PURE RED CELL APLASIA

Presenter: Sanaa S. Said

BIODATA

- JG
- 43 year old
- Male
- Originally from Nyahururu
- DOA: 20/5/14

Presenting complaint

- Pt came for routine check up post kidney transplant and was noted to be pale

History of presenting illness

- Diagnosed with ESRD secondary to ?CGN in 2007
- Underwent successful renal transplant on 26th Feb, 2014
- Tacrolimus 5mg BD, Mycophenolic acid 720mg BD, Prednisone 20mg OD, Isoniazid 300mg OD, Pyridoxine 25mg OD, Septrin 960mg OD

- Patient reported to be well
- Denied any easy fatigability, breathlessness on exertion, palpitations or lower limb edema
- No constitutional symptoms
- No bleeding tendencies
- No melena
- No itchiness or rash
- Reported adequate intake of vegetables and meat

- PMH as above
- FSH: works as a farmer.

Married with 2 children

Denied any history of alcohol, cigarette smoking or drug use

- Denied use of local herbs, over the counter medication or any exposure to agrochemicals

On examination

- In fair general condition
- Pallor, no jaundice, no cyanosis, no LL edema
- PR 117 bpm
- BP 120/70
- RR 18 bpm
- Temp 36.6°C

- No features of iron deficiency, no beefy tongue
- CVS: regular pulses, apex in 5th ICS MCL,

  S1 &S2, with a haemic murmur
- PA: Surgical scar rt iliac fossa, soft, non tender with a palpable mass RIF
- MSK: Non contributory
- RS: Non contributory

Differential diagnosis

- Infections
- Rejection
- Immunosuppressive medications
- Haemolysis

Investigations

	20.5.14
WBC	6.49
RBC	2.47
Hb	6.08
Hct	18
MCV	72.7
MCH	24.6
Plt	549
K	5.12
Na	138
Creat	115
Urea	3.7
eGFR	73
Tac	10.0

PBF:
RBC – Microcytic with severe hypochromasia
WBC – N 89%, L -8%, M – 3%
PLT – Increased
Comment: Anemia of chronic disease
Iron studies – S. iron 43.2 (11-28),
S. transferrin 25(26 -47),
S. Ferritin 304 (34 -310)
Reticulocyte count -0.5%
Stool for occult blood - neg

Management

- D/W hematologist
- Probable erythropoietin deficiency
- Plan was to optimise ePo
- Patient discharged for follow up in 2 weeks
- To do erythropoietin levels as outpatient

On follow up: 10/6/14

- Readmitted with worsening anemia:

WBC - 7.18

Hb - 3.61 g/dl

Hct - 10.4 %

MCV – 70 fL

MCH – 24.4 pg

Plt – 528

- Transfused 4 units packed red cells

BMA

Subsequently:

- Readmitted again twice with anemia underwent blood transfusion
- No blood transfusion requirements prior to transplant
- Total blood transfusion requirements post transplant 1.2 units/month

- Currently on:
- Tacrolimus 3mg BD
- Mycophenolic acid 360mg BD
- Prednisone 10 mg OD
- Septrin 960mg OD
- Isoniazid 300mg OD
- Pyrazinamide 25mg OD
- Nifedipine 40mg BD.

PURE RED CELL APLASIA (PRCA)

Clinical syndrome defined by the absence of mature erythroid precursors in an otherwise normo-cellular bone marrow

Essentials of Haematology. Shirish M Kalkawthar. JP Medical Ltd, Dec 2012

Causes

- Infections – Parvovirus, HCV, HBV, HIV

Author	Year	Location	n	findings
Egbuna et al	2006	USA	8	38%
Park JB et al	2009	Korea	143	23.5%
Bertoni et al	1997	Italy	63	6.3%
Carraturo et al	2012	Italy	64	4%
Zolnourian et al	2000	UK	110	1.8%

- Drugs – azathioprine, isoniazid, mycophenolate, azathioprine
- Hematological malignancies – Large Granular Lymphocytic Leukemia, B and T cell CLL

- Auto-immune disorders – RA, SLE, Type 1 DM
- Thymoma - 1-5% of PRCA patients[1]

1. TK Lahiri et al. Pure red cell aplasia associated with thymoma. Indian Journal of chest diseases and allied sciences. 2002, Vol 44.

