“Epidemiology of rickettsial infections”
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SRI LANKA

I have got 45 min....

First 15 min...
• A travel medicine physician...
• Evolution of epidemiology of rickettsial diseases in brief
• Expanded knowledge of rickettsioses vs travel medicine
• Determinants of Current epidemiology of Rickettsial infections
• Role of returning traveller in rickettsial disease epidemiology
• Current epidemiology vs travel health physician

Next 30 min...
• Clinical cases

People travel…
  Regionally and internationally

Bugs travel
  Regionally and internationally

Human Travel &
Human activity

Increased risk of contact between humans and bugs

Deforestation
Habitat fragmentation
Echo tourism

Change in global epidemiology

This man.. a returning traveler.. down with fever.. What can this be???

• This is the greatest challenge faced by an infectious disease / travel medicine physician

• compared to a physician attending to a well streamlined management plan of a non-communicable disease...
• A travel medicine physician...
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Rickettsial diseases

• Represent some of the oldest and most recently recognized infectious diseases
• Athens plague described during 5th century BC...

In 1916........

• *R. prowazekii* was identified as the etiological agent of epidemic typhus

By 1970s-1980s four endemic rickettsioses; a single agent unique to a given geography !!!

• Rocky Mountain spotted fever
• Mediterranean spotted fever
• North Asian tick typhus
• Queensland tick typhus

Family Rickettsiaceae

Genera Rickettsia

Spotted Fever Group (SFG)
Typhus Group (TG)

Transitional group between SFG and TG

• *R. australis*
• *R. akari*
• *R. felis*

• (evolutionary genetic relationships)
Genera Orientia

[Separated from Genera Rickettsia in 1995; antigenically diverse spp]

Transmitted by.....ticks, mites, fleas and lice...

- SFG: mainly ticks, also fleas (R. felis), mites (R. akari)
- TG:
  - R. prowazekii
  - Human body louse (Epidemic louse-borne typhus, recrudescent typhus)
  - Flying squirrel ecto parasites (Flying squirrel associated typhus)
    (Amblyomma ticks)
  - R. typhi (Murine typhus)
  - Fleas
- Orientia (Scrub typhus)
  - Larval mite (chigger).......
  - (Thomas Weizler)

Identification of rickettsial spp from pathogenic to non-pathogenic potential across the globe...

Eg: Rickettsia conorii complex (2005).....

(based on epidemiological and clinical differences)

- R. conorii-Astrakhan strain: Astrakhan fever, Southern Russia
- R. conorii-Israeli: Israeli spotted fever
- R. conorii-Indica: Indian tick typhus: India, Sri Lanka and Pakistan

Rickettsia spp..

- 30 validated species, incl. 17 pathogens
- > 100 unclassified rickettsial isolates
- Major human pathogens

Effect of global warming?
Global warming linked to changing epidemiology of MSF

- Effect of on tick behavior
  - (↑ incidence of *Rhs. Sanguineus* (Brown Dog Tick)-transmitted diseases)
  - ↑ period of activity
  - ↑ aggressiveness
  - ↑ biting of unusual hosts (humans)
  - Multiple eschars, severe forms


2003 heat wave

- Fatal MSF in France
  - one man; 22 attached ticks
  - Multiple eschars
  - 2–6% fatality reaching 30% in hospitalized patients


TBR: has become a worldwide disease (Parola et al. 2014)

*Orientia tsutsugamushi* (Scrub typhus)

- More than 20 antigenically distinct strains
- Originally, 3 prototype strains; Gilliam, Karp and Kato
- Later, additional antigenic types: Kawasaki, Kuroki, Shimokoshi etc and other distinct serotypes in the tsutsugamushi triangle
- Novel orientia species being described outside the tsutsugamushi triangle; Dubai (O. chuto) and
- in Chile (proved novel: “Named”, yet to be published (Thomas Weitzel)

This Antigenic heterogeneity of *Orientia tsutsugamushi*

reason for

- frequent outbreaks and reinfection
- Differences in Virulence among the strains
- Variation in the general course of the disease and the prognosis depending on the endemic strain

*Orientia Species Locations*

- Countries with Orientia
- Traditional Tsutsugamushi Triangle
Today........

