PYREXIA OF UNKNOWN ORIGIN
A DIAGNOSTIC DILEMMA

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HISTORY

• 4 years old/female child
• Developmentally normal
• Immunised for age
• No significant past illness

• H/O intermittent fever –1 month
• No other localising symptoms
• Had received multiple oral antibiotics
EXAMINATION

- Febrile, coated tongue.
- Abdomen – mild hepatomegaly.
- TC – 3100 (N 17, L 78), Hb – 9.4, Plat- 2.4L
- ESR - 40 mm/hr
- Blood culture - sterile.
TREATMENT

• Partially treated enteric fever - 5 days of IV Ceftriaxone
• She was afebrile for 24 hours
• Discharged on oral antibiotic (Cefixime) for a total duration of 2 weeks
• Plan was to repeat blood counts at review
FOLLOW UP

• Completed course of oral cefixime
• Persisting fever spikes – 8 weeks duration

• Repeat CBC - Persisting Leukopenia
  (TC – 3100, Hb - 9.4, Plat – 2.4 L)
• Hence she was readmitted for further workup
HISTORY - RELOOK

- H/O poor appetite – even before the illness
- No skin rashes/joint pain/joint swelling
- No H/O loss of weight
- No pallor / clinical bleeds
- No H/O contact with TB
- No H/O recent travel/contact with pets
- No H/O any drug intake
- No H/O surgery in past

Vegetarian by diet – no H/O intake of any raw food
EXAMINATION

- Febrile, not sick looking
- Pallor +
- Painless **Bilateral upper eyelid swelling** was seen
- Glossitis +. No oral ulcers
- No significant lymphadenopathy
- No skin rash/joint swelling/bone tenderness
- BCG scar + (No erythema)
- Systems – mild hepatomegaly
DIFFERENTIAL DIAGNOSIS

- Prolonged viral illness (EBV)
- Enteric fever
- Tuberculosis
- Collagen vascular disease
- Evolving malignancy
- Infection associated HLH
- Immunodeficiency – HIV
WORK UP

- TC - 3,500 cells
- DC - N 40/75, L 34/75, M 01/75
- Hb – 7.6 g/dl
- Platelet – 3.3 lakhs

- Peripheral smear – normocytic normochromic anemia, no evidence of hemolysis, no abnormal cells
- DCT – negative, Reticulocyte count - 1 %
- Serum LDH – 3740 (elevated)

- ESR - 119 mm/hr
• Renal function test - normal

• SGOT - 105 IU/L
• SGPT - 26 IU/L
• Serum albumin – 3.4 g/dl

• ECHO (to rule out Kawasaki disease / infective endocarditis) – Normal
Work up for infective etiology

- EBV VCA IgM – negative
- WIDAL – negative
- Blood & Bone marrow culture – sterile
- Urine microscopy & culture – normal
- CSF analysis was normal
- Scrub typhus IgM – Non reactive
  HIV ELISA - Non reactive
Work up for TB

• ESR – elevated (119mm/hr)

• Mantoux – negative

• CXR – normal

• CT chest – normal. No mediastinal nodes
Work up for malignancy

- Peripheral smear – no abnormal cells
- Bone marrow smear – reactive marrow. No atypical cells.
- USG abdomen – mild Hepatosplenomegaly
- Serum LDH – 3740
Autoimmune workup

• ANA – negative
• ds DNA - negative

Work up for infection associated HLH

• Ferritin – 898
• TGL – 329
• Fibrinogen – 375
Management

- Temperature monitoring
- NSAID - Ibuprofen
- Empirical doxycycline (to cover any atypical organism)
Ophthalmologist consult

‘BILATERAL DACRYOADENITIS’
?ORBITAL PSEUDOTUMOUR
underlying autoimmune disease or chronic infection

Advised CT Orbit/oral steroid
DACRYOADENITIS

- Inflammation of the lacrimal gland
- Acute or chronic
- Acute – Viral / Bacterial
- Chronic – Inflammatory disorders
- C/F: Painful swelling in the region of upper eyelid, fever, watering of eyes

Inv: CT/MRI, Biopsy

Treatment: Rest, warm compresses
ORBITAL PSEUDOTUMOUR

• Idiopathic, nonmalignant orbital inflammation
• Etiology – Not known
  Autoimmune etiology
• Present as a painful, unilateral orbital swelling
• Inv: MRI, biopsy
• Treatment: High dose steroids, immunosuppression, radiotherapy.
THE FINAL CALL

• Parents were given the option of further workup – CT orbit and proceed or to start the child on steroid and look for the response.

• “NO” – For further evaluation
• She was started on oral steroids.
• She was afebrile for 2 days in the hospital.
• Discharged on steroids.
FOLLOW UP

• She was afebrile.

• Eyelid swelling started resolving.
Investigations at follow up

2 weeks after discharge

- TC – 8300 cells/cu.mm, Hb – 7.6g/dl
- Platelet count - 6.4Lakhs/cu.mm
- ESR – 108 mm/Hr
- ECHO (? Kawasaki disease) - normal
Clinical diagnosis

? INCOMPLETE KAWASAKI DISEASE

• Started her on antiplatelet dose of aspirin.

• Advised to review in 2 weeks time.
At review

- Clinically afebrile.
- No new signs or symptoms.

Repeat investigations:
- TC 6600, Hb 10, Platelets 3.3 L
- ESR -24 mm/Hr
- CRP was negative
Possibilities:

• Can still be an incomplete KD, autoimmune disorder or evolving malignancy.

• She needs frequent follow up and re-examinations to make a definitive diagnosis.
ESR >100mm/hr

- Tuberculosis
- Kawasaki disease
- Autoimmune disease
- Malignancy
Baseline
- CBC, ESR, CRP, Peripheral smear
- Mantoux
- Bone marrow smear
- Cultures – blood, urine, CSF, bone marrow

Serology
- Infectious mononucleosis, brucellosis, enteric fever, rickettsial, leptospirosis, lyme’s disease
- ANA, dsDNA, ANCA

Imaging
- Chest x-ray, USG Abdomen, CT chest, whole body MRI, PET
- Bronchoscopy, laparoscopy, mediastinoscopy, GI scopy
TAKE HOME MESSAGES

• Be rationale in investigating a child with PUO.

• Don’t be in a hurry to label the child with a diagnosis.

• Counsel the family.

• YOUR PATIENCE IS ESSENTIAL.

Patience is not the ability to wait, but the ability to keep a good attitude while waiting.