Southern African HIV Clinicians Society

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Our Issues, Our Drugs, Our Patients

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South African HIV Clinicians Society

Managing adult treatment through case study discussion

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Referral summary

- 20-year-old male
- HIV infected, CD4 count = 17cells/mm^3
- Seen at a district hospital
- Problems: loss of weight, loss of appetite and night sweats
- Investigated for mycobacteria tuberculosis
  - GeneXpert: MTB not detected on 2 sputum samples
  - Sputum microscopy (auramine): negative repeatedly
- TDF/FTC/EFV commenced
- He developed jaundice 2 weeks later.

STOP and THINK

What are the considerations?

- Drug induced liver injury secondary to efavirenz
- Immune reconstitution syndrome
  - Viral: Hepatitis B, Hepatitis C, CMV (cholangiopathy)
  - Mycobacterial (TB or NTM)
  - Fungal infections (Histoplasmosis)
- Biliary obstruction due to non-benign process
- Haemolysis

Case

- ART was discontinued
- Referred to tertiary hospital
- Clinical presentation
  - Thin, generalized muscle wasting, ill looking
  - Fever 38°c
  - Alert and cooperative
  - Pale, deep jaundice
  - No peripheral lymphadenopathy
  - Hepatomegaly, liver span 16cm
  - Splenomegaly

Laboratory results

Assay	Result	Assay	Result
Haemoglobin (g/dL)	**7.2**	Bilirubin (umol/L) Conjugated bil	**312** **205**
Mean cell volume (fl)	91	ALT (IU/L)	**58**
Erythrocytes (cells/L)	**1.4×10^{12}**	AST (IU/L)	**153**
Leucocytes (cells/L)	5.7×10^{9}	ALP (IU/L)	**2074**
Platelets (cells/L)	**103×10^{9}**	GGT (IU/L)	**1046**
CD4 count (cells/mm^3)	**9**	HIV viral load (copies/L)	**227 226**

Case summary

- HIV infected patient
- Baseline CD4 count = 9 cells/mm^3
  - Jaundice 2 weeks after commencing ART
  - Bicytopaenia, erythrocytes and platelets
  - Hepatosplenomegaly

