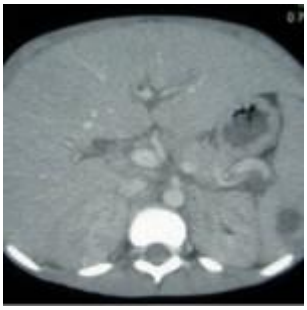
A case of a 10 year old boy with a 3 week history of diarrhoea, vomiting and cough



Patient Presentation

A 10 year old boy presents with a 3 week history of weight loss, diarrhoea, vomiting and a cough. No toxin ingestion has been noted and the family denies any use of traditional medicines.

Acknowledgement

This case study was kindly provided by Dr Bhadrish J Mistry, Paediatrician, Department of Paediatrics, Chris Hani Baragwanath Hospital and the University of Witwatersrand.

History

A 10 year old boy was brought into the emergency department by his mother because she was worried about ongoing diarrhoea for three weeks and vomiting following every meal. As a result he had lost a lot of weight and was extremely thin. She also noted that he was having difficulty walking and sitting up, and his hands would shake as he tried to pick things up. The mother was also worried about an on going cough. Although she had not noted any fever or night sweats and the cough was non-productive, she had been infected with TB one year before. She had completed her treatment and was now sputum negative, but the child had not received any TB prophylaxis at the time and she was worried he may also have TB.

Past Medical History

The mother reported occasional episodes of diarrhoea since age 1 year, which were treated at her local clinic. No other illnesses or hospitalisations were noted.

Birth History

The child was born term, with a normal vaginal delivery- no complications.
He was breast and formula fed, until age 2 years.
The mother does not know her HIV status, and was not treated with Nevirapine at the time of delivery.

Social History

The family live in Soweto in a two bedroom house. There are 4 adults and two older siblings aged 12 and 13, who are all reported as well. Two of the adults are employed and support the household. Water and electricity are available in the home.

Vaccinations

Up to date

Medication

No medication
No history of any traditional medication use (orally or via enema).

Allergies
None known

Differential Diagnosis

- Chronic gastroenteritis
- TB
- Extrapulmonary TB
- Cerebellitis (TB, viral, salmonella)
- HIV

Examination

Vitals

- Heart Rate- 130 beats per minute
- Blood Pressure- 76/52
- Respiratory rate- 22 breaths per minute
- Temperature- 38.0°C

Anthropometry
Severely wasted, weight 60% of expected weight for age (EWA)

General

- Mild pallor
- No jaundice
- No lymphadenopathy
- No oedema
- No dehydration
- No rashes

Cardiovascular
Normal heart sounds, no gallop, no murmurs

Chest

- Not in respiratory distress
- No adventitious sounds

Abdomen

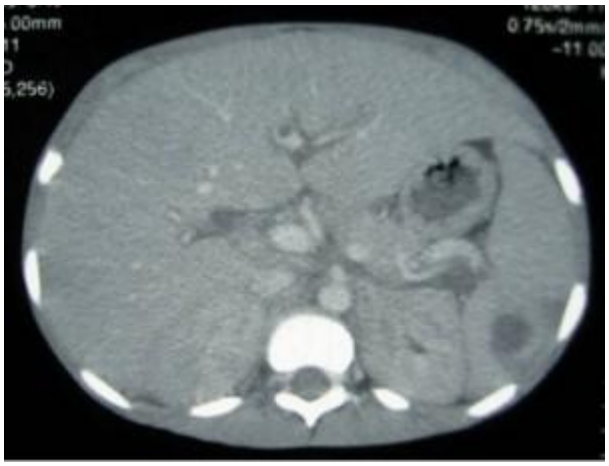
- Not distended, non tender
- No organomegaly
- Normal bowel sounds present

Neurological

- Confused, waxing and waning level of consciousness
- No neck stiffness
- Fundoscopy, no abnormalities detected
- Cerebellar signs
- Truncal ataxia & mild gait ataxia
- No nystagmus
- Intention tremor & past pointing
- Dysdiadochokinesis
- Possible staccato speech
- Bilateral long tract signs
- Increased tone bilaterally, upper limbs and lower limbs
- Brisk reflexes globally but no plantar reflex
- Cross adductors
- No weakness