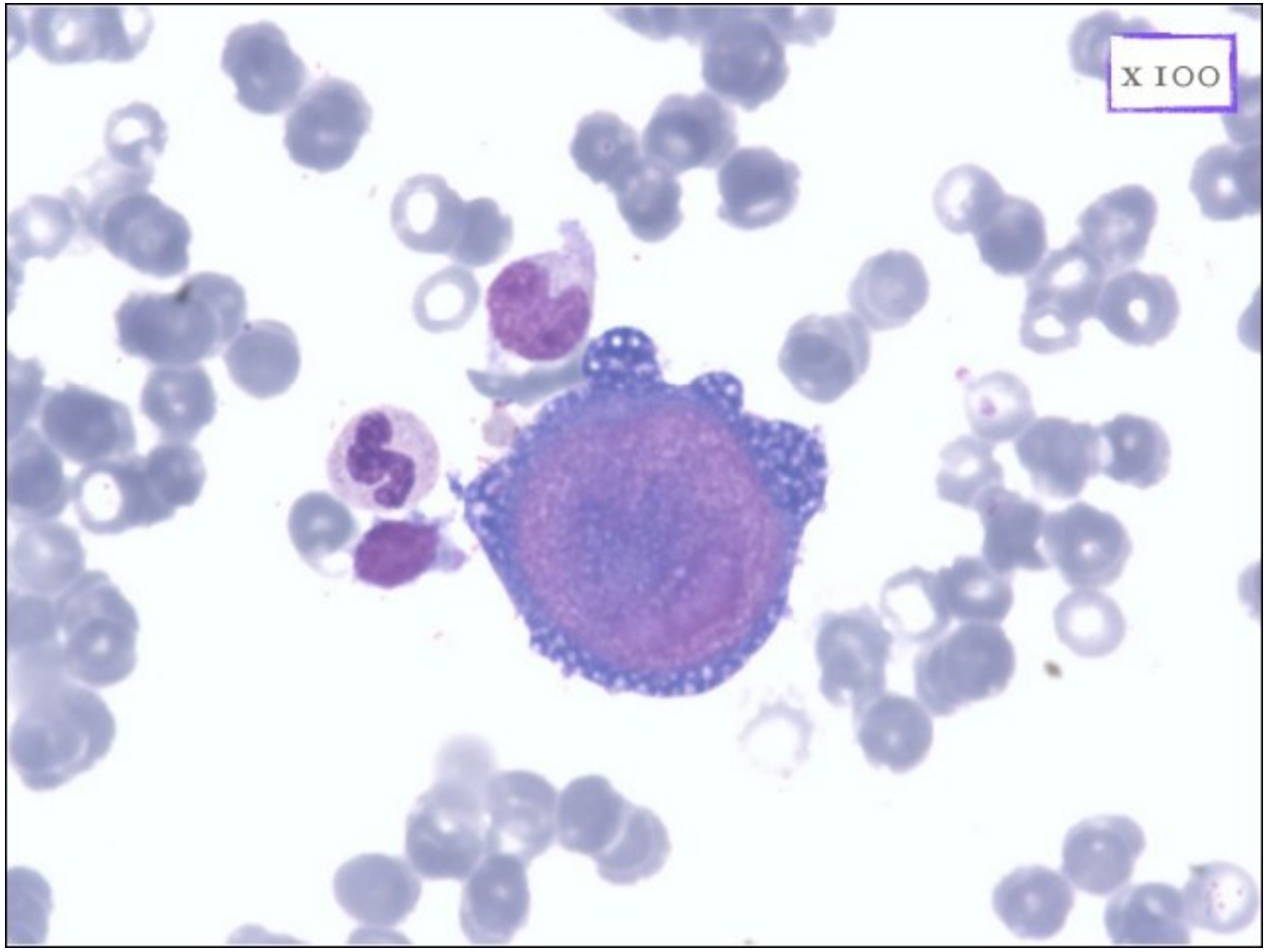
- Anti-erythropoietin antibodies – occurs in 27/100,000 among CKD pts