Many Organisms / Serotypes / Strains

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Historically
• Different species of prokaryotic pathogens were defined based
  • on the diseases they caused
  • regardless of other ecological or evolutionary considerations

• Clinical manifestations of most rickettsioses are neither specific to a particular agent nor to a geographic distribution

• Novel *Rickettsia* isolates
  • Very much less from one another
  • Is an overenthusiastic designation of many new species
• *R. africae* and *R. parkeri*
• *R. japonica* and *R. helongjiangensis*

show minimal differences

_Walker DH, Ismail N. Nature Reviews: 2008_

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**Epidemiology of Tick borne Rickettsioses**

1. Is based mainly on _Rickettsia_ isolated in Ticks
2. Reporting error vs rickettsial epidemiology

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**Most prevalent rickettsioses is**

• Based on
  • "Priority agents" for surveillance
  • Reportable rickettsial diseases
  • Rickettsioses which require medical attention
  • Rickettsioses that standout for their morbidity and mortality

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"Reporting error"; _RMSF_ in the Americas

Most Rickettsial disease diagnosis is based on IFA
Is still the primary tool in the diagnosis
Has a marked cross-reactivity within the SFG

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"cases"

• May reflect an unrelated exposure to a vector bearing a _Rickettsial_ agent that caused an immune response rather than the occurrence of a true rickettsiosis
IFA crossreactivity…

- Low pathogenic agents may have contribute to the apparent overall increased incidence of RMSF in Americas?

This fact led to the change in reporting of “RMSF” cases in the United States

- Now classified as “SPOTTED FEVER Group” Rickettsioses

In most resource poor countries… which are important for Travel Medicine…

- Rickettsial disease diagnosis is mainly on History and examination…
- Ix facilities are not widely available
- Even if available, its mainly serology based; “will not identify” the causative organism.. Will end up with an umbrella term “SFG”

Does this really mean…

- ”In your clinical practice.. you do not want to know what the organism is..??”
- But simply know that the illness is one of Rickettsial ??

Perspective of a pragmatist

“The laboratory diagnosis of rickettsioses can appear an academic exercise:

For each of > 25 ecologically, epidemiologically, and aetiologically distinct disease comprising ‘the rickettsioses’ responds to the safe, inexpensive, widely distributed, and highly effective antibiotic doxycycline”

Paddock CD

Is it really necessary to identify the causative agent in a returning traveler?
We have questions needing clarification...

Newer Rickettsioses: are they really low in numbers?
Will their impact be always small?

- Low pathogenicity?
- Low vector carriage?
- Low transmission potential?

Are we planning on preventive measures in travelers?
Fever in this returning traveler: Can this be rickettsial??...

• Epidemiology
• Clinical syndrome
• Exposure risk
• Incubation period
• Manageable
• DD
• Clinical judgement

Expected clinical syndrome of rickettsioses...

• Mostly a short incubation (6-7 days)

Clinical triad:

• Fever,
• Eschar,
• Maculo-papular rash

Important...!! Aneruptive fever

• R. helvetica (although the pathogenic role is unclear)
  (Ixodes ricinus ticks) European and Asian countries

• Fever, Headache, Myalgia

• No inoculation eschar or cutaneous rash in the warm season

• More severe infections are reported as septicemia and meningitis

• Almost all Scrub typhus in Sri Lanka NO rash!! (40-60% eschar)

Rickettsialpox

R. akari

A case of rickettsialpox in Northern Europe

United States, Ukraine, Croatia, South Africa, Bosnia, France, Italy, Costa Rica and Turkey

Vesicular enanthema:

Palate
Tongue
Mouth
Tonsils
Pharynx

Tick-borne lymphadenopathy (TIBOLA)

Scalp eschar and neck lymphadenopathy after tick bite (SENLAT)

Rickettsia slovaca, Rickettsia raoultii, R. candidatus and Rickettsia rjoja
R genotype 3640 (R. phillipi)

Europe and Central Asia, California
Lymphangitis-associated rickettsiosis (LAR)

