62- year-old man presented with-

- High grade continued fever
- Extreme anorexia and vomiting

2 months

# BACKGROUND

On 15th March 2004, presented with-

- severe pain, swelling, marked redness of ears, nose, eyes for 20 days
- pain in the throat
- high grade fever

# Investigations of first episode

- Hb: 7.9 gm/dl
- WBC: 11,500/µl
- Poly: 76%, Lym: 18%, Mono: 3%, Eos: 3%
- Platelet: 1,70,000/µl
- ESR: 150 mm in 1$^{st}$ hour
- ANA and Rose-Waalar test: Negative

- Diagnosed as polychondritis
- He was treated by prednisolone, 40 mg daily
- Features resolved completely over 7 days
- Steroid tapered off to 5 mg/d over next 3 wks

# SECOND EPISODE

- 17th April 2004
- Less severe than previous one
- Treated on outpatient basis by prednisolone 15 mg/d to continue
- Resolved completely

- Minor relapses occurred thereafter at about 3-month intervals
- Managed by temporary increases in the dose of prednisolone

# A MAJOR RELAPSE

- 13th January 2005
- More severe relapse with longer duration
- Methotrexate (7.5 mg weekly) was started along with prednisolone, 40 mg daily
- Partially recovered

# Lab Reports

- Hb: 10 gm/dl
- WBC: 5,000/µl
- Poly: 70%, Lym: 24%, Mono: 2%, Eos: 4%
- Platelet: 1,90,000/µl
- ESR: 140 mm in 1$^{st}$ hour
- Serum creatinine: 1.7 mg/dl
- Blood urea: 40.8 mg/dl

- After 2 months developed severe dizziness, weakness and abdominal discomfort
- Methotrexate was withdrawn
- Prednisolone was continued as 20 mg daily
- Remained well for 2 months

# NEXT RELAPSE

- 6th June 2005
- Cyclophosphamide (100 mg daily) plus Prednisolone (40 mg daily) was started
- Partially responded but residual debility was more than before

# August 2005

- Hb: 7 gm/dl

  WBC: 1,700/µl

  Poly: 78%, Lym: 15%, Mono: 7%, Eos: 0%

  Platelet: 1,30,000/µl

  ESR: 90 mm in 1$^{st}$ hour
- Cyclophosphamide was discontinued

# Late August 2005

- High grade continued fever
- Severe anorexia, vomiting
- Profound weakness
- Generalized aches

# Lab Reports

- Hb: 4.7 gm/dl
- WBC: 13,000/µl
- Poly: 80%, Lym: 10%, Mono: 8%, Eos: 2%
- Platelet: 30,000/µl
- ESR: 160 mm in 1$^{st}$ hour
- Peripheral blood film: anisochromia and anisocytosis, WBCs are mature, reduced platelets

- Treated with-

  - Inj. Ceftriaxon 1 gm i.v. daily for 7 days

  - Oral ciprofloxacin 500 mg daily for 5 days

  - Two units of whole blood transfusion
- No improvement

# IN OUR UNIVERSITY

Admitted on 31 October 2005

# Lab reports

- Blood count (10.11.05):

  Hb: 5.2 gm/dl

  WBC: 7,000/µl

  P: 85%, L: 10%,  M: 3%, E: 2%

  Platelet: 30,000 /µl

  ESR: 160 mm/h

- Peripheral blood film (10.11.05):

  Anisochromia & anisocytosis. WBC mature with neutrophilia. Platelets are reduced

- Blood for MP (08.11.05): Not found
- Blood for CS (9.11.05): No growth
- Urine for RE & CS (02.11.05):

  Albumin: +

  Pus cell: 1-3/HPF

  RBC: 1-2/HPF

  Gr cast: A few/HPF

  CS: No growth
- ECG (11.11.05): Sinus tachycardia

- S. electrolytes (06.11.05, in meq/L):

  Na: 133,  K: 4.3,  Cl: 101,  HCO3: 25
- S. creatinine (06.11.05): 1.1 mg/dl
- ALT (06.11.05): 35 IU/L
- USG of whole abdomen (11.11.05):

  - Mild hepatomegaly

  - Multiple right renal cortical cysts

  - Mild enlargement of prostate (PVR 88 ml)

- Bone marrow study (10.11.05):

  Hypercellular marrow with increased myeloid-erythroid ratio. Erythropoiesis is active with normoblastic features. Granulopoiesis is hyperactive and mature to segmented form. Scanty megakaryocytes. Plasma cells and lymphocytes are mildly raised.

# 13 November 2005

- Methylprednisolone, 1 gm followed by Prednisolone, 60 mg daily
- Total 4 units of whole blood transfusion
- Vomiting stopped. The fever responded initially for 7 days, then recurred as high grade quotidian

# Lab reports

- Blood count (27.11.05):

  Hb: 6.25 gm/dl

  WBC: 8,000/µl

  P: 95%, L: 05%

  Platelet: 30,000 /µl

  ESR: 70 mm/h
- PBF (27.11.05):

  Anisochromia, anisocytosis, significant spherocytes & tear drop cells. WBC mature with neutrophilia. Platelets are reduced

- Blood for CS (27.11.05): No growth
- Urine for RE & CS (24.11.05):

  Albumin: +

  Pus cell: 5-10/HPF

  RBC: 2-5/HPF

  CS: No growth
- Blood for MP (29.11.05): Not found
- S. ferritin (24.11.05): 12322.2 µg/L

- Serum electrolytes (in meq/L):

| | Na | K | Cl |
|---|---|---|---|
| 21.11.05 | 125 | 2.35 | 87 |
| 28.11.05 | 132 | 3.8 | 98.8 |

- Echocardiogram (14.11.05): Mild pericardial effusion (LVEF: 73%)
- Endoscopy of upper GIT (15.11.05): Normal upper GIT
- ECG (27.11.05): Sinus tachycardia

# PROBLEM LIST

What is the cause of

- Fever, weakness and anorexia
  - Infection?
  - RPC itself?
- Anemia and thrombocytopenia
  - Cyclophosphamide?
  - Early MDS?

# Infection?

- No focus identified clinically or at imaging, cultures negative
- Common antibiotics already tried

# Refractory RPC?

- If RPC itself is the cause, it is proving to be refractory to steroid
- Immunosuppressive agents reported effective in RPC, eg., MTX (could not tolerate), cyclophosphamide and AZT are myelosuppressive and thus contra-indicated

# Options?

- Treatment of undetected infection: Combination of antifungal, antibiotic and antiviral agents
- Biological agent (Anti TNF-$\alpha$): anecdotal evidence of efficacy, expensive
- Treatment of marrow failure
  - Cytarabine, considering early MDS
  - Erythropoietin and G-CSF (Filgrastim)

# THANK YOU ALL