



# Clinical Pearls



# A Young Boy with Fever and Hepato-splenomegaly



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- A 14-year-old boy
- From Norshindi, Bangladesh
- Admitted on 26<sup>th</sup> October, 2014, in BSMMU Hospital
- For evaluation of his fever
  - ✓ Duration: 1 month
  - ✓ Intermittent, daily
  - ✓ Peak 104°F
- Anorexia, malaise, fatigue
- Weight loss (5 KGs in 1 month)





- No organ-specific symptoms
- No significant past medical history
- Not travelled recently





- Before admission, locally treated with
  - ✓ Co-amoxiclav 375 mg TID for 4 days
  - ✓ Azithromycin 500 mg BID for 10 days
  - ✓ Ceftriaxone 1 gm BID for 5 days
  - ✓ Chloroquine, course completed
  - ✓ Quinine, course completed



- No clinical improvement
- No adverse effect





- Physical examination
  - ✓ Moderate anaemia
  - ✓ Temperature 102°F
  - ✓ Stable vitals
  - ✓ Hepatomegaly (3 cm)
  - ✓ Splenomegaly (20 cm)
- NO
  - ✓ Peripheral lymphadenopathy
  - ✓ Bony tenderness
  - ✓ Ascites

- 
- All other systemic examination:

Normal

# Initial Investigations

- Complete Blood Count
  - ✓ Hb: **8 gm/dl**
  - ✓ RBC:  $3.04 \times 10^{12}/L$
  - ✓ TC: **1,800/cmm**
    - ✓ N: 35%, L: 58%, M: 7%
  - ✓ Platelets:  **$100 \times 10^9/L$**
- PBF: Pancytopenia
- ESR: **05 mm in first hour**



# Initial Investigations...

- Liver function test
  - ✓ Serum Bilirubin: T- 43.3  $\mu\text{mol/L}$ , **D-33  $\mu\text{mol/L}$**
  - ✓ ALT: **202 U/L**
  - ✓ AST: **160 U/L**
  - ✓ Alkaline Phosphatase- **220 U/L**
  - ✓ Serum albumin: **24 gm/L**
  - ✓ LDH: **911 U/L**
  - ✓ PT: 15.6 sec (control 11-16)
  - ✓ INR: 1.31
  - ✓ APTT: 47.3 sec (control 20-40)

# Initial Investigations...

- USG of whole abdomen
  - ✓ Hepatomegaly with hypo-echoic parenchyma and prominent peri-portal echo, suggestive of hepatitis
  - ✓ **Huge splenomegaly**
- Chest x-ray P/A view: Normal skiagram

# Initial Investigations...

- Urine R/M/E: Normal
  - Blood C/S: No growth of bacteria
  - Urine C/S: No growth of bacteria
- } After discontinuation of antibiotics
- ICT for malaria: Negative
  - ICT for Kala-azar: Negative

# Initial Investigations...

- Bone Marrow Study
  - ✓ Normal, active marrow

# Hospital Course

- Remained febrile with very high peak (105°F)
- Repeat examination
  - ✓ Icteric (mild)
  - ✓ Pulse: 94/min
  - ✓ BP: 90/60 mm Hg

# Hospital Course...

- Started broad spectrum antibiotics
  - ✓ Meropenem 1 gm TID
- Normal saline infusion
- Remained febrile
- Added Fluconazole 100 mg OD

# Further investigation

- Liver function test
  - ✓ T. bilirubin: **64.4  $\mu\text{mol/L}$**
  - ✓ ALT: **150 U/L**
  - ✓ ALP: **874 U/L**
  - ✓ PT: 15.6 sec (control 11-16)
  - ✓ INR: 1.31
  - ✓ APTT: 47.3 sec (control 20-40)
  - ✓  $\text{NH}_3$ : 46  $\mu\text{g/dl}$
- Serum electrolytes
  - ✓ Na: **127 mmol/L**
  - ✓ K: 4.2 mmol/L
  - ✓ Cl: 98 mmol/L
  - ✓  $\text{TCO}_2$ : 22 mmol/L
  - ✓  $\text{Ca}^{2+}$ : 8.3 mg/dl
- Uric acid: 3.2 mg/dl
- RBS: 5.8 mmol/L
- S. creatinine: 0.7 mg/dl