- *Rickettsia sibirica mongolitimonae*: Greece, Portugal, South Africa and Southern France.
- Incidence is higher in spring or summer
- Fever, Headache, One or more frequently multiple eschars
- Maculopapular rash
- Enlarged lymph nodes and lymphangitis
- Case of retinal vasculitis reported

Clinical features

<table>
<thead>
<tr>
<th>Symptomatic</th>
<th>Asymptomatic</th>
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<tbody>
<tr>
<td>Virulent</td>
<td>Less virulent</td>
</tr>
<tr>
<td>RMSF (un Rx: 25% mortality)</td>
<td>Med SF (un Rx: 4% mortality)</td>
</tr>
<tr>
<td>Rash</td>
<td>Eschar</td>
</tr>
<tr>
<td>CNS, CVS</td>
<td>Multi-organ</td>
</tr>
<tr>
<td>Severe complications</td>
<td>ix</td>
</tr>
</tbody>
</table>

The clinical outcome of Rickettsioses

- Severity varies greatly from mild, self-limiting, to life-threatening diseases
- Mortality
  - 0% (*R. slovaca, R. africae, R. felis*)
  - 1% (*R. typhi*)
  - 2 - 5% (*R. conorii, R. rickettsii*)
  - 30% (*R. prowazekii*)

Severity of Rickettsioses: Is it solely the organism?

- Likely to be multifactorial....
- How the host responds to an infective aetiology...
  - Dengue
  - Leptospirosis
  - Rickettsial Infections

The most recent published paper on sever sepsis: JAMA, May 2019: Sepsis is NOT a Single Syndrome

- Comparison of parameters using artificial intelligence

Four types of sepsis

- α: commonest (33%) Fewest abnormal laboratory, least organ dysfunction: 2% death
- β: (27%) Older patients, most chronic illness and kidney dysfunction
- γ: (27%) elevated inflammatory measures, primary pulmonary dysfunction
- δ: least common (13%) most deadly, often liver dysfunction and shock; 32% death
Severity of rickettsial sepsis syndrome?

• What is the difference between a native (with background exposure) compared to a previously unexposed traveler?

For Rickettsial illness: Early diagnosis is the Key to prevent “severe sepsis syndrome” and subsequent multi-organ involvement and death…

Case 1; Male patient- 26 Years

• A traveler from Zurich Switzerland
• Three months of holiday in South & Eastern Asia

In Pakistan one month:

Early December’17 – Early January -18’

• Living with a farmer family
• Looking after cattle
• Farming in the paddy fields
• Sleeping in the field tents

Flying to Thaïwan; January two weeks

• Hiking
• Camping
Flying to Thailand- Late January 7 days stay

- First few days in Rural

From Google images

67

Last week in the city..

- Severe headache
- Body aches
- Fever
- On the day of departure

From Google images

68

Arrives in Negombo Sri Lanka (major tourist destination)

- Stayed with a friend for 4 days
- Fever continues
- Admits to Negombo hospital

- Ixs: Non conclusive
- No response to treatment

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Negombo- April 21

From Negombo to Ragama Teaching hospital: (40 min travel)

Admission

What do you notice?
Why was his illness missed?

- Did he evolve these signs over 40 min?

How would you approach to this patient?
Questions:
• What is the most obvious clinical syndrome?
• What is the most likely organism? (Where did he catch this illness?)
• What more clues (History / Examination) are needed?
• What are the confirmatory tests?
• What is the treatment?

Approach to diagnosis
• Syndrome + Geography based approach
• Syndrome + Geography + activity based approach
• Syndrome + Geography + activity + exposure based approach

Clinical syndrome
• Fever
• Erythematous maculo-popular rash
• Lymphadenopathy

Can this syndrome...a result of...

