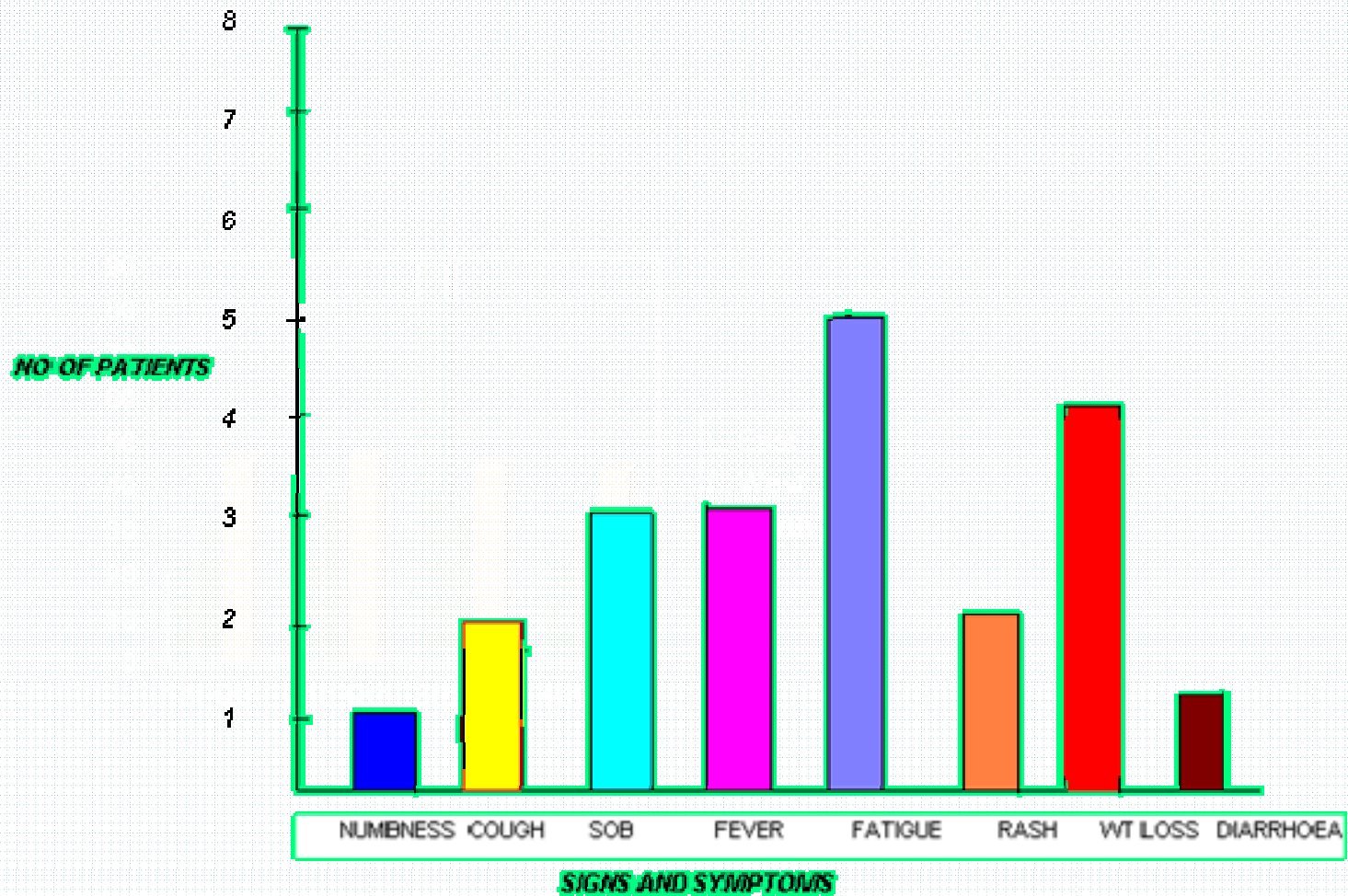
AGE



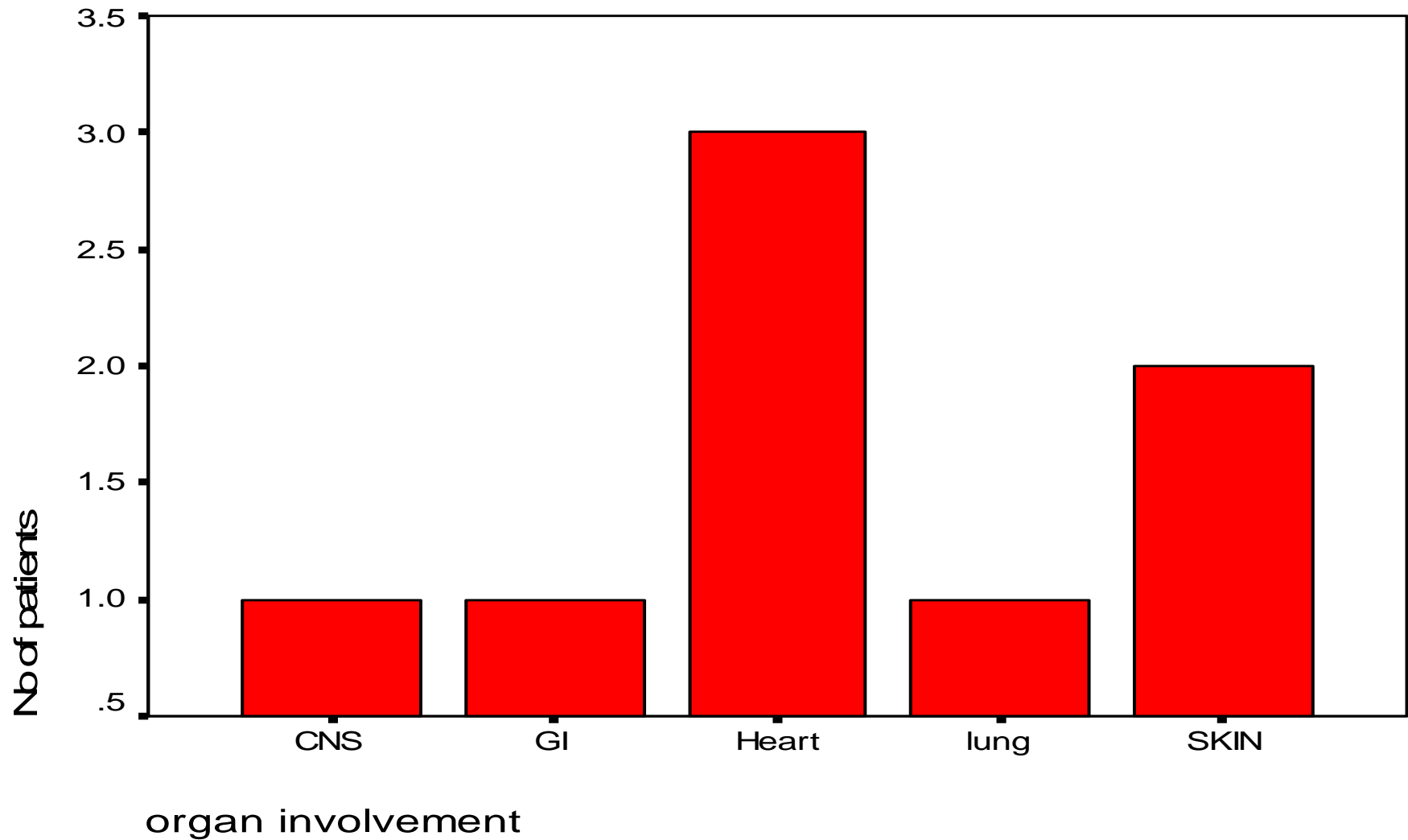
DURATION OF EOSINOPHILIA



