

Fever from SE Asia

Nick Beeching

Senior Lecturer in Infectious Diseases
Liverpool School of Tropical Medicine

NIHR HPRU in Emerging and Zoonotic Infections
ESCMID Study Group on Infection in Travellers
and Migrants (ESGITM)

Feb 2018 UK male age 40

Travelling for 5 months:

- UAE
- Singapore
- Hong Kong
- Extensively through China
- Cambodia
- Vietnam
- Thailand
- India

Extensive mix of rural and urban travel. Treks in jungle. Swam in local waters.

- Ate street food
- Back for 2 weeks from India
- Took malaria tablets in Cambodia, fully vaccinated

Symptoms

- Felt unwell on 2 days before return Thailand to Goa
- It is now 20 days later

- Progressive myalgia and worsening fatigue.
- Myalgia worse in legs, upper arms and neck (neck is not stiff)
- Fevers at night, night sweats (changed his bedding), no weight loss
- Now has bilateral retro-orbital eye pain

- No change in vision.
- No focal neurology.
- Pt has not noticed a rash
- No chest symptoms
- No abdominal symptoms.
- No neck stiffness, no photophobia
- No arthralgia

Social history

- MSM- in a relationship with same partner for 6 years
- Nil smoke
- Minimal alcohol
- Nil recreational drugs, over the counter medications

- Stressed as witnessed fatal road traffic accident

Examination

- Looks well
- HR 94, BP 136/81, RR 19, Temp 36.7, Sats 99%
- No peripheral stigmata of disease
- Chest- Chest clear and good air entry
- Heart Sounds - normal
- Abdomen soft and non-tender. Bowel sounds OK
- Joints normal

- Maculopapular rash over trunk- patient has not noticed this before





What is your diagnosis?

- Chikungunya
- Dengue
- HIV
- Leptospirosis
- Scrub typhus
- Syphilis
- Typhoid
- Zika
- Something else

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Results

- Full blood count
- Haemoglobin 153 g/l
- Total WBC $7.9 \times 10^6/l$
- Platelets $180 \times 10^9/l$
- Malaria screen negative (RDT, thick and thin films)

- CRP 10
- ALT 82 u/l (normal < 45), GGT 109 u/l (<60)
- Urea and electrolytes normal

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- Dengue
- HIV
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- Scrub typhus
- Syphilis
- Typhoid
- Zika
- Something else

36 hours later

- Discharged as probable dengue case after overnight stay
 - Received call from RIPL lab to clarify date of symptom onset.
 - Zika IgM strongly positive, IgG negative - from sample on day 2 of rash
 - Rest of arboviral panel negative, except CHIK which is still outstanding
-
- HIV and syphilis negative

Do you think this is Zika?

- No
- Yes

Clinic 16 days later

- ZIKV IgM+, DENV IgM-, though illness clinically feels more dengue like
- ALT rose to 224
- Still has a rash - homogenous erythema, mild, blanching, some islands of white
- Tired and lethargic, anxious
- No itching or de-squamation

- Recruited to arbovirus (Zika) study...

Serology

Test	Day 2 of rash	Day 25
DEN IgM	Neg	Neg
DEN IgG	Neg	Neg
DEN RNA	Neg	Not done
CHIK IgM	Neg	Pos
CHIK IgG	Neg	Neg
ZIK IgM	Pos	Pos
ZIK IgG	Neg	Neg
ZIK RNA	Neg	Not done
Scrub typhus	Both Neg	Both Neg
Leptospirosis		

What is going on?

Review of lab results at 9 days

Full blood count

- Haemoglobin 153 g/l
 - Total WBC $10.9 \times 10^6/l$ (upper limit 11)
 - Neutrophils $3.5 \times 10^6/l$ (2 – 7.5)
 - Monocytes $1.1 \times 10^6/l$ (0.2 – 0.8)
 - Lymphocytes $6.2 \times 10^6/l$ (1.5 – 3.0)
 - Platelets $196 \times 10^9/l$ (150 – 400)
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- ALT 224 u/l (normal < 35), GGT 159 u/l (<60)

Admission serology

Hepatitis BsAg : Negative
Hepatitis C Ab : Negative
HIV Ag/Ab : Negative
CMV IgM : Positive
CMV IgG : Negative
EBV VCA IgM : Negative
EBV VCA IgG : Positive

HIV antibody/antigen NOT detected

The results are consistent with **recent primary cytomegalovirus infection** and confirms a clinical diagnosis of infectious mononucleosis (glandular fever).
Consistent with past EBV infection

Diagnosis = acute CMV

Clues

- Long history
- Profuse sweats
- Late rash
- Later weight loss, lethargy ++
- Lymphocytosis, no thrombocytopenia

- False positive ZIK then CHIK IgM

He had confirmatory CMV IgG seroconversion later

Did we miss it on initial tests?

- NOT REALLY
- Full blood count on admission
 - Haemoglobin 153 g/l
 - Total WBC $7.9 \times 10^6/l$ (upper limit 11)
 - Neutrophils $3.9 \times 10^6/l$ (2 – 7.5)
 - Monocytes $0.7 \times 10^6/l$ (0.2 – 0.8)
 - Lymphocytes $3.2 \times 10^6/l$ (1.5 – 3.0)
 - Platelets $180 \times 10^9/l$ (150 – 400)
- Glandular fever screening test was negative

Lessons

- CMV is often missed
- Not all imported fevers are exotic
- Even with a blanching rash from Asia
- Do the simple things first
- Take note of early clues and revisit them
- IgM serology has problems:
 - Arbovirus cross reactions and mutual boosting
 - False positives with CMV, EBV, malaria etc