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<tr>
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<th>Yes</th>
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<tbody>
<tr>
<td>Ticks</td>
<td>Yes</td>
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<tr>
<td>Ticks</td>
<td>Yes</td>
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<tr>
<td>Insects</td>
<td>Yes</td>
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Most likely exposure Geography
• Asia / Eastern Asia
• An European traveler
Ten human rickettsial pathogens circulate in ticks in different and often overlapping parts of Eurasia:

- *R. conorii*
- *R. massiliae*
- *R. slovaca*
- *R. raoultii*
- *R. sibirica*
- *R. mongolotimonae*
- *Rickettsia heilongjiangensis*
- *R. helvetica*
- *R. rioba*
- *R. honei*

Major rickettsioses described by causative agent, clinical syndrome, and vector by region:

**Europe:**
- *R. conorii*
- *R. massiliae*
- *R. slovaca*
- *R. raoultii*
- *R. sibirica*
- *R. mongolotimonae*
- *Rickettsia helongjiangensis*
- *R. helvetica*
- *R. rioba*
- *R. honei*

**Asia:**
- *R. conorii*
- *R. massiliae*
- *R. slovaca*
- *R. raoultii*
- *R. sibirica*
- *R. mongolotimonae*
- *Rickettsia helongjiangensis*
- *R. helvetica*
- *R. rioba*
- *R. honei*

Flea Borne: A traveler from Europe / to Asia...

From Google Images
Transitional Group: *Rickettsia felis* (Flea borne)

Typhus group: *R. typhi* (Flea borne)

Mite Borne: A traveler from Europe / to Asia...

Orientia tsutsugamushi

Typhus group: *R. prowazekii*; Body louse / Amblyomma ticks

This syndrome... a result of...

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<th>Yes</th>
<th>Yes</th>
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<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Most likely etiology for the clinical syndrome (Fever/ Rash/Lymphadenopathy)

- Tick borne
  - *R. conori*
  - *Rickettsia heliologiangensis*
  - *R. helvetica*
  - *R. honei*

- Flea borne
  - *R. felis*
  - *R. typhi* (Murine typhus)

- Mite borne
  - *Orientia tsutsugamushi*

Questions:

- What is the most likely illness?
- What is the most likely organism?
- What more clues (History / Examination/ Ixs) are needed?
- Where did he catch this illness?
- What is the treatment?

What further clues may help?

While in Hospital

What is the diagnosis?

In the field

From Google Images
Most likely etiology for the clinical syndrome
(Fever / lymphadenopathy / Rash / eschar)

• Tick borne
  • R. conorii
  • Rickettsia helongjiangensis
  • R. helvetica
  • R. honei
• Flea borne
  • R. felis
  • R. typhi (Murine typhus)
• Mite borne
  • Orientia tsutsugamushi

Where did he acquire it?

<table>
<thead>
<tr>
<th>Switzerland</th>
<th>Pakistan</th>
<th>Taiwan</th>
<th>Thailand</th>
<th>Sri Lanka</th>
</tr>
</thead>
</table>

Common symptoms:
- High intermittent fever (101-103°F), chills and rigors for 8 days
- Severe frontal headache
- Nausea and vomiting

Rare clinical scenarios: Delay in the diagnosis

Case 2

• 39 years, housewife, two children
• High intermittent fever (101-103°F), chills and rigors for 8 days
• No response to oral co-amoxiclav by GP
• Severe frontal headache, nausea and vomiting
• Progressively severe pain in almost all large and small joints backache and neck pain limiting her movements; bedbound
• Yellowish discoloration of the sclerae and dark urine around the third day of fever
• IUCD one year; Intermittent offensive vaginal discharge 2 months
• Denied recent pregnancy or gynecological interventions
• A victim of floods 2 weeks prior to the onset of illness
• Not travels
• Had two pet dogs at home
• No contact with animals

Examination
• Very ill, icteric, pale and dehydrated
• No skin rash, oral ulcers or lymphadenopathy
• Severe neck stiffness and bilateral symmetrical large and small joint arthritis with distal interphalangeal joint sparing
• Abdominal examination non-tender enlarged liver 2 cm below the right costal margin

Examination contd..
• HR 100 beats/min, blood pressure 110/60 mmHg
• No cardiac murmurs
• Not tachypneic, lungs clear
• Vaginal examination unremarkable

DD?
• Leptospirosis
• Palindromic rheumatism with systemic involvement
• Severe bacterial sepsis with a meningitic process