SIGNS AND SYMPTOMS



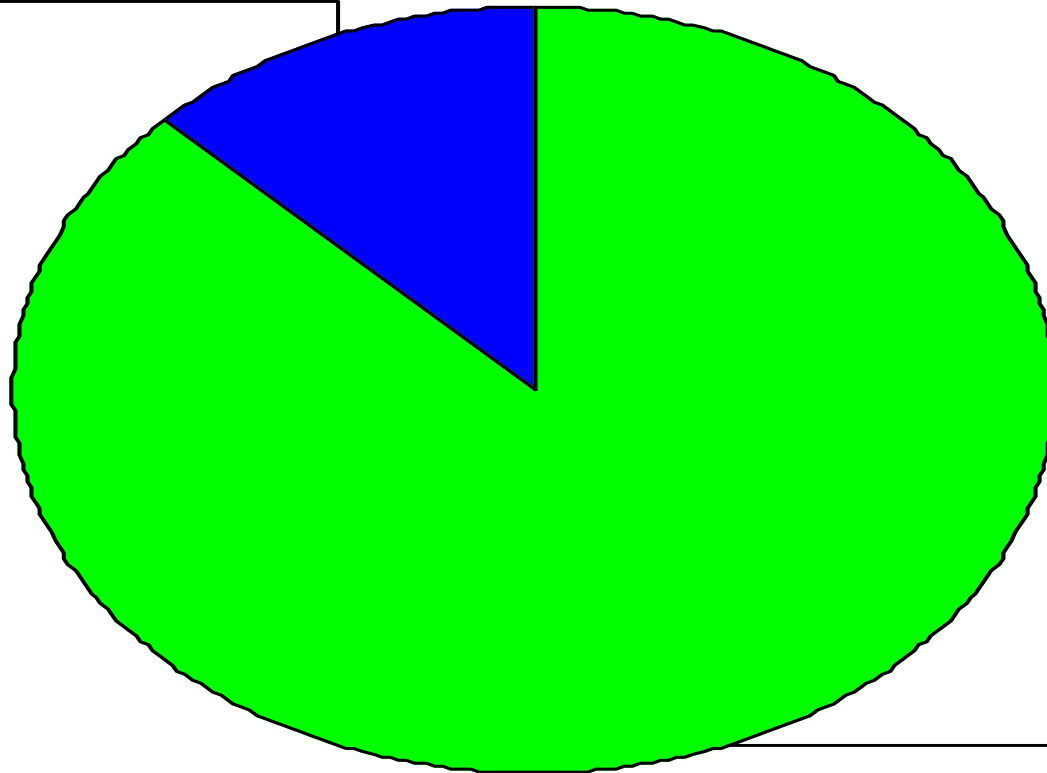
ORGAN INVOLVEMENT



Organs involved	I-HES (n=7)	m -HES (n=1)
heart	42.8%	
skin	28.7%	
nervous system	14.2%	
GIT	14.2%	
lung		100%

