refractory anaemia: a case study

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Background perspective

• FA, 10yr old ♂, orphan, NGO-based care
• 2001: diagnosed at 2yrs old, symptomatic
  HAART initiated: ZDV/3TC/RTNV
  re-HAART: ZDV/3TC/EFZ
• 2007: treatment failure (v/load-5.39; CD4-9%)
  changed HAART to d4T/3TC/KAL
• 2009: lipodystrophy, switched to ZDV/3TC/KAL
21/4/2011

history
• cough + lethargy x 4/7
• pale looking x 2/7

vital signs
• BP: 96/50; HR: 86; RR: 30
• afebrile
• hydration - moist oral mucosa
• perfusion: capillary refill time<2s, pulse volume √
Physical findings:

- Bilateral perforated tympanic membrane
- Cervical lymph nodes
- Soft, non tender
- No ascites
- Liver: 1cm
- Spleen: not palpable
- Apex: 4th LICS medial to MCL
- ESM at ULSE 2/6
- Pale
- Mildly jaundiced
- No pedal edema
diagnosis

- Retroviral disease on 2\textsuperscript{nd} line HAART
- Anemia
investigations

FBC
- WBC : 4.23 x 10⁹/L
- Hb : 3.2 g/dL
- MCV : 91 fL
- MCHC : 31.6 g/dL
- MCH : 28.8 pg
- Plat : 522 x 10⁹/L
- retic % : 0.18

others
- RP : normal
- LFT : normal
- TSB : normal
- LDH : normal
<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Reference Range</th>
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<tbody>
<tr>
<td>Ferritin</td>
<td>660 ug/L</td>
<td>(22 – 322)</td>
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<tr>
<td>Iron</td>
<td>42 umol/L</td>
<td>(11 – 28)</td>
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<tr>
<td>TIBC</td>
<td>43 umol/L</td>
<td>(52 – 77)</td>
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<td>Folate</td>
<td>14 nmol/L</td>
<td>(&gt; 12)</td>
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<tr>
<td>B 12</td>
<td>395 pmol/L</td>
<td>(156 – 672)</td>
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### Infectious serology

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<tr>
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<th>Result</th>
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<tbody>
<tr>
<td>Mycoplasma</td>
<td>-ve</td>
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<tr>
<td>EBV</td>
<td>IgG +ve</td>
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<td></td>
<td>IgM -ve</td>
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<td>CMV</td>
<td>IgG +ve</td>
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<td></td>
<td>IgM -ve</td>
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<tr>
<td>Hep Bs Ag</td>
<td>-ve</td>
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<tr>
<td>Hep C Ab</td>
<td>-ve</td>
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</tbody>
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### Others

- Stool occult blood: -ve
• FBP

severe anemia
normochromic, normocytic cells
thrombocytosis
poor reticulocyte response
Q1 Why is he anemic?

- A : HIV related chronic illness
- B : nutritional cause
- C : drug induced
- D : infection/inflammation
Discussion 1

• A
  Anemia’s common in adv HIV disease with normochromic, normocytic picture:
  -↓erythropoiesis
  -HIV infection of marrow progenitor cells

• B
  usually due to Fe, B12 folate ↓ - poor nutrition or small bowel function.
  FBP: hypochromic, microcytic or macrocytic megaloblastic picture
Discussion 1

• **C**
  ZDV-most common cause (1/3 of pts by 6/52 of Rx) antimicrobial/viral- PCP prophylaxis with TMP/dapsone; gangcylopir

• **D**
  Infections- esp in adv disease
  MAC, TB, histoplasmosis, cryptococcus.
  EBV, hepatitis B, mycoplasma, CMV(colitis-GIT blood loss)
  Malignancies- lymphoma
CLINICAL PROGRESS

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<td>Adm.</td>
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- Pallor 2/7
- Cough 4/7

AZT-induced Anemia

- HAART changed to
  - Kaletra
  - Didanosine
  - Lamivudine

Hb
- 3.2
- 5.3
- 5.8
- 9.7
CLINICAL PROGRESS

AZT-induced Anemia

Hb  3.2  5.3  5.8  9.7  5.7

Date  21/4  22/4  23/4  25/4  25/5
Adm.  D/C  Adm

Pallor 2/7
Cough 4/7

HAART changed to
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### CLINICAL PROGRESS

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<thead>
<tr>
<th>Date</th>
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**Hb**
- 3.2
- 5.3
- 5.8
- 9.7
- 5.7
- 9.1
- 11.8
- 7.4
- 7.2
- 6.7
- 3.4

**Notes:**
- **Pallor 2/7**
- **Cough 4/7**

**HAART changed**
- Kaletra
- Didanosine
- Lamivudine

**Cough 2/52**
- Pallor 4/7
- Conjunctivitis 2/7
- Atypical Pneumonia

**Electively admitted for transfusion**

**Giddy**

**AZT-induced anaemia**
Q2 What further tests?

• A just observe & treat symptomatically

• B investigate for causes not considered before

• C do invasive test/s
Discussion 2

• A
serial post transfusion
Hb’s were improving.
He’ll get better eventually
with expectant care!

