

Malaria in HIV

Julie Makani

Case history

- Juma was a 25-year-old man who presented to ward 3, Mwaisela block, MNH with high-grade fever and confusion.
- His relatives reported that he had been previously fit and well. He had recently returned from Kyela, Mbeya where he had been for 4 weeks. Three days ago, he complained of high-grade fever, muscle aches and pains accompanied by nausea and vomiting.
- He had gone to a local pharmacy and taken 3 tablets of Fansidar. As there was no improvement, he was then taken to a local clinic where a bloodslide was taken and he was told that he had malaria. Apparently, he was given a “drip” but his condition deteriorated. Earlier that day, he had a single generalised fit and so his relatives brought him to MNH.
- He was unmarried and without children. He had never been admitted to hospital before. He works as a trader dealing with fresh produce, which he brings from Mbeya and sells in Dar-es-Salaam.

Physical Examination

- Juma was pale, had a tinge of jaundice but wasn't wasted.
- He was breathing normally. There was no respiratory distress and the chest was clear. PR=110bpm, good volume and regular; BP=100/60mmHg. The jugular venous pressure was not raised and heart sounds were normal.
- Axillary temperature was 39.3°C, he had moderate dehydration and there was no oral thrush, peripheral lymphadenopathy, skin or joint lesions. The abdomen was soft without palpable organomegaly.
- Although conscious when seen initially in the casualty department, when re-assessed shortly afterwards Juma opened his eyes only when spoken to but was confused and responded to questions with inappropriate answers. He was not able to respond with active movements of limbs when asked to do so, but reacted to the application of painful stimulus by withdrawing
- The neck was supple and Kernig's sign equivocal. His confusional state limited examination, but no deficits were detected in the cranial or peripheral nervous systems.

Differential Diagnosis

- Cerebral malaria
- Meningoencephalitis
- Septicaemia

Others

- Diabetic coma precipitated by infection
- Cerebrovascular accident (CVA)

GENERAL MANAGEMENT

- ❖ Resuscitation
- ❖ Rapid clinical assessment – ABC
- ❖ Blood slide – don't wait for results
- ❖ Intravenous cannula
- ❖ Check for hypoglycaemia – or give glucose
- ❖ Look for other causes of presentation
- ❖ Monitor therapeutic response
- ❖ Regular checks on Hb, glucose, U&C, electrolytes

Results

- Microscopy of thick and thin blood films reveals
 - **Thick film:** an average number of 207 *P.falciparum* trophozoites /hpf (equivalent to 103,500 parasites/ μ L blood)
 - **Thin film:** *P.falciparum* trophozoites can be identified. Red cells show mixed population of cell size and colour suggestive of both hypochromic, microcytic and megaloblastic anaemia. lymphocytes: normal in number and morphology
- Capillary blood sugar was <2 mmol/L. A venous sample sent to the laboratory at the same time was later reported to show RBG = 2.1mmol/l.
- Hb=10.7g/dl, WCC=9,100 x 10⁹/L and an inconspicuous differential count
- CSF appeared clear and colourless with glucose = 3.2 mmol/L and protein = 2.4g/L. Microscopy of CSF showed no organisms on Gram, Ziehl Neelsen or Indian ink staining. No reagents were available for CSF culture for bacteria.
- Arterial blood gas analysis: pH: 7.38; pCO₂: 5.3kPa; BE: 26; pO₂: 11kPa
- creatinine= 188 micromoles/mL.

Why malaria?

Geographical residence

- Malaria transmission varies considerably within Tanzania. Juma's relatives reported that he was born and raised in Kyela, Mbeya, a non-malarious area and, therefore, it is likely that he had developed little protective immunity against malaria. He has been living in Sinza, Kinondoni, a highly endemic area for the past 2 years.

Pre-hospital treatment

- It is often difficult to get a clear history of treatment. On further questioning, his brother produced a note from the clinic which showed that Juma had received 3 doses of IV quinine 600mg. When he developed the convulsion, he had received 10mg diazepam IM.

Why HIV?

High prevalence of HIV

- In areas like Dar-es-salaam where HIV prevalence is high, HIV should always be considered.