Investigations
• WBC 12.7 x 10^3/mL (N 80% L 16%)
• Blood picture showed toxic granules in polymorphonuclear leukocytes together with a left shift
• C-reactive protein (CRP) 327 U/L (Normal < 5 U/L)
• ESR 72 mm/1st hr
• Urinalysis 2+ proteinuria with occasional leukocytes and red blood cells
• Serum creatinine 229 µmol/L (normal 45-90)
Investigations

- AST 92 U/L (normal 0 – 35 U/L).
- ALT 45 U/L (normal 0 – 35 U/L).
- Bilirubin 95 µmol/L (normal 5.0–17.0 µmol/L).
- Direct 40 µmol/l.
- Serum alkaline phosphatase 255 U/L (normal 50-100 U/L).
- Anti-nuclear antibodies and rheumatoid factor were negative.
- Urine culture, blood culture were negative.

Empiric treatment

- Treated as for leptospirosis or severe sepsis with intravenous ceftriaxone, 1g twice daily together with intravenous hydration, antipyretics and analgesics.
- Despite the above treatment, she continued to deteriorate rapidly with worsening of symptoms.

On the 2nd day of admission (10th day of illness)

Further Ix

- Blood picture showed fragmented red cells and thrombocytopenia suggesting early DIC.
- Hemoglobin dropped to 8.6g/dL from 10g/dL and the platelet count was 76x10^3/mL.
- APTT 40 s with INR 1.3 and elevated D-dimers of 1.2 ng/ml (normal<0.5ng/ml).
- No active bleeding.

DD?

- Infective endocarditis.
- Meningococcal or gonococcal septicaemia.
- Severe staphylococcal or streptococcal sepsis.
- Acute flare of connective tissue disease with vasculitis.
- Cryoglobulinemia.
- Hemorrhagic form of leptospirosis.
- Rickettsial infection.

Further Ixs

- Transesophageal and transthoracic echocardiograms normal.
- ASOT titre was <200 U.
- Chest radiograph normal.
- Ultrasound scan of the abdomen; hepatomegaly.
- Leptospira antibodies were negative.
- The IFA IgG titre against Rickettsia conorii Ag titre of 1:8192.
Oral doxycycline and azithromycin were added on the 3rd day of admission.

Reduction in fever by the 2nd day of doxycycline (5th day of admission).

Complete recovery from acute kidney and liver injury by the 4th treatment day.

Skin rash and the joints became very painful over the 2nd-4th days of treatment.

All these resolved completely within 5 days of treatment (9th day of admission), and she was discharged on the 11th day of admission.

Purpura fulminans

- Characterized by rapidly progressive purpuric lesions; develop into extensive areas of skin necrosis, and peripheral gangrene.

- Associated with consumptive coagulopathy and is often fatal.

- PPs usually associated with many infections, meningococcal, staphylococcal, streptococcal infections.

- SFG rickettsioses (R. conorii indica)

- Queensland tick typhus (R. australis)
Case 3

- 56yrs, School teacher
- Intermittent fever for 10 days - chills, rigors
- Dry cough, SOB on exertion
- Progressive confusion 1 day
  - No visits
  - Previously healthy

Examination

- Conscious
- Confused
- No neck rigidity
- No Kernig's sign
- No focal neurological signs
- Fundi-normal
- 2cm hepatomegaly

Investigations

- Mild neutrophil leucocytosis
- Urine: Alb +, Red cells +, B. Urea normal
- Malaria film-ve
- ESR 60 mm 1st Hr,
- C-Reactive Protein 78 mg/dl
- Slightly raised AST/ ALT Normal bilirubin
- Blood culture: negative
- Electrolytes: normal
- CT scan Brain: Normal

Empiric treatment

- IV ceftriaxone (High dose)
- IV acyclovir
- IV Quinine

Investigations

- Lumbar Puncture: mild raised proteins
  - Lymphocytes (30-40)
  - Neutrophils (5-8)
  - Sugar 2/3 of blood levels
Rapid clinical deterioration

Third day of admission (13th day of illness)

• clinical evidence of pneumonitis and myocarditis (confirmed by chest X-ray/ECHO)

• Patient developed progressive hearing loss, coarse tremors on extremities, oscillating eye movements in all directions

• In matter of few hours .. was stoneDeaf...!!