• B
Logical!
Hbs aren’t getting better
Blood for C+S
Serology for infections/
inflammations

• C
It’s time to do a
BMA/trephine biopsy!
CLINICAL PROGRESS

Date 21/4 22/4 23/4 25/4 25/3 25/5 26/5 16/6 17/6 21/6 22/6 5/7 6/7 12/7
Hb 3.2 5.3 5.8 9.7 5.7 9.1 11.8 7.4 7.2 6.7 3.4 11.4
Adm. D/C Adm D/C Adm D/C Adm D/C Adm D/C Adm D/C
Pallor 2/7 Cough 4/7
HAART changed
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Cough 2/52 Pallor 4/7 Conjunctivitis 2/7 Atypical Pneumonia
Electively admitted for transfusion
Parvovirus IgM +ve
BMA
IVIG IVIG

Giddy
Further investigations

- Negative results for C+S/ serology for TB/fungal/CMV/EBV/Mycoplasma

- Parvovirus B19 serology: IgM +ve
Bone marrow aspiration

- Erythroid Precursor
- Histiocytes
- Megakaryocytes
- Eosinophils
- Lymphocytes

NORMAL

PURE RED CELL APLASIA
• Erythroid precursor markedly reduced
• Reduced granulopoiesis/ megakaryopoiesis
• No evidence of leukemia/ intra-cytoplasmic organisms
• Increased macrophages (AFB/fungal culture negative)
Final Diagnosis

Chronic Anemia $2^0$ to Pure Red Cell Aplasia due to Parvovirus B19 infection in a child with underlying retroviral disease
ANEMIA IN HIV PATIENTS

↓
RBC Production

HIV infection
Drugs
Infection
Infiltration-Neoplasm

↑
RBC Destruction

Hemolysis
Auto Ab
DIVC
Haemophagocytic syn

≠
RBC Production

Nutritional Deficiency
Malabsorption
Pediatric Causes of Acquired Pure Red Cell Aplasia

- **Infections**
  - Parvovirus B19, EBV, Mumps, Hepatitis, Mycoplasma, etc
- **Immunologic**
- **Autoimmune**
  - SLE, JCA
- **Oncologic**
  - Lymphoma, ALL
- **Drugs/Toxins**
  - Antibiotics, Anticonvulsants
Parvovirus B19

- Single stranded DNA
- Virus binds to blood group P antigen
- P antigen is found on
  - Erythroid precursors
  - Megakaryocytes
- discovered by chance in 1975
Parvovirus B19 in immuno-suppressed patients

May be absent
Lack of immunological response
Failure to mount Ab response
Chronic PVB19 infection
Chronic Anemia
PVB19 serology may be negative
DNA PCR more sensitive
IVIG : neutralizing antibody against PVB19
Q3 Parvovirus B19 red cell aplasia treatment modalities in RVD patients?

• A regular symptomatic blood transfusion

• B IVIG infusion

• C HAART
Discussion 3

• A Patient may need serial/regular blood transfusion to tie over the anemic period

• B In resource limited settings, this modality is expensive, patient may require repeated infusions although side-effects are rare. Relapse of anemia can occur(30%)

• C HAART initiation will restore immune function & cause resolution of anemia
FA’s serial hemoglobin parameters (post treatment)

Δx at 1 yr old $^+$

↓Hb/Parvovirus+

ddI/3TC/Kal

Retic count %

0.5 1.0 1.5 2.0 2.5

12 yr

POSHE
FA’s progress

- CD4
  - %: 40, 35, 30, 25, 20, 15, 10, 5, 0
  - nmbr: 800, 700, 600, 500, 400, 300, 200, 100, 0
- Viral load
  - 12 yr

- Δx at 1 yr old
- ↓Hb/Parvovirus+
- ddI/3TC/Kal
- AZT/3TC/Efz
- d4t/3TC→Cmbvr/Kal
- defaulted

- Undetectable limit <20

POSHE
Lesson pearl

• in a child with HIV infection presenting with refractory anemia and poor reticulocyte response;
• pure red cell aplasia secondary to parvovirus B19 infection needs to be considered.