- Common with ePo alfa

- Treatment

- Long term outcomes of individuals with PRCA and ePo antibodies in patients treated with recombinant ePO: a follow up report from the Research on Adverse Drug Events and Reports (RADAR) project. CL Bennet et al. Blood, 15 Nov, 2005. Vol 106 No 10

BMA



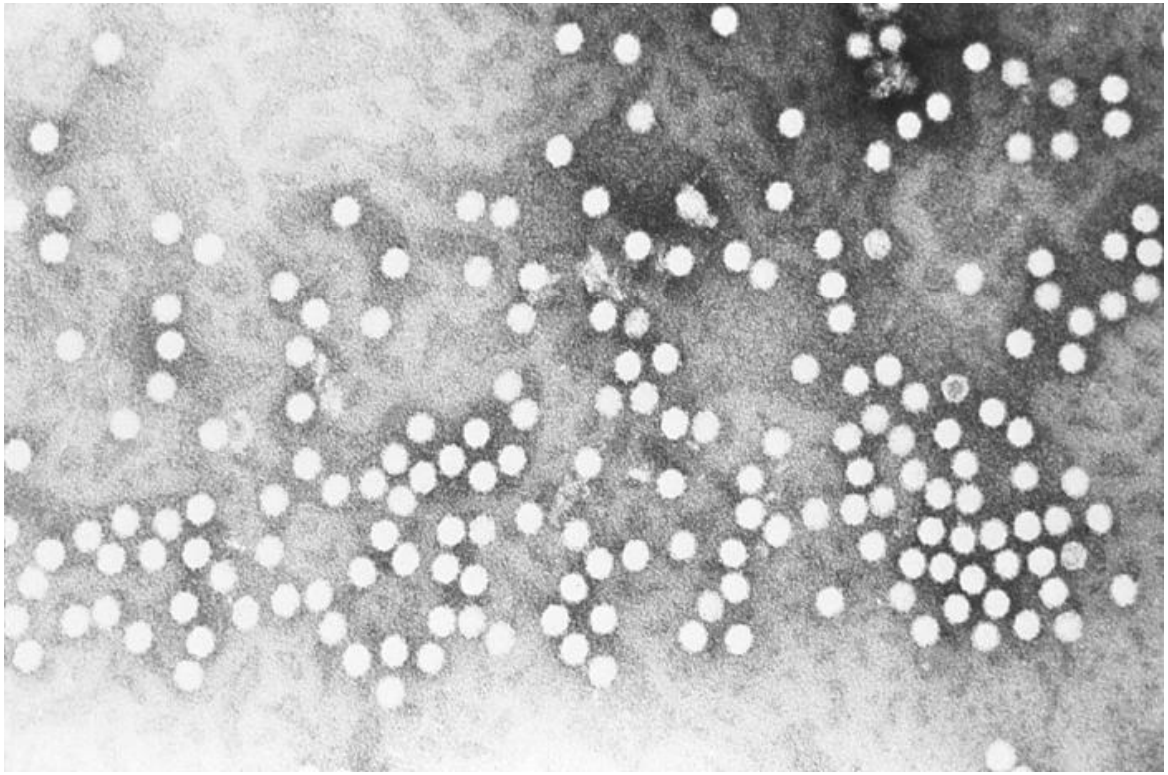
- M:E ratio is 5:1
- Erythropoiesis is reduced with presence of giant erythroblasts that are vacuolated and have intranuclear inclusions.
- Late forms of the erythroid series are reduced
- Granulopoiesis is normal.
- Megakaryocytes are increased and show activity.