Risk Factors for HIV

- Although Juma did not appear wasted and was said to have been well previous to this illness, risk factors for HIV infection were assessed. There was a positive history of genital ulcer, penile discharge and chronic illness.
- This patient did not show any evidence of HIV infection, however during acute seroconversion (which could be possible here) there is a risk of opportunistic infections as the CD-4+ count falls.
- Opportunistic infections should be considered too.
 - causes of meningitis in HIV positive adults, SPN, TB and cryptococcal meningitis.
 - Cerebral toxoplasmosis and CNS lymphoma complicating HIV are less likely in this case because of the high fever and absence of focal neurological signs. However, herpes encephalopathy complicating HIV does not cause focal neurology and could present in this manner.

CLINICAL FEATURES OF MALARIA

SYMPTOMS

Aches – head, back, etc

Dizziness

Malaise

GI symptoms

Fever

Chills

SIGNS

Fever

Anaemia

Postural hypotension

Tender

hepatosplenomegaly

Severe manifestations of malaria

CLINICAL

- Prostration*
- Impaired consciousness*
- Convulsions*
- Respiratory distress*
- Abnormal bleeding
- Jaundice
- Circulatory collapse

LABORATORY

- hypoglycaemia
- Severe anaemia*
- Haemoglobinuria
- Hyperparasitaemia
- Hyperlactataemia
- Renal impairment
- Pulmonary oedema

INVESTIGATIONS IN SEVERE MALARIA

- ❖ Blood glucose
- ❖ Blood film for mps
- ❖ Full blood count
- ❖ Biochemical screening
- ❖ Dipstick urine testing, microscopy, C&S
- ❖ Blood culture and sensitivity
- ❖ Dipstick urine testing, microscopy, C&S
- ❖ Chest radiograph
- ❖ Lumbar puncture*
- ❖ Urine microscopy, C&S

ANTIMALARIAL CHEMOTHERAPY

Quinine plus S-P	Artemether/ Artesunate plus S-P	Artemether/ Artesunate plus Mefloquine
------------------------	--	---

Factors determining treatment

- ❖ Severity of infection
- ❖ Age of the patient
- ❖ Degree of background immunity
- ❖ Likely pattern of susceptibility
- ❖ Cost and availability of drugs

SUPPORTIVE & ANCILLARY TREATMENTS

Recommended

- ❖ Antipyretics
- ❖ Anticonvulsants
- ❖ Exchange blood transfusion

Unclear benefits

- ❖ Mannitol

No benefit

- ❖ Aspirin*
- ❖ Hyperimmune serum*

Harmful

- ❖ High dose corticosteroids*

Nursing Care

Emergency care

- ❖ Maintain clear airway
- ❖ Semilateral or prone position with two hourly turning
- ❖ Insert nasogastric tube

Monitoring

- ❖ Monitor vital signs four hourly
- ❖ Report any changes
- ❖ Reduce high temperatures

Fluid balance

- ❖ Insert urethral catheter
- ❖ Careful record of fluid input /output
- ❖ Note appearance of haemoglobinuria or oliguria
- ❖ Check infusion of fluids frequently

MANAGEMENT - SPECIFIC PROBLEMS

Hypoglycaemia

- ❖ Check blood glucose 4 hourly or if conscious level deteriorates
- ❖ If < 3.5 mmol/L, give 50mls of 50% dextrose iv and start infusion of 10% dextrose

Hypotension

- ❖ Give colloid or blood if Hb < 5 gm/dL

Convulsions

- ❖ Recheck blood glucose
- ❖ Diazepam 10 mg bolus slow injection or intrarectally

Pulmonary oedema

- ❖ Excessive fluids or ARDS
- ❖ Mechanical ventilation may be needed

Epidemiology and recent developments

- Immunity
 - Geographical distribution (Malaria Transmission in Tanzania)
 - Age
 - Seasonality
- Effect of intervention
 - Insecticide treated nets
 - Malaria chemotherapy (ACT)
- Widespread drug resistance of *P falciparum*
- Increasing understanding of pathogenesis of disease at genetic and molecular level.

Relationship of HIV and Malaria

Does Malaria worsen HIV disease?

Does HIV worsen Malaria?

