High Fever, Cytopenia and Hepatosplenomegaly in HIV patient on ART

INFECTIOUS DISEASES CLINIC

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History

- A 35 year male labor worker from Dungarpur, Rajasthan presented with
  - Fever, high-grade with rigor

- Past History:
  - HIV +ve since 2003
  - On presentation had H/O LNTB, Incomplete AKT
  - Lost to follow-up from 2003 to NOV 2008
  - Worked in Kuwait for 2 years before 10 years

Presenting Illness

- On presentation
- Fever with chills
- Anorexia
- Weight loss (3 kg)
- Weakness
- No GI/GU/Respiratory/Musculoskeletal complaints
- He was off ART except he took Tab Duovir for 2 – 3 days

1 Month

Physical examination

- Vitals: Normal
- Pallor ++, Dehydration ++
- No palpable lymph nodes
- Hepatosplenomegaly (both 1 finger below costal margin, soft, non-tender)
- RS, CVS, CNS: NAD

Investigations

- HB:**7.1** gm%, TC: **13,200**/cmm, DC: 67/26/1/6/0, PC:2.23 lacs
- SGPT: **81** IU/L, Bilirubin:**1.98/.74/1.51mg**%, S.ALK: 195IU/L, LDH: **2636** IU/L
- Bl.urea: **145.2**mg%, S.creat**: 4.9**mg%, Na+:132 meq/dl, K+: 4.23meq/dl, Ca++:4.88mg%, S.uric acid: 5.58 gm%,
- CD4: 234 cells/cmm
- Urine: 2-3 pus cells, **albumin+**
- X-ray chest: NAD
- USG Abdomen: **Bilat. Mild renal disease, sludge filled GB, minimally enlarged spleen**

Differential diagnosis

- Cause of Fever
  - ? Tuberculosis
  - Bacterial Infections/ GNB infection
- Renal failure:
  - ?pre-renal
  - HIV associated renal disease
  - Secondary to Sepsis
- Anemia:
  - Hemolysis
  - Nutritional
  - Chronic Infection

Treatment

- Hospitalized and Hydration
  - IV fluid/ oral hydration
- Antimicrobials
  - IV ceftriaxone
  - Oral Fluconazole
  - TMP-SMX
- Supportive therapy (B12, folic acid, multivitamine)
- Later on transfused 2 PCV before discharge
- Patient improved over period of one week

Lab FU

ART Started

Parameter	10/11/08	14/11/08	17/11/08	26/11/08	13/1/09
Hb	7.1	6.4	10.3	10.7	10.0
TC	13,200	2760	4640	3010	5900
DC	67/26/1/6/0	65/24/1/5/0	78/15/4/1/	45/37/2/6	34/55/4/6
PC	2.23	1.47	1.32	1.09	1.61
SGPT	81	35		22	24
Alop4	195	135			
S.Creat	4.9	4.0	2.9	2.11	.96
LDH	2636			963	

Follow Up

- ARV (d4T+3TC+EFV) started on 26/11/08
- Patient was better at first follow up
- Occasional fever (once in 7-10 days, low grade)
- S. Creatinine remained normal

Final Diagnosis

- Bacterial Infection with Sepsis and prerenal azotemia with Anemia (Chronic disease/Nutritional) in HIV infected patient

Clinical course on ART

- **Tolerated ART well, no complaints**
- **Came for follow up unscheduled visit on 2/2/09** (After 2months and 8 days of ART)
- **Fever, high-grade with rigor - 5 days**
- No cough, chest pain, body ache, headache, abdominal pain, diarrhea, vomiting, dysuria
- PE:
  - Temperature: + nt, Pulse: 96/min, BP: 110/70 mmHg
  - Pallor +++
  - Liver; +1 finger
  - Spleen: 6 finger below costal margin, firm to hard & non tender
  - RS, CVS, CNS: NAD
  - No rash/petechie/ no lymphadeopathy