- Plasma cells and lymphocytes are within normal limits.
- No foreign cells or parasites seen.
- Stainable iron is absent

Comment:

- Features are suggestive of parvovirus infection. This may be compounded by iron deficiency

PARVOVIRUS



Parvovirus B19

- Infection is global
- Common in childhood and antibody seroprevalence increases with age

Sources of infection

- Respiratory droplets
- Nosocomial infections – 30% among HCW [1]
- Blood products -
- Vertical transmission – 33% infected mothers [2]
- Through a donor organ – Incidence 2% [3]

1. Human Parvo Virus B19 Infection among Hospital Staff Members after Contact with Infected Patients. LM Bel et al. N Engl J Med 1989; 321:485-491

2.Bulletin 13. Parvovirus B19 and pregnancy. State of Alaska

3. Paravirus B19 infection: diagnosing and treating a kidney transplant patient. LR Leon et al. Nefrologia 2010;30(6):704-704

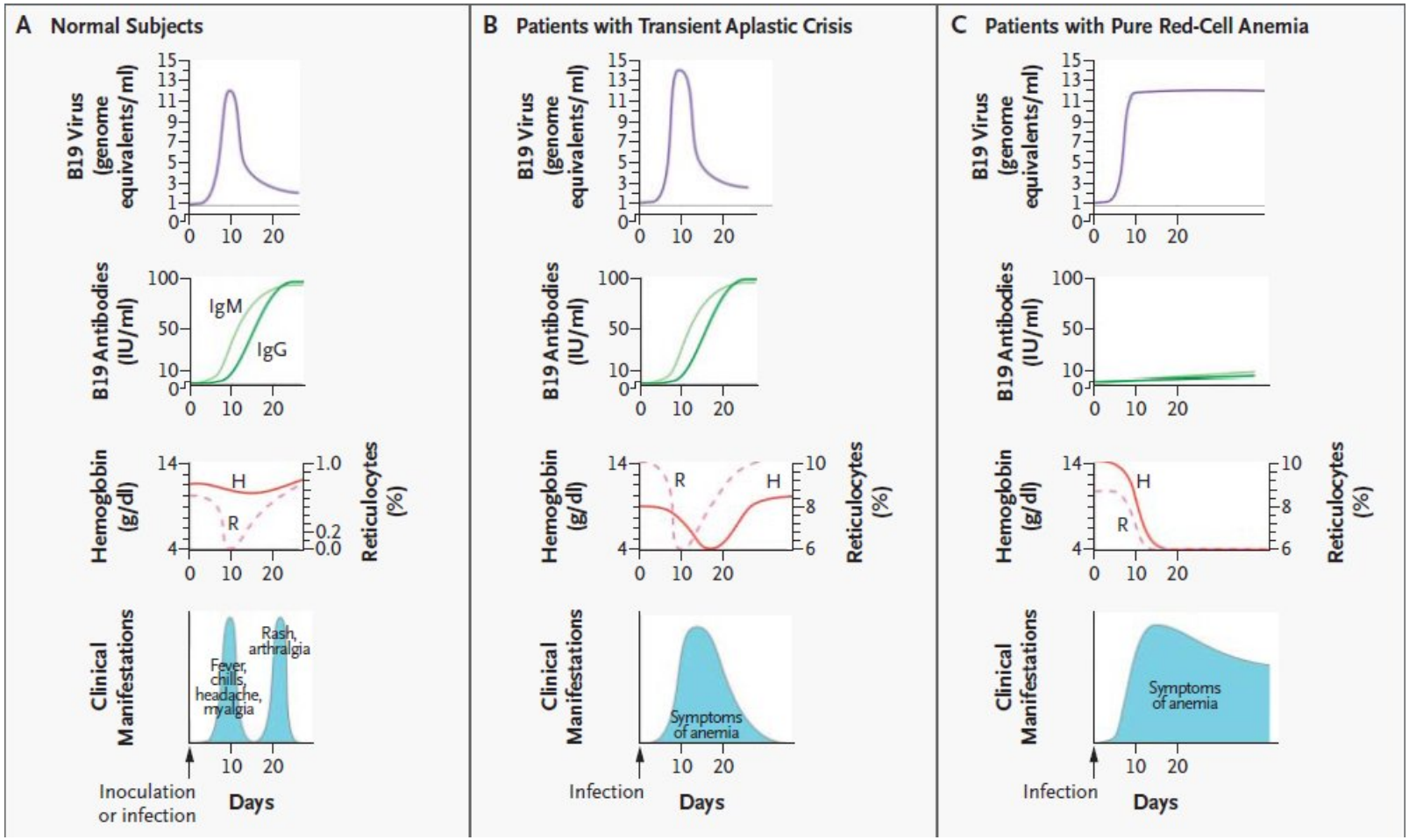
Presentation

Table 1. Major Diseases Caused by Parvovirus B19.