Intact sensation but positive Romberg sign

Investigations



Values	Normal Limits	
WBC	4.95 (diff 4.6 neutrophils and lymphocytes 0.3)	
HB	9.6999999999999993	(4-12x109/l)
MCV	78.599999999999994	(12.1-15.2 g/l)
Platelets	195	(140-450x109/l)
CRP	110	(<1mg/l)
ESR	84	
NA	123	(135-147 mmol/l)
K	3.3	(3.5-5.1 mmol/l)
CL	84	(95-107 mmol/l)
C02	23	(22-23 mmol/l)
UREA	7.2	(2.5-6.7 mmol/l)
CREAT	53	(70-150 umol/l)
TBIL	14	(3-17 umol/l)
INDIR BIL	1	(0.0-0.3 mg/dl)
TPROT	80	(60-80 g/l)
ALB	34	(35-50 g/l)
ALP	61	(30-150 u/l)
GGT	34	(11-51 u/l)
ALT	23	(5-35 u/l)

Values	Normal Limits	
AST	193	(5-35 u/l)

Lumbar Punch
Protein: 0.25
Glucose: 3.5
Chloride: 112 No cells, culture negative

Blood Cultures:
Negative

Urine Culture:
Negative

PPD
Negative

CT Brain
Mild involutional changes, no space occupying lesions, no raised intracranial pressure.

Chest X-Ray
Hilar lymphadenopathy
No cavitations

The patient was treated empirically with high dose Cefoxatime.

Five days later
Patient still has a fever, he has now developed jaundice and abdominal distension.

Additional Investigations on day 5
Stool MC and S-negative
Widal – Negative
HIV Elisa – Reactive

	Values	Normal Limits
WBC	5.05	
HB	---	(4-12x109/l)

	Values	Normal Limits
MCV	77	(80-96 fl))
Platelets	138	(140-450x109/l)
TBIL	22	(3-17 umol/l)
INDIR BIL	13	(0.0-0.3 mg/dl)
TPROT	66	(60-80 g/l)
ALB	27	(35-50 g/l)
ALP	111	(30-150 u/l)
GGT	65	(11-51 u/l)
ALT	26	(5-35 u/l)
AST	284	(5-35 u/l)

Abdominal Ultrasound

Hepatomegaly, coarse echogenic pattern, no focal lesions.
Splenomegaly, diffuse hypoechogenic lesions with large 2.8 x 1.6 cm hypoechogenic lesion.
Free fluid

Abdominal CT Scan

Hepatomegaly, no focal lesions.
Splenomegaly, 1.45 x 1.62 cm hypoattenuating lesion with no enhanced or thickened wall, no calcifications.
Moderate ascites.Para-aortic & coeliac axis lymph nodes.
Small right pleural effusion.

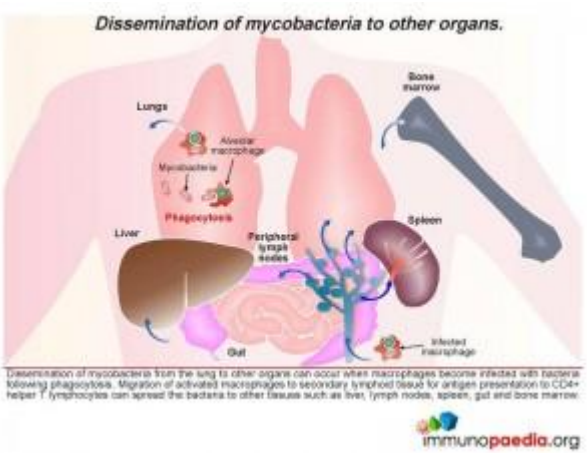
Bone marrow aspirate & trephine

Megaloblastoid features.
Disordered erythropoeisis.
Moderate-severe plasmacytosis – underlying chronic infection.
Ill defined granulomas

Discussion

Splenic tuberculosis although uncommon is considered an important manifestation of abdominal TB, especially in developing countries. Its prevalence is increasing with the epidemic of HIV-TB co-infection and subsequent rise in extrapulmonary TB. To best understand this disease process one has to look at the immunological processes which occur with dissemination of mycobacteria to extrapulmonary sites and HIV dissemination to secondary lymphoid tissue.

Dissemination of mycobacteria from the lung to other organs can occur when macrophages become infected with bacteria following phagocytosis Migration of activated macrophages to secondary lymphoid tissue for antigen presentation to CD4+ helper T lymphocytes can spread the bacteria to other tissues such as liver, lymph nodes, spleen, gut and bone marrow.