RESPONSE TO STEROIDS

non responders 12%



responders 88%

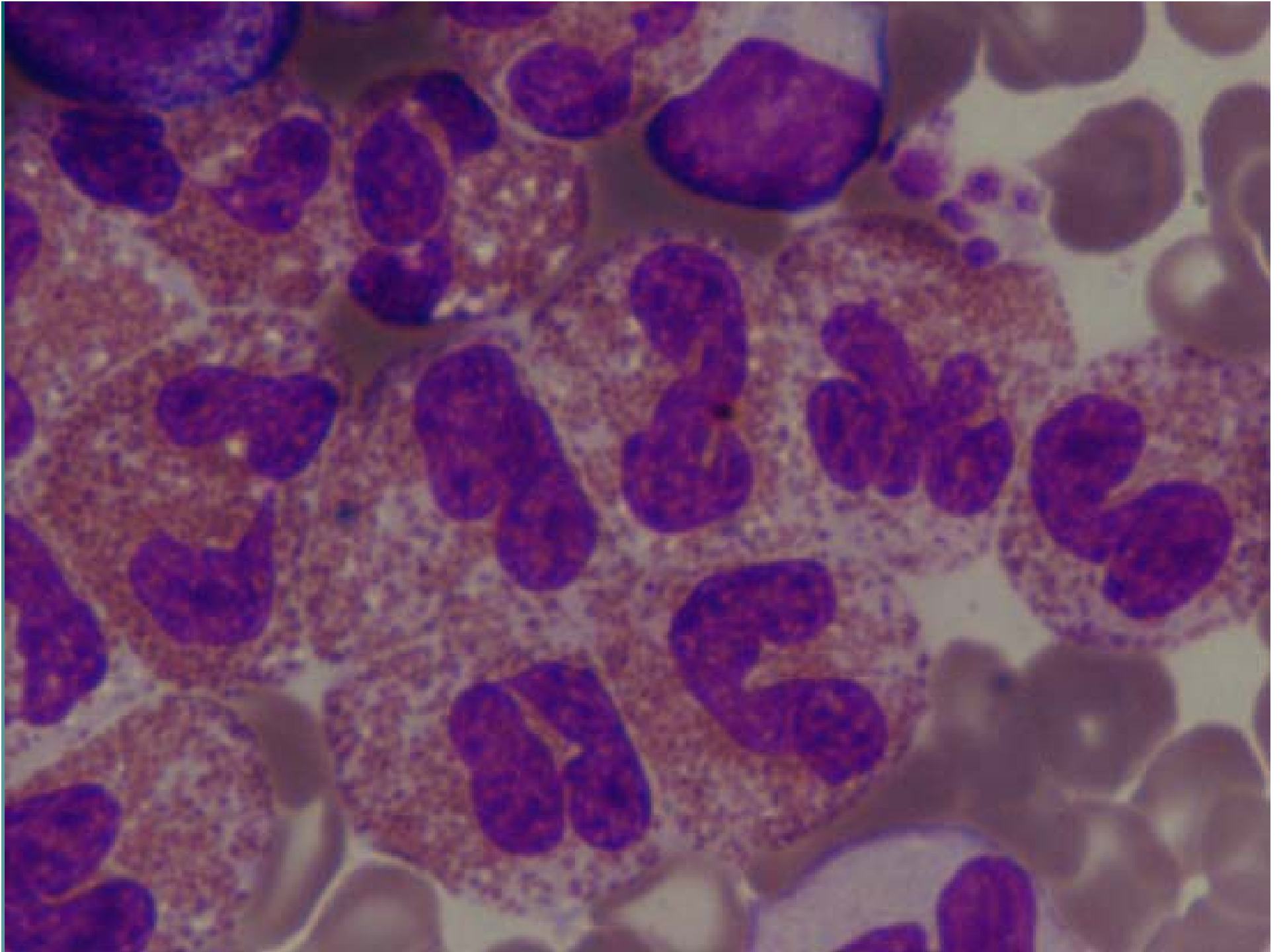
HAEMATOLOGICAL PARAMETERS

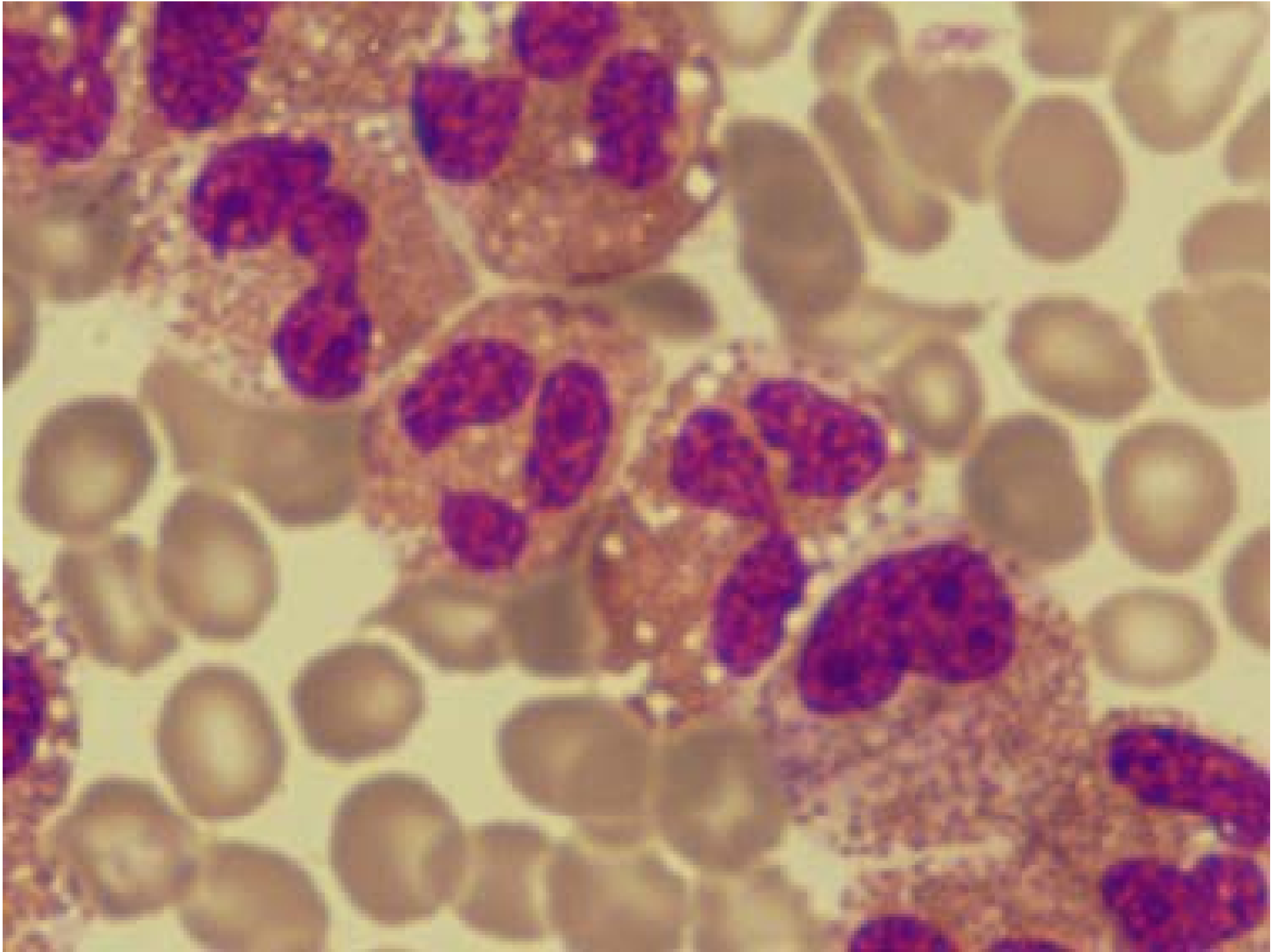
	Hb (g/dl)	TLC (x10 ⁹ / l)	Plts (x10 ⁹ / l)	AEC (x10 ⁹ /l)
Mean	10.4	27.7	411.6	16.0
Standard Deviation	2.2	12.2	308.6	11.1
Minimum	5.2	14.5	169	7.0
Maximum	12.3	54.0	1110	37.8