DD?

• Careful Re-examination of the patient

Left axilla

Treatment

• Doxycycline 100mg b.i.d
• Chloramphenicol iv

• Afebrile within 48 hours
• Rapid improvement in her clinical condition
• 50% hearing improvement in 2 weeks
• IFA- IgG against OT(Carp) > 1: 8192

Clinical Infectious Diseases 2006

Case 4

• 62-years, healthy male
• High fever associated with chills and rigors for 17 days
• Complained of malaise, myalgia and arthralgia
• Treatment from a local hospital; no clinical improvement
• 5th day of the clinical illness; intermittent resting tremor in his right arm and leg
• Generalized stiffness

• Difficulty to carry out normal work with the right hand
• Difficult to walk due to unusual stiffness and heaviness of the right leg
• Difficulty to smile with others and felt very distressed
• Denied similar previous episodes

Acknowledgements

• For all authors of google images included in this presentation

• No associated psychiatric illness, seizures, or altered level of consciousness
• Had been working in his garden 7 days prior to the onset
• No previous medication
lx

• Full blood count was 13.4x10^9/L (N-43%, L-56%)
• ESR was 80mm/1st hour
• Urine analysis, liver and renal function tests normal
• The CT scan of the brain and the EEG normal

DD?

• Acute febrile illness with a Parkinson syndrome
• ??

• Careful examination ...<2mm!!

• IFA-IgG titre against Orientia carp antigen was 1:1024 which rose up to 1:16384 after two weeks
• Rectal doxycycline: within 48 hours and demonstrated some improvement in his Parkinsonism features, discharged from hospital in 4 days
• Reviewed after two weeks of discharge: showed complete improvement

CASE REPORT

Scrub typhus mimicking Parkinson’s disease


Abstract

Background: Scrub typhus is a re-emerging infection in Sri Lanka, is often poses a diagnostic challenge and tends to present as a febrile illness of uncertain origin. Undiagnosed illness may progress to serious multi-systemic complications, hence we report a case of scrub typhus presenting with features of Parkinsonism.

Case report: An 81-year-old male patient presented with high fever, malaise, myalgia and arthralgia for 17 days. On the 14th day of illness he developed progressive rigidity in the right arm and leg associated with arthralgia. Difficulty in carrying out normal work and difficulty in smiling. He derived similar previous episodes. There were no other associated neurological manifestations. Clinical examination revealed a high amplitude tremor in resting position in the right hand, a mask-like face and mild diurnal tremor in the right hand. The patient also complained of loss of sense of smell, loss of facial expression except for an eater over the abdomen. No investigations revealed lymphocyte leucocytosis, high erythrocyte sedi-mentation rate and urine protein positive except for a urinary tract infection. The investigations revealed typhus fever which was positive with rising titre. With oral doxycycline and analgesics his fever settled within 48h and a complete recovery of
Nervous system presentations

- Late onset meningitis / meningo encephalitis syndrome
- Acute Parkinson syndrome in a febrile patient
- Transverse myelitis in late febrile phase (Case presented in November 2011: Manchester, UK, a doctor returning from an endemic country)
- Vasculitis related focal neurological syndromes

Case 5

- 54 years, male (Medical student’s father)
- High intermittent fever for 6 days
- Loss of appetite
- Frontal headache with fever and vomited twice
- Mild joint pains
- Obtained treatment from GP
- Watery diarrhea on the 10th day of illness

DD: Fever with late onset diarrhoea

- Typhoid
- Paratyphoid
- Viral: Dengue
- Antibiotic induced?

Can this be considered a “travelers diarrhea”??