STOP and THINK

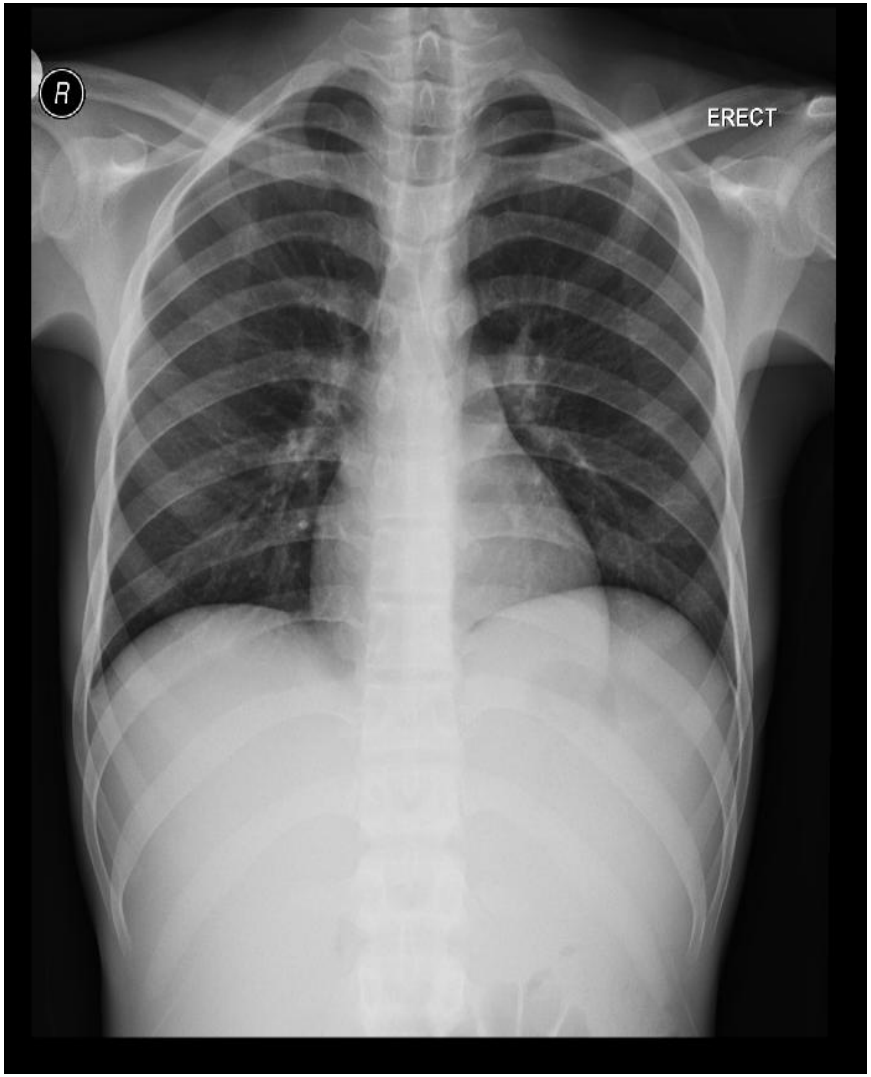
Reasons for the bicytopenia

- Bone marrow infiltration
  - Infective: mycobacterial, fungal
  - Malignant: lymphoma, myeloproliferative disorder
- Sequestration
  - Hypersplenism
- Peripheral destruction
  - Thrombotic thrombocytopenic purpura
  - Platelets low, erythrocytes low

New considerations?

- Lymphoma
- Infective
  - TB or NTM
  - Fungal
- Portal hypertension
  - No features of chronic liver disease
- Drug induced liver injury less likely

Investigations



Investigations

- Ultrasound abdomen
  - Confirming hepatomegaly, increased echogenicity
  - Splenomegaly with splenic hypodensities
  - No dilated bile ducts
  - No lymphadenopathy
  - Small amount of ascites
- Hepatitis B surface Ag negative
- Hepatitis C antibody negative
- CMV IgM negative
- Plan to perform a liver biopsy

Investigations

- Peripheral smear
  - Anisocytosis, scanty polychromasia, mild target cells, scanty schistocytes
  - Leucopenia
  - Adequate platelets
- Reticulocyte count
  - Absolute reticulocyte count = **0.013×10^{12}** (0.05-0.1)
  - Reticulocyte production index = **0.1** (<1 inadequate bone marrow response)

Investigations

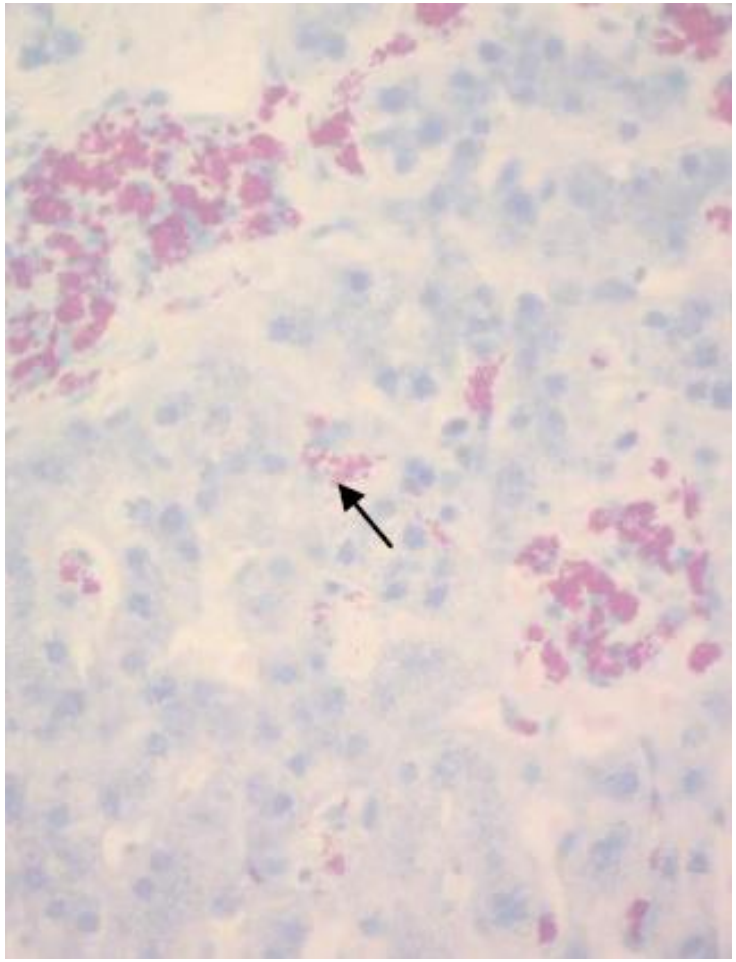
Assay	Results	Normal values
Iron	7.9 umol/L	11.6 – 31.3 umol/L
Transferrin	1.17 g/L	2.15 – 3.65 g/L
Percentage saturation	27%	20 – 50%
Ferritin	5249 ug/L	24 – 336 ug/L