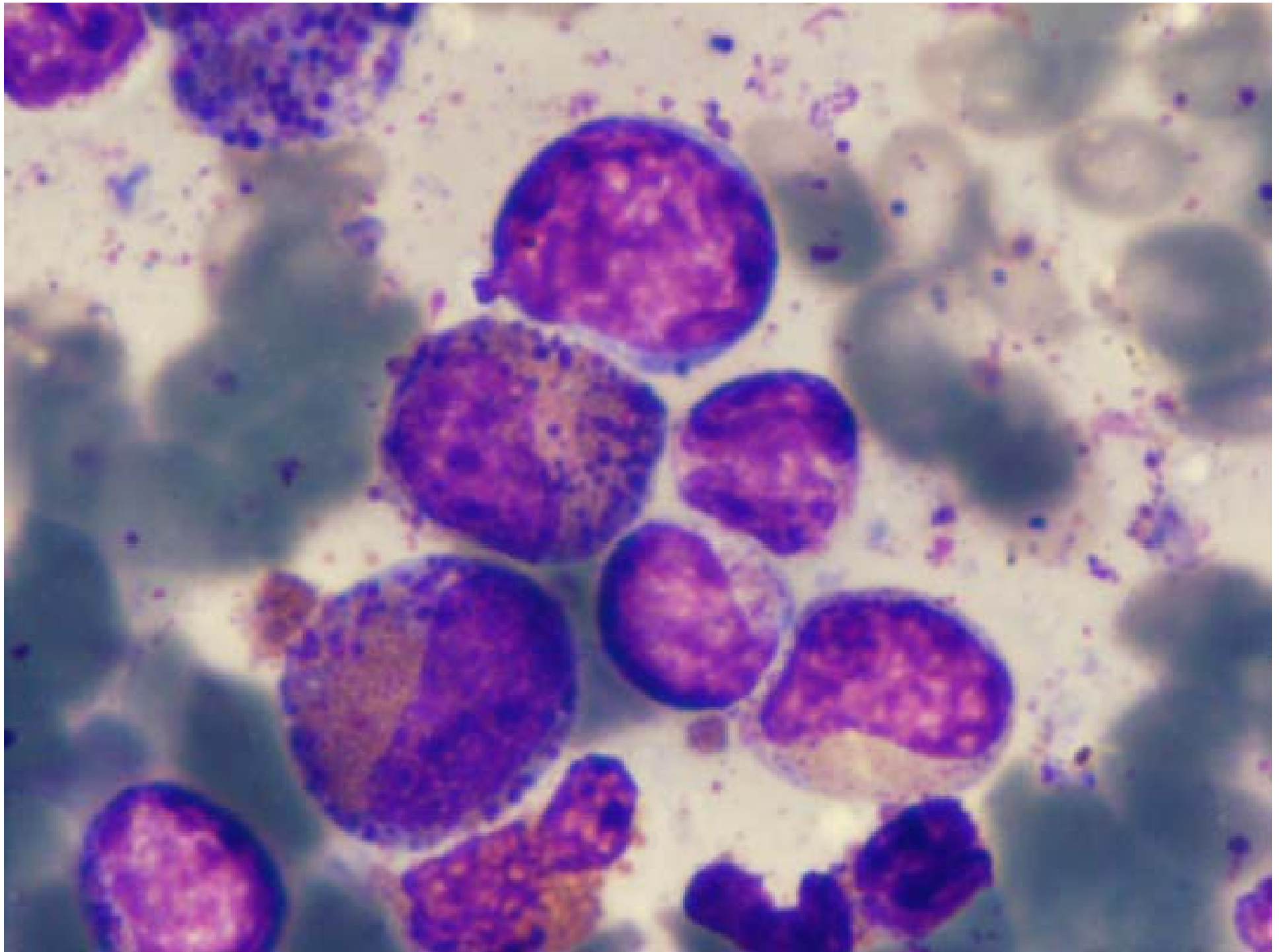
Wednesday, April 29, 2009

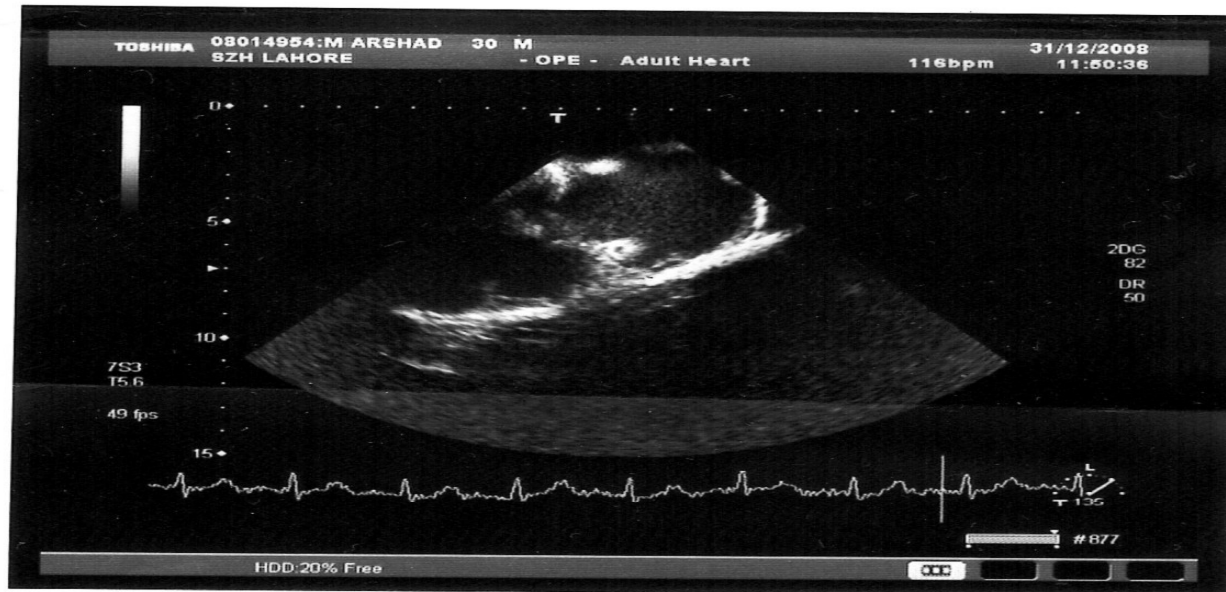
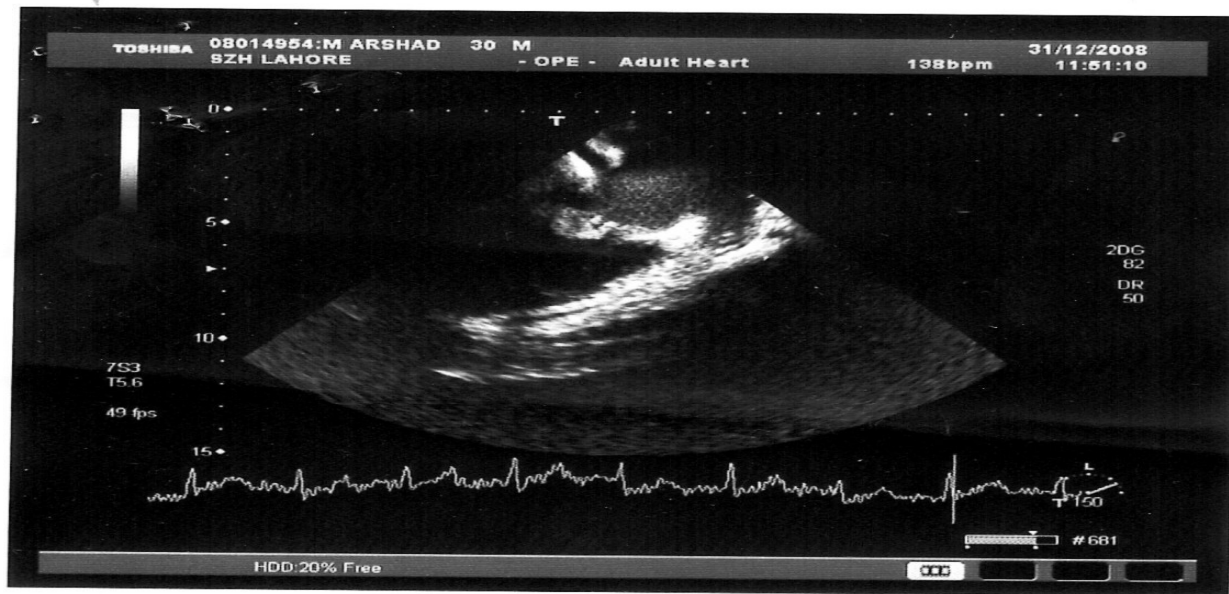
FINDINGS IN m-HES

- ◆ **Male** patient
- ◆ Splenomagaly
- ◆ **Blasts** in peripheral blood 1%
- ◆ Bone marrow **Blasts** 3%
- ◆ Bone marrow **fibrosis**
- ◆ Bone marrow **Mast cells**
- ◆ **High vit B12 level**
- ◆ **Ph¹** chromosome negative
- ◆ **No response to steroids**









HISTORY

- 🕒 1968 - Hardy and Anderson first introduced the term HES

Diagnostic Criteria
for
Idiopathic Hypereosinophilic Syndrome
(HES)

1. Persistent eosinophilia of over $1500/\text{mm}^3$ for longer than 6 months
2. Lack of evidence of other known causes of secondary hypereosinophilia (SH)
3. Multiple organ involvement.