Clinical examination

- Not pale, not icteric, No LN
- Mild dehydrated
- CVS, RS, CNS-normal
- Abdomen- soft spleen 2cm below LOM

ls

- Hb= 12.4g/dL
- WBC-3500, N-35%, L-52%
- Blood picture: Leucopenia with relative lymphocytosis
- CRP-24mg/dL
- UFR: Albumin +, RBC- few HPF
- LFTs- mild deranged
- S. creatinine- 1.8mg/dL
Likely diagnosis?

- Typhoid / Paratyphoid

Examination revealed an eschar hidden (Not noticed)
IFA: 1: 1024 for O.tsutsugamushi
Rx: Oral Doxycycline

Scrub typhus mimicking enteric fever

Case 6: A group of soldiers

- An acute outbreak of fever and cough (severe pneumonia) among a group of military serving in the Forward Defense line in Palali Jaffna during late 2008; Some were air lifted to National Hospital, Colombo, Sri Lanka on a Sunday

Examination

- Very ill; some were dyspnoic at rest
- Chest examination: scattered coarse crepitations
- Reduction in capillary oxygen saturation in seriously ill patients
• Chest X-ray

Investigations
• FBC: WBC 5600; N 58%, L 38%
• UFR: Alb ++, RBC 4–8,
• Blood culture: A/W
• CRP 94 mg/dL
• BU/SE/S.creatinine (Mild elevations)
• LFT&Mild derangements: AST 210 iu/L, ALT 156 iu/L

DD?
• Atypical pneumonia
• Bacterial pneumonia
• Bio-terrorism (ANTHRAX)

What do you notice?

Why many affected?
• Mite islands

• Detected on the face….
• Final diagnosis of Scrub typhus resulting in severe pneumonia
Case 7

- A 24-yr-old bus driver who used to sleep in the bus over night
- Admitted during O'HKG outbreak
- Intermittent high Fever 14 days (101-102°F)
- Progressive severe multiple joint pains: Ankles, knees, Shoulders; Difficult to walk
- Stooped posture

Examination

- Not pale, not icteric, mild conjunctival injection, No LN
- Erythema nodosum over both shins, obvious arthritis
- Hepato-splenomegaly

Investigations

- Hb: 11.7 g/dL
- WBC: 7600; N-56%, L-38%
- Platelets: 110,000
- Blood picture: Non reactive, few toxic granules in neutrophils, no pus cells
- ESR-108 1st Hr
- CRP-64 mg/dL (Normal <6)
- Urine- Red cells 5-10/HPF, Alb+-
- AST-98 iu/L, ALT-- 65 iu/L, Alk Po4- 114iu/L
- S.Creatinine –1.2mg/dL
- ANA - ve, Rheumatoid Fact - ve, S.Ferritin - Normal

DD?

- Chikungunya
- Sero negative arthritis
• Resolved completely with oral doxycycline over 7 days (afebrile within 48 hours)
• Diagnosis: scrub typhus

Case 8
• 58 yrs, female with low grade intermittent fever for 16 days
• Intermittent cough
• Mild joint pains
• Mild loss of appetite
• Worked abroad: (Returned from Middle East 5 years back)

Examination
• Average built (Says has lost weight)
• Few cervical nodes 0.5cm
• 2 finger splenomegaly
• CVS no murmurs
• Resp normal
• ONS/Optic fundi: normal

Lx
• Hb: 9.8g/dl
• WBC: 5600, N 45%, L 52%, Platelets 154,000
• Blood picture: No abnormal cells, no toxic granules, no viral lymphocytes
• ESR: 78 1st hr, CRP 96iu/l
• Normal Chest Xray
• UFR: albumin +, RBC 2-4 HPF, Pus cells: negative, B. urea: 45mg/dl
• AST: 125 iu/L, ALT: 256 iu/L
• Mantoux test -ve
• ANA, RF -ve, S. ferritin -ve
Rxs

- Antibiotics: (short courses: penicillins / 3rd gen cephalosporins)
- Anti malarials: CHQ

USS abdomen L & Sp enlarged, ? Pelvic mass
CT abdomen and pelvis normal
ECHO cardiography Normal (Trans thoracic + Trans oesophageal)

Treatment trials

- No response to Co-amoxyclav + clarythromicin over 5 days
- No response to ceftrioxone for 4 days
- No response to meropenum for 4 days

