Failure to thrive despite appropriate treatment

Patient presentation

A two year 1 month old boy who has been on TB treatment and antiretroviral therapy for the past 9 months presents with failure to thrive despite adherence and nutritional counseling.

Acknowledgement

This case study was kindly provided by Dr Claire Egbers from the Wits Paeds HIV Clinics.

History

At 13 months:

- Patient admitted for Kwashiorkor. At this time he was

also diagnosed with HIV infection.

At 14 months:

- 6.6 kg, height 64 cm (below 5th centile for height and weight)
- He showed signs of HIV infection which included generalised lymphadenopathy, 2cm hepatomegaly and less then 60% estimated weight for age (Marasmic Kwashiorkor). He was classified as WHO stage IV due to severe failure to thrive (FTT)
- Child exhibited a chronic cough
- Monocytosis on full blood count
- Chest X-Ray (CXR) showed right lung multilobar consolidation
- Night sweats, family or contact history of TB, fever, lethargy and anorexia were all nil of note.
- Gastric washings for acid fast bacilli (AFB) were negative
- Patient was diagnosed empirically with TB based on the above criteria
- TB treatment of Rimcure (rifampicin, isoniazid and pyrazinamide) was started

At 16 months:

- 6.6 kg, height 70 cm (below 5th centile for height and weight)
- HAART was started, calculated using weight specific doses and body surface area (BSA):

Stavudine(d4T) = 7mls
Lamivudine(3TC) = 2.3mls
Kaletra = 1.3 mls

Ritonavir boost dose = Kaletra dose * 0.75
= 1.3 * 0.75
= 1ml

At 19 months (3 months after starting HAART):

- 7 kg, height 72 cm (below 5th centile for height and weight)
- Clinically stable, no admissions for acute illnesses at this time.
- However weight gain was still inadequate despite treatment adherence and nutritional counseling.

At 22 months (6 months after starting HAART):

- 8 kg, height 76 cm (below 5th centile for height and weight)
- Intensive adherence counseling was given to the mother, but no adherence problems were found. Another sibling in the mothers care was fully suppressed on ART
- CXR changes had not resolved
- TB treatment was continued for a further 3 months
- Induced sputum and TB Bactec done, which were negative

Currently at 25 months (9 months after starting HAART):

- Weight gain has remained inadequate

Diagnosis

- Non compliance to medication
- Poverty, inadequate nutrition
- Multi drug resistant (MDR) TB

Examination

Initial visit, 14 months – TB treatment initiated	16 months, HAART started	19 months	22 months	
Age	14 months	16 months	19 months	22 months
Weight	6.6	6.6	7	8
Height	64	70	72	76
CD 4%	3.95		4.58	3.15
CD4 count	160		261	176
Viral load	660 000		46 000	58 000

Investigations

Age	Investigation	Result
13 months	Elisa test for HIV	Positive
14 months	FBC	Monocytosis
	CXR	Right lung multilobar cons
	Mantoux test (PPD)	Negative
	Gastric washings and AFB culture	Negative
	CD4%	3.95
	CD4 count	160
	Viral load	660 000
16 months	HAART was started, no further investigations done at this time	

Age	Investigation	Result
19 months (3 months after starting HAART)	CD4%	4.58
	CD4 count	261
	Viral load	46 000
22 months (6 months after starting HAART)	CXR	No change. Right lung multilobar consolidation
	Gastric washings and Bactec	Negative
	CD4%	3.15
	CD4 count	176
	Viral load	58 000
25 months (9 months after starting HAART)	Sputum cultures	Positive TB
	Sensitivity	Rifampicin, ethionamide and isoniazid resistant

Discussion

Elisa or PCR

When performing an HIV test on an infant it is important to know the patient's age as it will determine whether to use PCR or ELISA:

• < 18 months old use PCR testing as this will detect actual virus

• > 18 months use Elisa as the maternal antibodies have now cleared

The guidelines for diagnosis of TB in Children:

It is difficult to obtain bacteriological confirmation therefore we need to rely on a cluster of suggestive factors:

HISTORY of positive contact

- Mantoux skin test (PPD)
- Chest X-ray
- Sputum microscopy and culture
- Culture of other body fluids
- Biopsy specimens

ALGORITHMS for guiding decision to treat:

Feature:	0	1	2	3	4	Score
General						
Weeks of illness	<2	41731		>4		
Nutrition (% weight for age)	0.8	60-80%		0.6		
Family history of TB	None	Reported by Family		Proved sputum positive		
Mantoux Test				Positive		
Malnutrition				Not improved after 1 month Rx		
Unexplained Fever			No response to Rx			

Feature:	0	1	2	3	4	Score

Feature:	0	1	2	3	4	Score
Local						
				Lymph nodes		
				Joint or bone swelling		
				Abdominal mass or ascities		
				CNS signs, CSF abnormal		
X-Rays				Broad mediastinum due to enlarged hilar glands	Gibbus	

Total = score for general features + score for local features (any score ≥7 is suggestive of TB

This patient scored 12

Mantoux test

Utilises the fact that the body's Cell Mediated Immunity (CMI) reacts against foreign protein

- 2TU of Purified Protein Derivative (PPD) injected intradermally on left forearm (mid-third)
- Read 48 to 72 hr later
- Area of transverse induration measured (in millimetres)

Many factors influence body's response to PPD

The following can give rise to a negative result:

- Acute viral infection e.g. measles
- Overwhelming bacterial infection
- Overwhelming TB
- HIV infection
- Immunosuppressive therapies
- Malnutrition
- Recent live viral vaccine
- Incorrect PPD administration technique

The following can give rise to a false positive test:

- Previous BCG vaccination
- Previously treated TB
- Exposure to environmental mycobacteria

Interpretation

- Skin test ≥ 5 mm denotes TB infection in HIV positive children
- A positive skin test means TB Infection, not necessarily TB Disease

	Previous BCG	**No previous BCG**	**HIV Positive**
Mantoux	>15 mm	>10 mm	>5 mm

At the patients 12 month visit (28 months old), he had been on MDR TB treatment for 3 months and had gained over a kilo in weight and was clinically well. These were his results:

Age	**28 months**
Weight	9.5kg
Height	79cm
CD4%	8.39
CD4 count	607
Viral load	<25

Evaluation – Questions & answers

What is the Diagnosis at 25 months of age?

Multi drug-resistant tuberculosis (MDR TB)
What is the definition of this disease?

MDR TB is a form of tuberculosis that is resistant to two or more of the primary drugs, isoniazid and rifampicin used for the treatment of tuberculosis.
How does drug-susceptible TB become drug-resistant TB?

Drug resistance arises due to the improper use of antibiotics

in chemotherapy of drug-susceptible TB patients. This improper use is a result of a number of actions, including administration of improper treatment regimens by health care workers and failure to ensure that patients complete the whole course of treatment. Essentially, drug-resistance arises in areas with poor TB control programmes.

What are the advantages of TB Diagnostic Algorithms?

• Relies on History, Examination and Mantoux test
• X-ray is not considered to be an important part of the diagnostic workup
• Highlights fact that sputum AFB determination is not necessary to diagnose Childhood TB

What are the disadvantages of TB Diagnostic Algorithms?

• Their usefulness has not been tested in controlled clinical trials
• They tend to detect cases with longstanding disease whereas most childhood TB is an acute presentation of recent infection.

Why should TB ideally be excluded or treatment started before starting HAART?

This is done to reduce the chance of Immune Reconstitution Inflammatory Syndrome (IRIS) which is a paradoxical clinical deterioration after starting HAART.

What is the treatment for MDR TB?

Choice of drugs will depend on the results from sensitivity testing. The following drugs are amongst those used to treat MDR TB:

• Pyrazinamide (PZA)
• Ethionamide
• Ofloxacin
• Ethambutol
• Amikacin

Would you change the ART regimen at this stage?

Yes, the Ritonivir boost can be stopped because the patient is no longer on a rifampicin containing regimen.