Disease	Acute or Chronic	Host
Fifth disease	Acute	Normal children
Arthropathy	Acute or chronic	Normal adults
Transient aplastic crisis	Acute	Patients with increased erythropoiesis
Persistent anemia	Chronic	Immunodeficient and immunocompromised patients
Hydrops fetalis and congenital anemia	Acute or chronic	Fetus

Mechanisms of disease: Parvovirus B19. NS Young et al. NEJM. 2004;350: 586-97

Pathophysiology



Mechanisms of disease: Parvovirus B19. NS Young et al. NEJM. 2004;350: 586-97

Diagnosis

- BMA is characteristic
- PCR is required to confirm diagnosis
- Bone marrow PCR is more sensitive than blood [1]

1. Intravenous Immunoglobulin Therapy for Pure Red Cell Aplasia Related to Human Parvovirus B19 Infection: A Retrospective Study of 10 Patients and Review of the Literature. Y Crabol et al. CID 2013:56

Treatment

- No antiviral therapy approved
- IV immunoglobulin at dose of 0.4g/kg body weight for 5-10days

Prevention

Vaccine

Volume 31, Issue 37, 20 August 2013, Pages 3872–3878

Generation of a parvovirus B19 vaccine candidate

Sumana Chandramouli[a], Angelica Medina-Selby[b], Doris Coit[b], Mary Schaefer[a], Terika Spencer[a], Luis A. Brito[a], Pu Zhang[a], Gillis Otten[a], Christian W. Mandl[a], Peter W. Mason[a], Philip R. Dormitzer[a], Ethan C. Settembre[a,]

Consequences of treatment vs no treatment

No treatment

- Spontaneous cure -8% [1]
- Persistent infection leads to glomerulopathy:

a) FSGS
b) Collapsing glomerulopathy
c) Endocapillary proliferative glomerulopathy [2]