◆ Two main types

- Myeloproliferative variant (m-HES)
- Lymphoproliferative variant (l-HES)

👉 differentiation is important as course and t/m are different

Myeloproliferative variant (m-HES)

- ◆ Male : female ratio - 9:1
- ◆ mean age of onset -33 yrs(range 20-50y)
- ◆ Course - indolent...fulminant...rapidly fatal
- ◆ mean duration of disease of 4.8 yrs (range, 1-24 y)
- ◆ Acquired clonal abnormality of myeloid lineage
- ◆ chromosomal **del on band 4q12** leading to **FIP1L1-PDGFR** fusion gene.
- ◆ karyotypic abnormalities -rare

Clinical and Biological features

- **are of MPD**
- ◆ anemia
- ◆ Thrombocytopenia
- ◆ splenomegaly
- ◆ high B₁₂ level
- ◆ altered LAP score
- ◆ Inc leucocyte precursors
- ◆ leukemic transformation

Bain BJ, Fletcher SH, Chronic eosinophilic leukemias and The myeloproliferative variant of HES. Immunol Allergy Clin North Am 2007;27:377

Wednesday, April 29,
2009

➤ due to Eosinophils which infiltrate multiple organs and release granule proteins

ie

- eosinophil peroxidase
- major basic protein
- eosinophil-derived neurotoxin
- eosinophil cationic protein

➤ Heart, GI, lungs and nervous system are effected

➤ Progression to eosinophilic leukemia is more common

- CBC
 - anemia (50%)
 - eosinophil count ($>1.5 \times 10^9/L$)
 - Neutrophilia
 - Thrombocytopenia (31%)
 - thrombocytosis (16%)
 - very high TLC, immature forms may indicate leukemia
- peripheral smear
 - Teardrop cells and nucleated erythrocytes
 - Eosinophils can exhibit cytoplasmic vacuolization, nuclear hypersegmentation, a decrease in granule number/size
- Bone marrow *increased eosinophils, mast cells, fibrosis*
- IgE elevated in 38%
- Inc serum tryptase levels
- ECG
- Echo
- s. troponin
- PFTs

Treatment of *m*-HES

- ◆ Imatinib mesylate ,a tyrosine kinase inhibitor
- ◆ Chemotherapeutic agents (hydroxyurea, vincristine, etoposide ,chlorambucil)
- ◆ Anticoagulants and antiplatelet agents
- ◆ Long-term remission after allogeneic stem cell transplantation

Lymphoproliferative variant (L-HES)

- ◆ Male: female ratio - 1:1
- ◆ Course ... indolent
- ◆ cytokines ; A clone of T cells produces eosinophilo-poietic cytokines ie **IL-5 , IL-3** and **GM-CSF**
- ◆ Pathogenesis-not known but many pts have past h/o atopy

Clinical and biological features

- ◆ Skin
- ◆ Heart
- ◆ Pulmonary
- ◆ Nervous system
- ◆ Gastrointestinal system

- ◆ May evolve into **lymphoma**

HEART INVOLVEMENT IN HES

Acute necrotic phase.....

clinically silent...endocardial damage
myocardial infiltration with eosinophils
eosinophils degranulation
myocardial necrosis-formation of
microabscesses

Intermediate stage.....thrombus formation

Fibrotic stage...fibrosis...scarring

NERVOUS SYSTEM

- ◆ Cerebral Thromboembolism
- ◆ Encephalopathy
- ◆ Peripheral neuropathy

SKIN

- ◆ Angioedematous /Urticarial Rash
- ◆ Erythematous rash
- ◆ Papules and nodules

Treatment of ϵ -HES

- ◆ Corticosteroids
- ◆ Corticosteroids + IFN alpha
- ◆ Cyclosporine A
- ◆ Anti-IL-5 mAb
- ◆ If malignant transformation CHOP, fludarabine, 2-CDA

Prognosis

- ◆ Initial case series -----poor prognosis
mean survival of 9 months
a 3 year survival of 12 %
- ◆ A 1989 French series of 40 patients with HES
(including 17m-HES)
80 % survival at 5 years
42 % survival at 15 years
- Prognosis improves with
Earlier diagnosis of HES
close clinical and echocardiographic monitoring
medical and surgical management of cardiac
complications

- ◆ Identification of specific variant of HES will help to guide treatment regimens. as I-HES responds better to steroids
- ◆ Trial of glucocorticoids in all pts even asymptomatic, response to glucocorticoids is associated with better prognosis
- ◆ Serial assessments should be made as patients of HES may develop clonal cytogenetic abnormalities like translocation of 5q33 or 8p11,transcription of FIP1L1-PDGFR.

Delay in starting treatment may result in permanent organ damage.

THANKS