Malaria and HIV - Effect of HIV on Malaria

- **High incidence of clinical malaria in HIV positive**
 - Malaria not considered OI
 - ↑ burden of Disease
 - Frequent use of antimalarials
 - results in ADR
 - ↑ risk of drug-drug interactions
 - ↑ antimalarial drug resistance
 - ARV role in malaria Rx
- **Increase frequency of malaria with falling CD4 counts**
- **Increase severity of malaria**
- **Incidence of malaria is higher than other OI eg PCP, CPM**
- **Loss of Malaria Immunity in HIV immunosuppression**

Co-morbidity of HIV and Malaria

- **Cause of fever**
 - Malaria
 - HIV
 - OI
 - Drugs
- **Overdiagnosis and overtreatment of malaria**
 - 38% “cerebral malaria”; 7.5% parasitaemia; 1% WHO criteria
 - Asymptomatic parasitaemia (10%)
- **UnderDx of HIV-related causes**

Co-morbidity of HIV and Malaria

- **Anaemia**
 - Px: haemolysis, BM dyserythropoiesis, HIV, OI
 - ? Faster progression of HIVD
 - ± parasitaemia or anaemia does not exclude malaria as cause of anaemia
- **Respiratory syndromes**
 - Malaria may present with cough/respiratory distress
- **GI syndromes**
 - Acute malaria
 - OI, ADR, Immune reconstitution
- **Neurological syndromes**
- **Lactic acidosis**
 - Severe malaria

Malaria and HIV - Effect of Malaria on HIV

- Elevates viral load
- May increase risk of HIV transmission
- Reduces CD4 count
 - Misclassification
 - Premature start of ART
 - MisDx of Rx failure

Management of Malaria in HIV

Diagnostic and Management algorithms

- Follow National Guidelines for Malaria and HIV
- Harmonize HIV-Malaria Policy

Research areas in HIV and Malaria

- Description of Malaria (frequency, severity) in HIV patients \pm ART
- Description of CD4, Viral load in HIV patients \pm ART with Malaria.
- Guidelines of diagnosis, management of
 - Malaria (in HIV)
 - HIV (during malaria)
- Pharmacological studies
 - Antimalarial pharmacodynamics in HIV
 - ART pharmacodynamics during malaria

References

- Brentlinger, P.E., C.B. Behrens, and J.G. Kublin, *Challenges in the prevention, diagnosis, and treatment of malaria in human immunodeficiency virus infected adults in sub-Saharan Africa*. *Arch Intern Med*, 2007. **167(17): p. 1827-36.**
- Herrero, M.D., et al., *HIV and malaria*. *AIDS Rev*, 2007. **9(2): p. 88-98.**
- Hewitt, K., et al., *Interactions between HIV and malaria in non-pregnant adults: evidence and implications*. *Aids*, 2006. **20(16): p. 1993-2004.**
- Whitworth, J.A. and K.A. Hewitt, *Effect of malaria on HIV-1 progression and transmission*. *Lancet*, 2005. **365(9455): p. 196-7.**
- French, N., et al., *Increasing rates of malarial fever with deteriorating immune status in HIV-1-infected Ugandan adults*. *Aids*, 2001. **15(7): p. 899-906.**
- Wang, S.J., et al., *Rapid urban malaria appraisal (RUMA) II: Epidemiology of urban malaria in Dar es Salaam (Tanzania)*. *Malar J*, 2006. **5(1): p. 29.**
- Makani, J., et al., *Admission diagnosis of cerebral malaria in adults in an endemic area of Tanzania: implications and clinical description*. *QJM*, 2003. **96(5): p. 355-362.**
- Kawo, G., et al., *Prevalence of HIV type 1 infection, associated clinical features and mortality among hospitalized children in Dar es Salaam, Tanzania*. *Scand J Infect Dis*, 2000. **32(4): p. 357-63.**
- Kahigwa, E., et al., *Risk factors for presentation to hospital with severe anaemia in Tanzanian children: a case-control study*. *Trop Med Int Health*, 2002. **7(10): p. 823-30.**
- Archibald, L.K., et al., *Fatal Mycobacterium tuberculosis bloodstream infections in febrile hospitalized adults in Dar es Salaam, Tanzania*. *Clin Infect Dis*, 1998. **26(2): p. 290-6.**