Multi drug resistant Kala-azar – is it really present?

Dr. Habib Ahmed
Indoor Medical Officer
Department of Medicine
Dhaka Medical College Hospital
Particulars of the Patient

Name – Mr. Surja Hajon
Age - 35 years
S/O – Mr. Okul Ritchil
Sex - Male
Occupation - Farmer
Marital status – Married
Religion - Christian
Date of admission - 24 Nov. 2007

Address:
Village - Magonti Nagar
P.O. - Jolchotra
Upazilla - Modhupur
District - Tangail
Source of referral - Medical Officer (Disease control), Modhupur Thana Health Complex, Modhupur, Tangail
Source of history - Patient
Presenting Complaints

- Fever – 3 years
- Generalized weakness – 3 years
- Mass in abdomen – 5 months
- Loss of appetite – 5 months
- Loss of weight – 5 months
History of Presenting Complaints

- Reasonably well 3 years back
- Developed intermittent fever with peak of temperature in the morning and evening
- Associated with chills and rigors
- Not subsided after taking antipyretic.
- Not associated with vomiting, cough, haemoptysis, chest pain or burning sensation during micturation or abdominal pain, impaired consciousness or convulsion
- Developed generalized weakness and unable to continue his job.
3 months following fever he was diagnosed as a case of Kala-azar by ICT for the first time at the Modhupur Upazilla Health Complex.

Treated with injection sodium stibogluconate for 20 days.

Fever subsided and he remained well for about one year.

After one year he again developed same pattern of clinical features and was again treated with injection sodium stibogluconate for 20 days
History of Presenting Complaints contd…. 

- Remained well for another year and then he developed features as before. This time he was treated with Miltefosine capsule 50mg, twice daily for 28 days and became well.

- About 5 months after completion of treatment with Miltefosine he noticed a mass in the left upper abdomen which was gradually increasing in size but was not painful.

- Developed loss of appetite and significant weight loss this time.
History of Past Illness

- No history of Jaundice, Diabetes Mellitus and Hypertension or Tuberculosis, previous surgery or travel to Malaria endemic area.
- No history of previous hospitalization

Treatment History

- Injection Stibatin – for two occasions, first time 3 years back and the other 2 years back. Duration of treatment was 20 days on each occasion
- Capsule Miltefosine, 50mg twice daily – 1 year back for 28 days.
Family History

- Parents are alive with good wellbeing
- Married for 15 years
- Two daughters and two sons
- One brother, three sisters
- None of his family members suffered from similar illness.
Personal History

- Ex-Smoker, smoked 2 pack years for 4 years.
- Occasional alcohol drinker (Traditional)
- Abstained from smoking and drinking alcohol for the last three years
Socio-economic History

- Low socio-economic condition.
- Lives in tinshed mud house with cracks and crevices in the wall of the house.
- Cow shed and poultry shed about 08 feet away from the house.
- Drinks tube well water.
- Uses sanitary latrine.
History contd.

- **H/O Immunization**

  Complete immunization according to EPI schedule.
General Examination

- Appearance – ill looking
- Co-operative & conscious
- Weight - 47 kg
- Nutritional status – average
- BMI – 20 kg/m²
- Decubitus – on choice
- Anaemia (++)
- Jaundice – absent
- Oedema – absent
- Dehydration – absent
- Pulse – 84 beats/min, regular in rhythm and normal in volume.
- BP – 120/70 mm Hg
- Temperature - 100°F
- R/R – 15 breaths/min
- Clubbing – absent
- Koilonychia - absent
- Leuconychia – absent
General Examination contd.

- Skin condition – normal
- Hair – normal distribution
- Stigmata of CLD – absent
- Splinter haemorrhage - absent
- Cyanosis – absent
- Bony tenderness - absent
- Thyroid gland – not palpable
- Lymph nodes – not enlarged
- Neck veins – not engorged
Alimentary System Examination

- Mouth and oral cavity – normal

Abdomen Proper

Inspection

- Abdomen is slightly distended
- Flanks are normal
- Umbilicus centrally placed and inverted
- No scar marks or engorged veins
- No visible peristalsis or no visible impulse.
- Hair distribution is normal.
Alimentary System
Examination...Abdomen Proper

**Palpation**

- Superficial palpation – no tenderness, palpable mass in the left hypochondriac region of the abdomen

- Deep palpation –

**Liver:**

- Enlarged, 3 cm from right costal margin at the mid clavicular line, non tender, border is sharp, surface is smooth, firm in consistency, moves with respiration, upper border of liver dullness was in right fifth intercostal space.
- **Spleen**
  - Enlarged, 12 cm from left costal margin along its long axis, non tender, firm in consistency, border is rounded, surface is smooth, notch is palpable, moves with respiration and dull on percussion

- **Para aortic lymph node**
  - Not palpable

- **Percussion**
  - Ascites is absent, evidenced by negative shifting dullness.

- **Auscultation**

- Bowel sound is normal.