- Persistent anemia with frequent transfusion

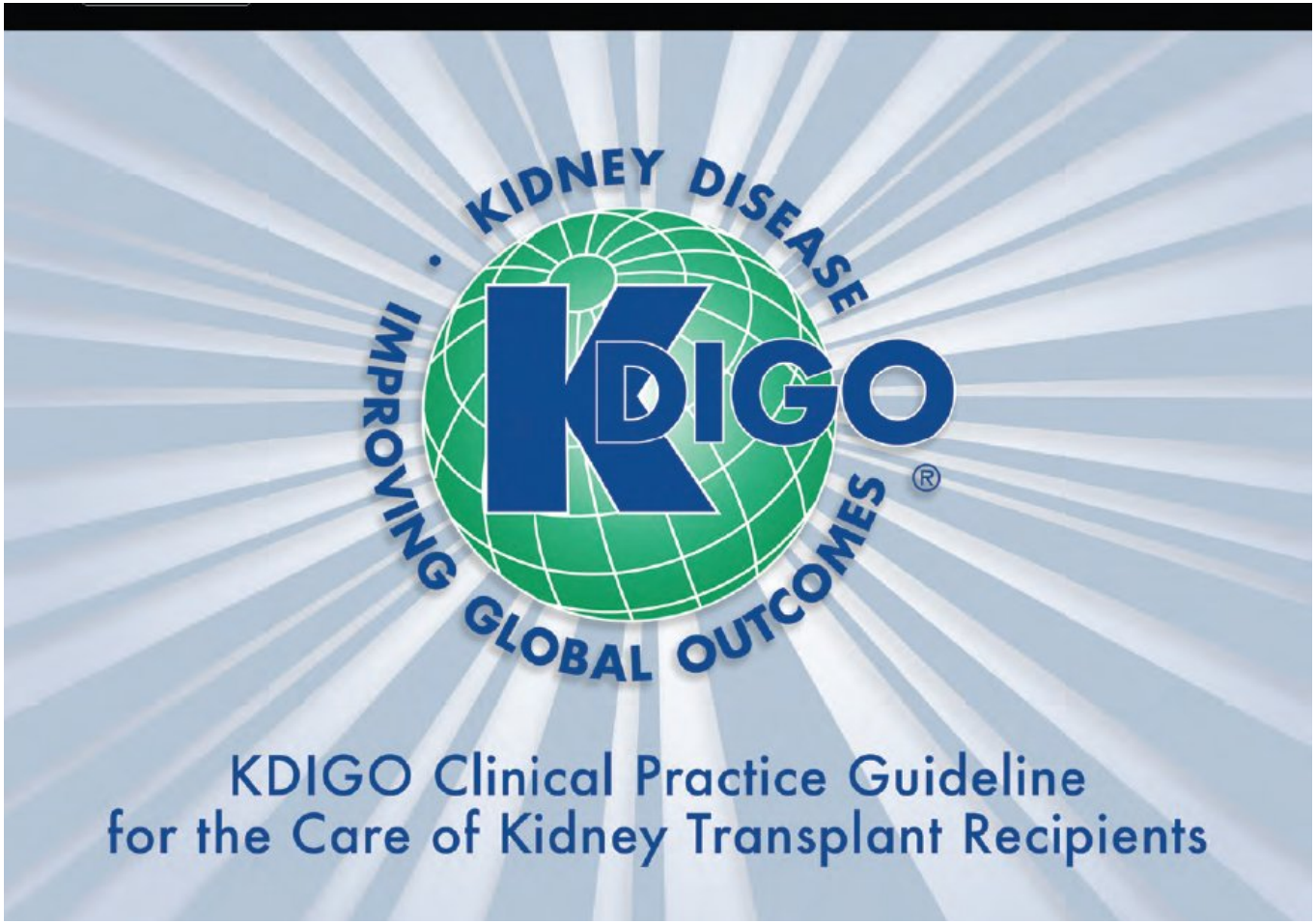
- 1. Intravenous Immunoglobulin Therapy for Pure Red Cell Aplasia Related to Human Parvovirus B19 Infection: A Retrospective Study of 10 Patients and Review of the Literature. Y Crabol et al. CID 2013:56
- 2. Treatment of Parvovirus B-19 (PV B-19) Infection Allows for Successful Kidney Transplantation Without Disease Recurrence. NR Barsoum et al. *American Journal of Transplantation 2002; 2: 425–428.*

Treatment

- Cost
- Nephrotoxic effect of IVIG [1]
- 34% show relapse in 4.3 months [1]
- Switch from tacrolimus to cyclosporine

- 1. Intravenous Immunoglobulin Therapy for Pure Red Cell Aplasia Related to Human Parvovirus B19 Infection: A Retrospective Study of 10 Patients and Review of the Literature. Y Crabol et al. CID 2013:56

Screening


KIDNEY DISEASE
IMPROVING GLOBAL OUTCOMES
KDIGO
KDIGO Clinical Practice Guideline
for the Care of Kidney Transplant Recipients