# Further Investigation

- Complete Blood Count
  - ✓ Hb: 8.3 gm/dl
  - ✓ TC: **1,500/cmm**
  - ✓ Platelet: **30,000/cmm**
- Fibrinogen: 146 mg/dl



# Further Investigation...

- Chest x-ray: Normal skiagram
- CT scan of whole abdomen
  - ✓ **Huge hepatosplenomegaly**
  - ✓ **Abdominal lymphadenopathy**  
(peri-portal & pre-pancreatic)
  - ✓ Mild ascites

# Further Investigation...

- Bone marrow trephine biopsy
  - ✓ Partly hypoplastic
  - ✓ In other parts: normocellular
  - ✓ No granuloma or malignancy seen.
- BM sent for mycobacterial and fungal culture
  - ✓ Fungal culture: No growth

# Further Investigation...

- HBsAg & Anti-HCV: negative
- Endoscopy of upper GIT
  - ✓ Bulb of duodenum shows deep irregular ulcer on posterior wall with few tiny nodules.
  - ✓ Post bulbar area is normal.
  - ✓ *Possibility of lymphoma cannot be excluded*
  - ✓ *D/D: TB*
- Biopsy from ulcer margin:
  - ✓ Chronic gastritis with intestinal metaplasia

# Hospital Course...

- Condition was deteriorating
- Started gum bleeding
- Developed spontaneous bruising & ecchymosis

# Further Investigation...

- Complete Blood Count
  - ✓ Hb: **6.5 g/dl**
  - ✓ TC- **1,500/cmm**
    - ✓ N-72% , L- 19%, M- 8%
  - ✓ Platelet: **15,000/cmm**
- Reticulocyte count: 2.17%
- ESR: **05 mm** in first hour
- Repeated transfusion of PRBC & platelet concentrate

# Hospital course & Further Investigation...

- Serum electrolytes
  - ✓ Na: **123 mmol/ L**
  - ✓ K: 3.5 mmol/L

# Further Investigation...

- Bone marrow trephine biopsy sent for review
  - ✓ Trilineage haematopoiesis
  - ✓ Patchy 30-60% cellularity
  - ✓ Focal megakaryocytes clustering fair number of tingible body macrophage
  - ✓ Scattered epithlioid-like cells
  - ✓ NO evidence of malignancy
  - ✓ *Comment: Granulomatous lesion should be excluded*

# Further Investigation...

- **Fasting Lipid Profile**
  - ✓ Total cholesterol: 289 mg/dl
  - ✓ HDL: 5 mg/dl
  - ✓ LDL: 244 mg/dl
  - ✓ TG: 459 mg/dl
- **Plasma fibrinogen:** 110 mg/dl
- **Serum ferritin:** 11022 ng/ml



# Further course...

- Patient decided to continue further management abroad
- Discharged with
  - Suspicion of **Haemophagocytic lymphohistiocytosis**
  - Further plan to go for laparoscopic lymph node biopsy

# Course abroad

- Review of BM slide
  - ✓ Mildly hypercellular marrow
  - ✓ mild erythroid hyperplasia
  - ✓ increase in RE activity
  - ✓ few **Haemophagocytes**
- Repeat BM trephine biopsy
  - ✓ Normocellular marrow
  - ✓ **Ring granuloma & foci of Haemophagocytosis**
  - ✓ No AFB in cultures & PCR
    - Sent for Brucella and CMV PCR

# Clinical course abroad...

- Lymph node biopsy
  - ✓ Sinus histiocytosis
  - ✓ Focal **Haemophagocytosis**
  - ✓ No evidence of lymphoma  
(Immunohistochemistry done)

# Course abroad...

- ANA: negative
- C3, C4: normal
- HIV: negative
- Anti-EBV-Ig M: negative
- Widal and WELL-FELIX: negative

# Final Diagnosis



- **Haemophagocytic lymphohistiocytosis**

# Course abroad...

- Treated with antibiotics and Injectable Methylprednisolone
- Plan to start chemotherapy
- Condition gradually deteriorated
- He ultimately succumbed to his disease