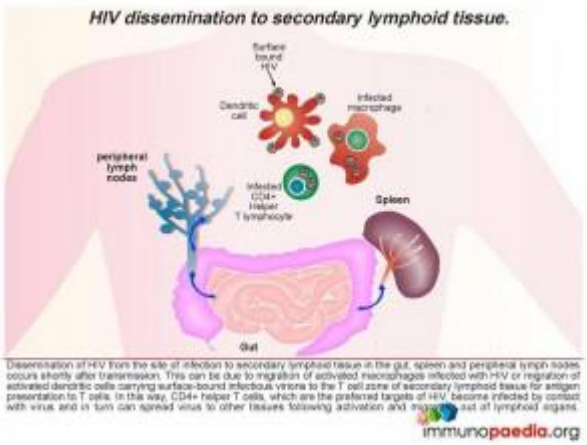


Looking specifically at the spleen which alongside removal of aged erythrocytes has a major function of detecting blood borne antigens entering the organ via arterial blood flow, we see inflammatory responses being initiated. This occurs in the lymphoid tissue known as the white pulp which is rich in lymphocytes and antigen-presenting cells. Foreign antigen is detected here and inflammatory responses become activated. The blood then continues to flow into specialised sinuses called the red pulp where macrophages remove aged erythrocytes by phagocytosis. Macrophages infected with mycobacteria may then enter the spleen and spread bacteria to other macrophages. In HIV infection the immune response to mycobacteria is weakened and bacteria are able to replicate more readily.

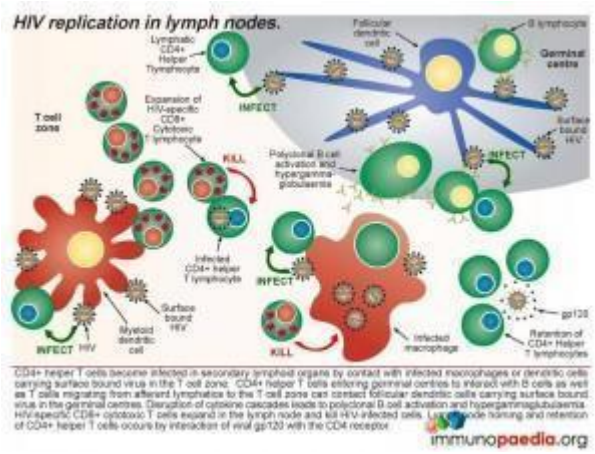
As explained TB infection occurs in macrophages which are

found either in tissues or lymphoid organs. TB effector cells play a role in containing infection, which culminates in granulomatous formation. However in the presence of HIV these microenvironments become depleted of these antigen specific responses resulting in breakdown and no local TB control i.e. TB infection with no granulomatous formation.

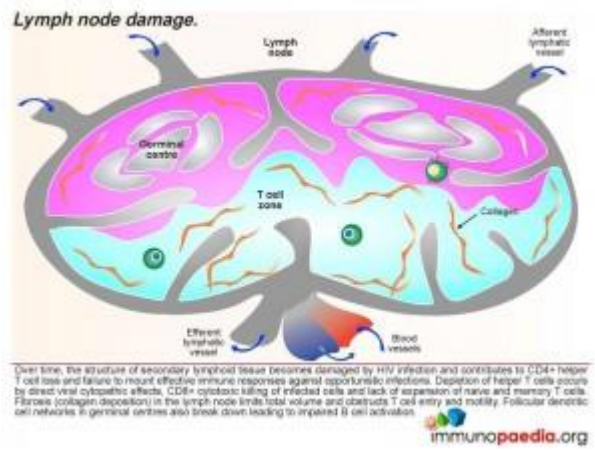
Dissemination of HIV from the site of infection to secondary lymphoid tissue in the gut, spleen and peripheral lymph nodes occurs shortly after transmission. This can be due to migration of activated macrophages infected with HIV or migration of activated dendritic cells carrying surface-bound infectious virions to the paracortical zone of secondary lymphoid tissue for antigen presentation to T cells.



Macrophages infected with HIV can infect CD4+ T helper lymphocytes during cell contact in the T cell zone of lymphoid organs as well as dendritic cells carrying infectious virus particles on the cell surface. Follicular dendritic cells in the germinal centres of lymph nodes also trap infectious virus on the cell surface and can infect T cells entering the lymph node via afferent lymphatics or T cells associated with B cells in germinal centres. Activated CD8+ cytotoxic T cells expand in the lymph node to kill the infected T cells. Viral gp120 antigen accumulates in the lymph node and interacts with CD4 receptors on helper T lymphocytes causing retention of these cells. In this way, CD4+ T helper lymphocytes which are the preferred targets of HIV, become infected by contact with virus and in turn can spread virus to other tissues following activation and migration out of lymphoid organs.