- There is no renal bruit, no hepatic bruit and no splenic rub.
Other Systemic Examination Revealed No Objective Abnormality
Mr. Surja Hajon, 35 years old, smoker, normotensive, alcoholic, poor farmer hailing from Magonti Nagar, Jolchotro, Modhupur, Tangail was admitted in Dhaka Medical College Hospital on 24 Nov. 2007 with the complaints of intermittent fever & generalized weakness for three years, loss of appetite, loss of weight and left sided abdominal mass for 5 months. Fever was associated with chills and rigors and was not subsided by taking antipyretics. There was rise of temperature in the morning and in the evening. He was diagnosed as a case of Kala-azar in Modhupur.
Thana Health Complex and was treated with injection Sodium Stibogluconate for two occasions and with capsule Miltefosine for one occasion with an interval of one year between them. Inspite of treatment with Sodium Stibogluconate and Miltefosine his symptoms reappeared and he was referred to Dhaka Medical College Hospital. On admission, he was febrile and anaemic. He was non icteric non oedematous and no lymphadenopathy. His pulse was 84 beats/min, regular, BP was 120/70 mm of Hg, temperature was 100°F, R/R was 15 breaths/min. Examinations of the abdomen revealed hepatosplenomegaly. All other systems revealed no objective abnormality.
Provisional Diagnosis

Treatment failure Kala-azar.
Differential Diagnosis

Malaria

Haemolytic anaemia with Kala-Azar

Kala-Azar, reinfection case,

Lymphoma
## Investigations...Complete Blood Count

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<tr>
<th>Date</th>
<th>Hb%</th>
<th>TC (mm$^3$)</th>
<th>DC (%)</th>
<th>TPC</th>
<th>ESR (1st hr)</th>
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TPC = 80,000

TPC = 189,000
Urine for R/M/E on 25.11.07

Physical Examination

Chemical Examination

Microscopic Examination

No abnormality

S. Creatinine

02/12/07 – 1.1 mg/dl

12/12/07 – 1 mg/dl

24/12/07 – 1.2 mg/dl

RBS on 25.11.07

3.93 mmol/l
Peripheral Blood Film – ON 09/12/07

Anisochromia with anisopoikilocytosis

Plenty of thick target cells and Spherocytes

Increased rouleaux formation

WBC are mature with normal count.

Neutrophil decreased in distribution.

Platelets are reduced.
Hb Electrophoresis

**ID:** 311516  
**Name:** Surja Hazam  
**Ref. By:** MU-1, Green (DMCH)  
**Sex:** F  
**Age:** 35 y  

**Hb Capillary Electrophoresis**

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<thead>
<tr>
<th>Name</th>
<th>%</th>
<th>g/dl</th>
<th>Normal Values %</th>
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<tr>
<td>Hb F</td>
<td>3.0</td>
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<td>Hb E</td>
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<td>Hb A2</td>
<td>5.3</td>
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**Comments**
Suggestive of Hb E disease.

MD. MASHIUL AZAM  
B.Sc.(Hons) M.Sc. (Biochem)  
Consultant Biochemist  
Popular Diagnostic Centre
## Investigations...L.F.T.

<table>
<thead>
<tr>
<th>Date</th>
<th>Test</th>
<th>Result</th>
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<tr>
<td><strong>On 24/11/07</strong></td>
<td>Prothrombin time:</td>
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<td>Control – 13 sec</td>
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<td>Patient – 14 sec</td>
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<td>Prothrombin index – 92.85 %</td>
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<td>Patient ratio – 1:1.07</td>
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<td>INR – 1.1</td>
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<td><strong>On 02/12/07</strong></td>
<td>Total protein – 99 gm/l</td>
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<td>Albumin – 35 gm/l</td>
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<td>Globulin – 64 gm/l</td>
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<td>A G ratio – 0.5:1</td>
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<td>Serum Bilirubin – 1.6 mg/dl</td>
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<td>SGPT – 10 U/l</td>
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Investigations...L.F.T.

**On 12/12/07**
- Total protein – 110 gm/l
- Albumin – 45 gm/l
- Globulin – 65 gm/l
- AG ratio – 0.7:1
- Serum Bilirubin – 1.6 mg/dl
- SGPT – 10 U/l

**On 08/12/07**
- Serum Bilirubin – 1.4 mg/dl
- SGPT – 10 U/l
ICT for Kala – Azar
On 24.11.07

Positive
CXR & USG of whole Abdomen
Splenic Smear
• ICT Malaria on 25.11.07  
  – Negative.

• Screening Test for HIV on 30.11.07  
  – Negative.

• Culture for Leishmaniasis  
  – Not done.
Confirmatory Diagnosis

Treatment failure Kala-azar with Haemoglobin E disease
Treatment

- Inj sodium stibogluconate 20 mg/Kg body weight daily intravenously for 30 days (started on 27.11.07).

- Two units of whole blood transfusion was given.

- Follow up: clinically by abatement of fever, physical well-being, decrease in size of spleen, increase in weight.
Treatment contd…

- No evidence of complication of treatment: hepatotoxicity assessed by hepatic enzyme and cardiotoxicity like arrythmia, ischaemia etc. evidenced by ECG.
- No myalgia, no arthralgia was present.
# Sodium Stibogluconate (Stibatin) Injection in Kala-azar

Name of the Hospital: DMCH
Regd No.: 45/43/12
Ward/Unit: 
Name: Sujan Hazan
Age: 35 yrs
Contact Address: 

Date of Admission: 24.11.07
Date of Treatment Start: 27.11.07
Date of Discharge: 
Diagnosis By: Bone Marrow, Spleen Puncture
ICT for Kala-Azar

C/F: 
Outcome: Improvement: Clinically By Lab: BM, Spleen Puncture
Others: 

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<th>Followup Chart For Stibatin Injection</th>
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<td>Day &amp; Dose</td>
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শিরার গতি ও তাপমাত্রার চার্ট

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<td>তাপমাত্রা (ফারেনহাইট)</td>
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After 30 days of inj. SAG Treatment

Splenic Smear:
LD body found
Final Diagnosis

Multi Drug Resistant Kala-azar with Haemoglobin E disease

Plan: Amphotericin B injection
Further treatment:

- Following treatment with inj. amphotericin B (1 mg/kg body weight, 15 doses in every alternate day) his splenic smear for LD bodies becomes negative.
Aims of this case report

• Drug resistant Kala azar is gradually increasing with a substantial threat of multi drug resistant Kala azar.

• The efficacy of currently available drugs should be carefully evaluated.

• There should be a search for multi drug resistance in kala azar.
Thank you