ACKNOWLEDGEMENTS

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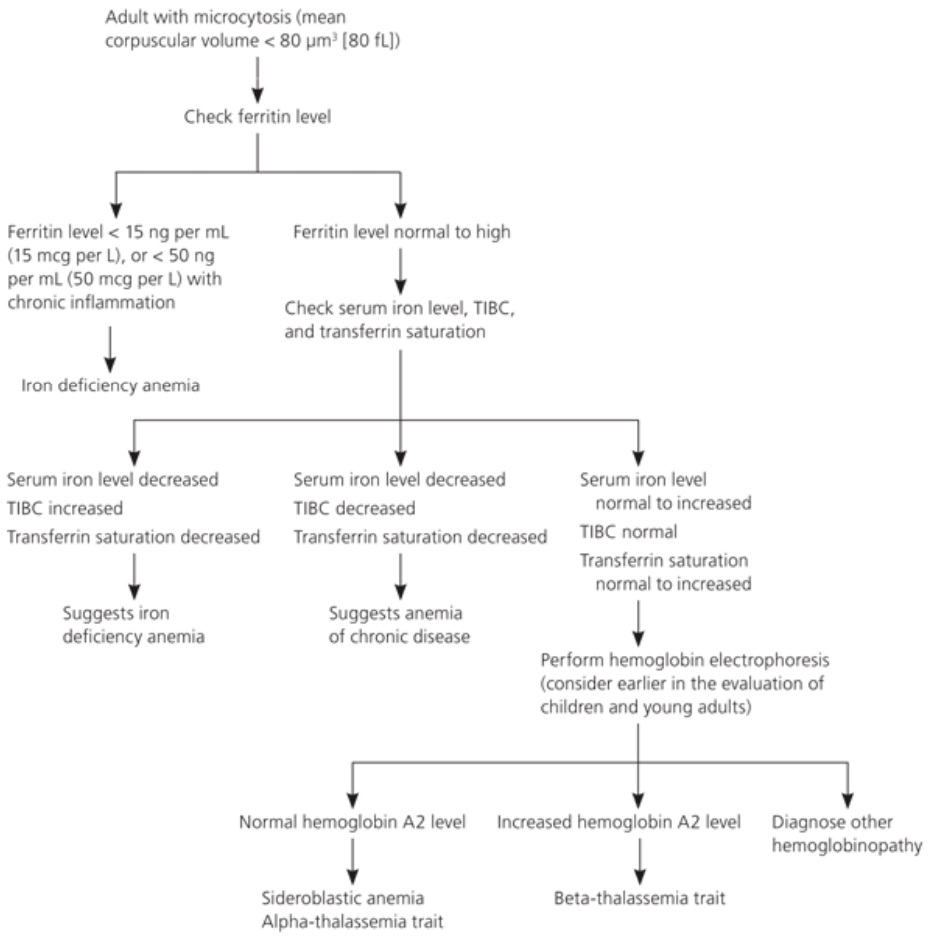
- Dr Rajab
- Dr MD Maina
- Prof Kayima
- Nancy Wang’ombe

"Without the organ donor, there is no story, no hope, no transplant. But when there is an organ donor, life springs from death, sorrow turns to hope and a terrible loss becomes a gift."
- UNOS

References

- Mechanisms of disease: Parvovirus B19. Neal S. young and Kevin E Brown. NEJM 2004;350:586-97
- Long term outcomes of individuals with PRCA and ePo antibodies in patients treated with recombinant ePO: a follow up report from the Research on Adverse Drug Events and Reports (RADAR) project. CL Bennet et al. Blood, 15 Nov, 2005. Vol 106 No 10

- Essentials of Haematology. Shirish M Kalkawthar. JP Medical Ltd, Dec 2012
- Uptodate version 19.3


Adult with microcytosis (mean corpuscular volume < 80 μm³ [80 fL])
Check ferritin level
Ferritin level < 15 ng per mL (15 mcg per L), or < 50 ng per mL (50 mcg per L) with chronic inflammation
Iron deficiency anemia
Ferritin level normal to high
Check serum iron level, TIBC, and transferrin saturation
Serum iron level decreased
TIBC increased
Transferrin saturation decreased
Suggests iron deficiency anemia
Serum iron level decreased
TIBC decreased
Transferrin saturation decreased
Suggests anemia of chronic disease
Serum iron level normal to increased
TIBC normal
Transferrin saturation normal to increased
Perform hemoglobin electrophoresis (consider earlier in the evaluation of children and young adults)
Normal hemoglobin A2 level
Sideroblastic anemia
Alpha-thalassemia trait
Increased hemoglobin A2 level
Beta-thalassemia trait
Diagnose other hemoglobinopathy