Clinical impression

- P. falciparum Malaria
- Acute viral infection ?? Not sure
- IRD: TB (Unusual and late; baseline CD4: 234 cells/cmm, 2 months and 8 days after ART)
- Chronic liver Disease with Portal HT? or Splenic/Portal Venous thrombosis
- Hematological malignancies

Investigation

- HB:**6.1** gm%, **TC: 760/cmm**, DC: 34/47/7/1/9, PC:1.15 lacs, Reticulocyte count: **5.79**%
- Urine: 5-6 pus cells, **albumin+**
- SGPT: 23 IU/L, Bilirubin:**1.56/.56/1.0mg**%, S.ALK: **839** IU/L, S.protein: **5.4/2.4/3.0gm%**
- S.creat: **1.24**mg%, Na+:134 meq/dl, K+: 4.1meq/dl, LDH: **20856** IU/L, S.Ferritin: **15592**
- CD4: **57** cells/cmm
- CRP: **170** mg%
- X-ray chest: NAD
- USG Abdomen: Hepatosplenomegaly, fatty liver, fluid filled colon

Clinical summary

HIV +ve patient on cART for 2 months presented with sudden onset high-grade fever with anemia, leucopenia and hepatomegaly and massive splenomegaly

Differential diagnosis

- Marrow Suppression:
  - Drug toxicity (TMP/SMX, d4T)
  - Marrow Infections (B19 Parvo, CMV, MAC, disseminated TB other systemic fungal infections)
  - Nutritional deficiency
- P. Falciparum Malaria
- Treatment failure & HIV disease progression (Patient took Duovir for 2 -3 days prior to current ART)
- Leukemia/lymphomas
- HPS

Treatment

- Rehospitalized
- IV Ceftriaxone & IV Metronidazole
- IV leucoverine 15mg, IV Optineuron
- S/C Neupogen 300µg
- PCV transfusion
- Supportive treatment

Hospital course

- Patient continue to spike very high-grade fever not responding to paracetamol
- Received neupogen for 2 days
- Hematologist involved and Bone marrow biopsy done

Follow up Lab reports

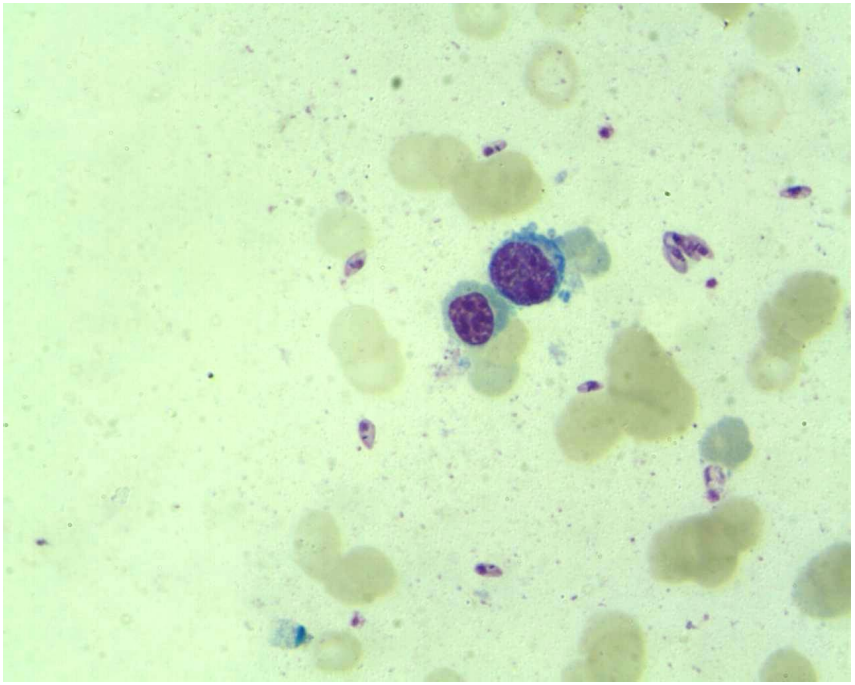
Parameter	2/2/09	3/2/09
Hb	6.1	5.6
TC	760	1030
DC	34/47/7/1/9	47/36/8/2/5
PC	1.15	1.2
SGPT	23	
Alop4	839 (7X ULN)	
S.Creat	1.24	
LDH	20,856	
Ferritin	15,592	TG: 220

Bone marrow biopsy

- Hypocellular marrow
- Myeloid hypoplasia
- Erythroid series: megaloblastoid erythroid maturation with delayed hemoglobinization
- Megakaryocyte: Adequate
- Iron adequate

Bone marrow biopsy: Contd.

