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 26\textsuperscript{th} 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 5<sup>th</sup> 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

<table>
<thead>
<tr>
<th></th>
<th>20.5.14</th>
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<tbody>
<tr>
<td>WBC</td>
<td>6.49</td>
</tr>
<tr>
<td>RBC</td>
<td>2.47</td>
</tr>
<tr>
<td>Hb</td>
<td>6.08</td>
</tr>
<tr>
<td>Hct</td>
<td>18</td>
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<tr>
<td>MCV</td>
<td>72.7</td>
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<tr>
<td>MCH</td>
<td>24.6</td>
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<tr>
<td>Plt</td>
<td>549</td>
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<tr>
<td>K</td>
<td>5.12</td>
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<tr>
<td>Na</td>
<td>138</td>
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<tr>
<td>Creat</td>
<td>115</td>
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<tr>
<td>Urea</td>
<td>3.7</td>
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<tr>
<td>eGFR</td>
<td>73</td>
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<tr>
<td>Tac</td>
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**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

Causes

- Infections – Parvovirus, HCV, HBV, HIV

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Location</th>
<th>n</th>
<th>findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egbuna et al</td>
<td>2006</td>
<td>USA</td>
<td>8</td>
<td>38%</td>
</tr>
<tr>
<td>Park JB et al</td>
<td>2009</td>
<td>Korea</td>
<td>143</td>
<td>23.5%</td>
</tr>
<tr>
<td>Bertoni et al</td>
<td>1997</td>
<td>Italy</td>
<td>63</td>
<td>6.3%</td>
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<tr>
<td>Carraturo et al</td>
<td>2012</td>
<td>Italy</td>
<td>64</td>
<td>4%</td>
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<tr>
<td>Zolnourian et al</td>
<td>2000</td>
<td>UK</td>
<td>110</td>
<td>1.8%</td>
</tr>
</tbody>
</table>
• 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

• Anti-erythropoietin antibodies – occurs in 27/100,000 among CKD pts
  - Common with ePo alfa
  - Treatment

• 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
• Blood products -
• Vertical transmission – 33% infected mothers
• Through a donor organ – Incidence 2%

Table 1. Major Diseases Caused by Parvovirus B19.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Acute or Chronic</th>
<th>Host</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fifth disease</td>
<td>Acute</td>
<td>Normal children</td>
</tr>
<tr>
<td>Arthropathy</td>
<td>Acute or chronic</td>
<td>Normal adults</td>
</tr>
<tr>
<td>Transient aplastic crisis</td>
<td>Acute</td>
<td>Patients with increased erythropoiesis</td>
</tr>
<tr>
<td>Persistent anemia</td>
<td>Chronic</td>
<td>Immunodeficient and immunocompromised patients</td>
</tr>
<tr>
<td>Hydrops fetalis and congenital anemia</td>
<td>Acute or chronic</td>
<td>Fetus</td>
</tr>
</tbody>
</table>

Diagnosis

• BMA is characteristic
• PCR is required to confirm diagnosis
• Bone marrow PCR is more sensitive than blood

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

Generation of a parvovirus B19 vaccine candidate

Consequences of treatment vs no treatment
No treatment

• Spontaneous cure -8% 
• Persistent infection leads to glomerulopathy:
  a) FSGS
  b) Collapsing glomerulopathy
  c) Endocapillary proliferative glomerulopathy
• 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
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

KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients
ACKNOWLEDGEMENTS

• Dr Andrew Odhiambo
• 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


• 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

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