Over time, the structure of secondary lymphoid tissue becomes damaged by HIV infection and contributes to CD4+ helper T cell loss and failure to mount effective immune responses against opportunistic infections. Depletion of helper cells occurs by direct viral cytopathic effects, CD8+ cytotoxic killing of infected cells and lack of expansion of naive and memory T cells. The lymph node also becomes fibrosed due to collagen deposition which further impairs lymph node functioning. Clinically this is noted as small lymph nodes or no detectable lymphadenopathy.



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Splenic TB

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Treatment

After 5 days the patient was commenced on metronidazole and cloxacillin. However he continued with persistent spiking fevers for a further two days.

The patient was then started on ciprofloxacin, amikacin and ethambutol.

Further investigations, day 10:

	Values	Normal Limits
WBC	2.7	(4-12x109/l)
HB	8.6999999999999993	(12.1-15.2 g/l)
MCV	77	(80-96 fl))
Platelets	46	(140-450x109/l)
TBIL	59	(3-17 umol/l)
INDIR BIL	48	(0.0-0.3 mg/dl)
TPROT	55	(60-80 g/l)
ALB	22	(35-50 g/l)
ALP	104	(30-150 u/l)
GGT	91	(11-51 u/l)
ALT	73	(5-35 u/l)

	Values	Normal Limits
AST	697	(5-35 u/l)
INR	1.83	
D-DIMERS	1.75	
LDH	4725	

He then underwent a sonar guided aspiration of the splenic abscess, which yielded 10 ml of very viscous pus which was sent for MC&S and TB culture. The culture was positive for Mycobacterium tuberculosis.

Mycobacterium tuberculosis was also cultured in sputum and blood culture specimens.

The hepatitis resolved and the patient was commenced on 4 drug TB treatment.

Splenic TB is usually associated with dissemination, usually with accompanying liver involvement. There are 3 categories of tubercular abscesses of the spleen which include splenic, splenohepatic and splenohepatoglandular abscesses.

The gold standard for management of splenic abscess used to be splenectomy however splenic preservation has now been shown to be important because of the immunologic functions of the spleen, especially in children. Successful treatment of single and multiple splenic abscesses in children is therefore achieved with antibiotic therapy.

TB splenic abscesses in children is becoming increasing common since the advent of HIV.

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Final Outcome

- The patient’s weight has increased from 60 to 71% of expected weight for age.
- A repeated abdominal U/S showed no splenomegaly or focal lesions.
- The patient was then commenced on ARV’s. He was closely monitored for an IRIS reaction which did not occur.
- He has been improving and has been transferred to an outpatient paediatric HIV facility

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Evaluation – Questions & answers

What is the diagnosis?

TB splenic abscess
Which cell is a target cell for mycobacteria in TB infections?

Macrophages
How does the bacteria spread to extrapulmonary tissues, including the spleen?

Migration of activated macrophages infected with bacteria to secondary lymphoid tissue for antigen presentation to CD4+ helper T lymphocytes can spread the bacteria to other tissues such as liver, lymph nodes, spleen, gut and bone marrow.
How does dissemination of HIV to secondary lymphoid tissues occur?

Dissemination of HIV occurs shortly after transmission when migration of activated macrophages infected with HIV or dendritic cells carrying surface-bound virus travel to the

paracortical zones of secondary lymphoid tissue for antigen presentation to T cells.

In the lymph node what happens to the infected T cells?

Activated CD8+ cytotoxic T cells expand in the lymph node to kill the infected T cells or infected CD4+ T cells die as a result of the cytopathic effects of HIV.

What happens to lymphoid tissue after years of HIV infection?

It becomes involuted due to the micro-anatomical structure disintegrating along with a build-up of fibrotic tissue. Follicular dendritic cell networks break down in the germinal centres and retard B cell activation. Collectively, this results in failure to mount effective humoral and cell-mediated immune responses against opportunistic infections

How does involuted lymphoid tissue manifest clinically?

Clinically this is noted as small lymph nodes or no detectable lymphadenopathy.

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Multiple Choice Questions

Earn 1 HPCSA or 0.25 SACNASP CPD Points – Online Quiz

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