- RE activity is increased with presence of intracellular and extracellular organisms
  - ? Histoplasma
  - ? Leishmania :
- Pathologist was confident about diagnosis of Leishmaniasis
- Trephine Bx report awaited



Visceral Leishmaniasis

Point against the Dx

- Never visited Endemic area, worked at Kuwait for 2 years before 10 years and lived at Dungarpur, Rajasthan

In Favour of Dx

- Cytopenia, fever
- Massive splenomegaly
- Organisms with features of amastigote forms of leishmania

Hospital course

- Started treatment with Ampho B 35mg/day
- From 2nd day increased to 40mg/day (S.creatinine: Normal)

Parameter	2/2/09	3/2/09	6/2/09	8/2/09
Hb	6.1	5.6	10	10.1
TC	760	1030	850	1050
DC	34/47/7/1/9	47/36/8/2/5	61/28/2/2/1	43/45/6/1
PC	1.15	1.2	90,000	94,000
SGPT	23			
Alop4	839			
S.Creat	1.24		0.94	
LDH	20,856			
Ferritin	15,592	TG: 220		

Follow up on Ampho B 23/2/09

- Patient received Ampho B at Hospital for 5 days and took another 10 days at Dungarpur
- Good clinical response, Afebrile
- Spleen regressed to 3 finger below costal margin
- Total 20mg/kg total dose received

Follow up lab reports

23/2/09

- HB:10.3 gm%, **TC: 1850/cmm**, DC: 40/41/7/2/1, PC:2.15 lacs,
- SGPT: 25 IU/L, S.ALK: **318** IU/L,
- S.creat: 0.89mg%, K+: 4.1meq/dl
- LDH: **781** IU/L, S.Ferritin: **1725**
- CRP: **16.8** mg%

Visceral Leishmaniasis in HIV

- Facultative intracellular pathogen
- Transmitted by sandfly bites
- Over 90% of cases of VL occur in five countries: India (especially the Ganges and Brahmaputra plains), Bangladesh, Nepal, Sudan, and northeastern Brazil
- Over 20 species of leishmania
- *Leishmania donovani* is the primary cause of visceral leishmaniasis in the Indian subcontinent and East Africa
- *L infantum* in the Mediterranean region, and *L chagasi* in the New World
- Reservoir:
  - Human beings are the only known reservoir of *L donovani*
  - Canines, especially domestic and stray dogs reservoir for *L infantum* and *L chagasi*

Visceral leishmaniasis in HIV

- Not commonly described in AIDS patient
- Risk factors: malnutrition, immunosuppressive drugs and HIV co-infection
- Co-infected patients may be difficult to diagnose, respond poorly to treatment and relapse repeatedly
- Involve liver, spleen and bone marrow
- Presenting features:
  - Fever, cough, abdominal pain, diarrhoea, epistaxis, splenomegaly, hepatomegaly, cachexia, and pancytopenia
  - Peripheral lymphadenopathy is common in some foci

Diagnosis

- Demonstration of the parasite
- Intracellular leishmania can be identified or cultured from aspirates of spleen, bone marrow, lymph node or liver
- Diagnostic yield is highest, about 98%, for spleen aspirates
- Serologic tests
- PCR

Treatment

- Pentavalent 20 mg/kg daily for 20–40 days
  -resistance, toxicity, cost
- Amphotericin B 7–20 mg/kg total for up to 20 days
  - toxicity, IV use, effective for visceral form
- Lipid preparations of Ampho B
  - Cost, effective for visceral form
- Miltefosine 100 mg/day for 4 weeks
  - Oral form, not US FDA approved, not effective against all species

Thank you