STOP and THINK

Biopsy

- Liver
- Bone marrow

Liver biopsy



- ZN stain multiple AFB
- Poorly formed granuloma
- Culture: MTB antigen test negative

Bone marrow biopsy

- Intracellular clumps of linear bead-like structures are seen within the distorted areas
- Ill-defined area of loosely formed granulomas

Gastroscope and Duodenal biopsy

- ZN stain showed AFB
- Stained with PAS
- Suggestive of NTM

Common Acid Fast Pathogens Found in HIV Infected Hosts.
Consider the following:

(i) all mycobacteria including *M. tuberculosis, M. leprae, and M. avium-intracellulare,*

(ii) *Actinomyces nocardia,*

(iii) *Cryptosporidium parvum,*

(iv) *Isospora belli.*

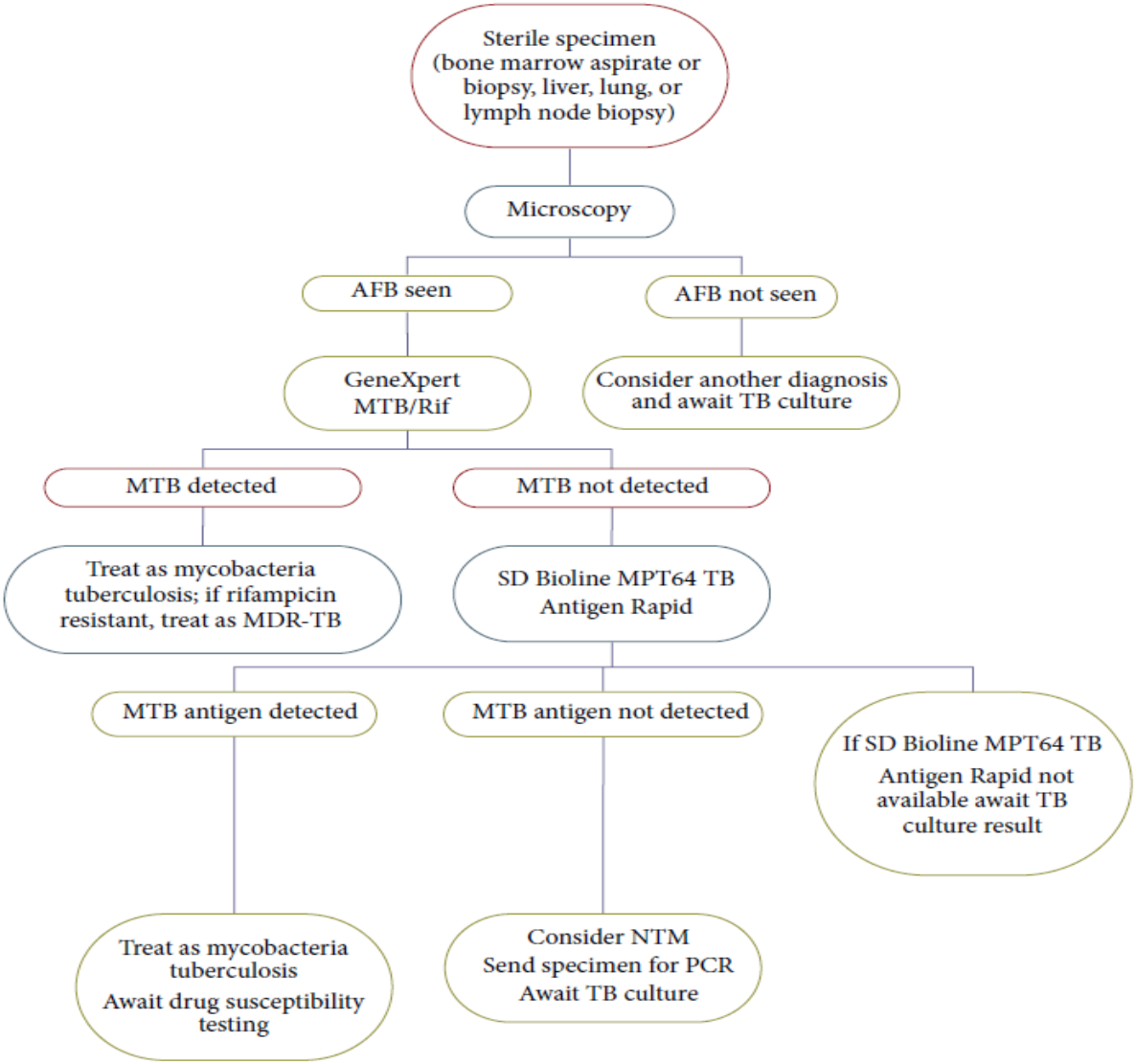


FIGURE 3: Proposed diagnostic algorithm for NTM.

Management?

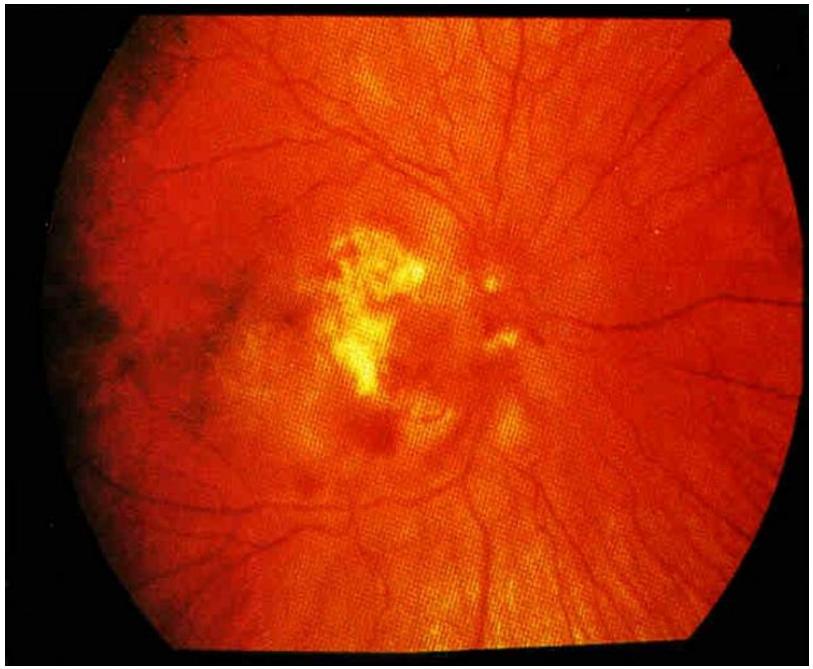
- Rifampicin
- Isoniazid
- Pyrazinamide
- Ethambutol
- Rifafour®
- Clarithromycin

Our management

- Rifafour
- Clarithromycin
- Treated patient for 2 weeks
- Initiated ART, TDF/FTC/EFV
- Patient slowly recovered
- Until…

Case

- Complained of blurring of vision and decreased visual acuity
- CMV PCR positive
- CMV Viral load 1000 copies/mL
- CD4 count = 61 cells/uL (baseline 9 cells/uL)
- Treated for CMV retinitis



Proposed Criteria For Diagnosis of IRS*

- HIV positive
- Receiving HAART :
  - Decrease in HIV-RNA from baseline
  - Increase in CD4 count from baseline (may lag)
- Symptoms consistent with inflammatory process
- Clinical course not consistent with:
  - Expected course of previously diagnosed opportunistic infection
  - Expected course of newly diagnosed opportunistic infection
  - Drug toxicity

* Shelburne et al J Antimicrob Chemother 2006,57:167-170

Conclusion

- High index of suspicion for an opportunistic infection in patients with low CD4 counts
- High index of suspicion for IRS in patients with low CD4 counts
- The drug isn't always the culprit