Viral screen

- CMV-negative
- EBV-negative
- Toxoplasma-negative
- HIV-negative

Repeat blood counts- illness > 3 weeks

- Hb: 8.2 g/dl
- WBC: 3200, N 34%, L62%
- Platelets: 96,000
- Blood picture: No abnormal cells. Few large lymphocytes with normal morphology
- LDH-760

DD

- Infiltrative illness / BM / Liver involvement
- TB
- Malaria (Previous experience of a child with falciparum malaria)
- Brucellosis
• Being planned for anti-TB treatment trial
• BM Biopsy carried out: + sent for TB cultures / PCR

• BM Bx: Reactive with haemo-phagocytosis
• Cells are being engulfed by macrophages

• Reexamined the patient:
Patient was strongly positive for Orientia tsutsugamushi and had a dramatic recovery with oral doxycycline.

Transactions of Royal Society of Tropical Medicine and Hygiene 2009

Consider rickettsial illness following a travel to an "endemic region"
• Fever and a rash
• Fever and lymphadenopathy
• Fever and any systemic manifestation especially when not responding to "appropriate non-rickettsial antibiotics"
• Fever alone...!!
• Do not delay the diagnosis
• Try to identify the offending organism...

Conclusion ...

Be the next clinician to describe a....
• New endemic region
• Or a novel rickettsial agent..!!
More important!!!

We are trying hard to figure out what is unseen...

- We have utterly failed to prevent what was obviously seen...

DECISION FROM HELL. Sri Lanka attacks: Brit dad forced to make agonising choice over which of his two kids to save - before both were tragically killed in blast

A Danish billionaire says 3 of his 4 children died in the Sri Lanka bombings
This lecture is dedicated to all those who died of this brutal attack.

I wouldn’t have been here today.... not for their generous sharing with me....

Greg  David  Stephen
Mareena  Yupin  Amanda  Blanton

What are the problems in the diagnosis?

• Lack of awareness
• Poor attempt at history taking
• Poor examination

How do I suspect rickettsioses?

• Fever
• Associated with chills, severe headache, and body aches
• Not feeling very ill in between fever spikes
• Acute phase: more frequent, high grade

"Thousands of candles can be lit from a single candle, and the life of the candle will not be shortened. Happiness never decreases by being shared."
Lord Buddha...

Thank you...
Fever

• Untreated chronic phase: Low grade intermittent

Common clinical syndromes

• Early signs and symptoms usually are nonspecific or mimic benign viral illnesses
• Chills, and headache (possibly severe).
• Associated with malaise and myalgia. Nausea, vomiting, and anorexia are common in early illness

Exposure Risk???

• Outdoor recreational or occupational activities
• If the activity takes place near high vegetation/scrub land (e.g., camping, hiking, gardening)
• Frequent contact with animals and those who have pets
• A history of tick bites (most do not realize they have been bitten)
• Mite bites are never noticed.

Signs: Conjunctival injection and sub conjunctival haemorrhages

• A patch of redness in the lateral limbus of each eye, more prominent when febrile
• Severe conjunctival injection
• Rarely associated with sub-conjunctival hemorrhages

Lymphadenopathy

• Regional
• Generalized

Eschar: Presumptive diagnosis
Eschar: DD

- Cutaneous anthrax
- Tularaemia
- Necrotic arachnidism (brown recluse spider bite)
- Rat bite fever (*Spirillum minus*)
- Staphylococcal or streptococcal ecthyma
- *Bartonella henselae*

**Commoner in Scrub typhus (20-87%)**

In some SFG:
- *R conorii* (Except in Israel / Indian) - 80% in MSF
- *R australis*
- *R japonica*
- *R. africae* (Usually multiple)
- *R. parkeri*
- *R. slovaca*
- *R. honei*
• Vector climbs until finds a resistance
  • Skin fold
  • Strap of a garment
  • Usually one bite by one vector

What are the other sites you will see them? Basically anywhere.

Rash

• Wide variability in the evolution, distribution, and appearance
  • Appears 3-5 days after fever but may occur early or late
  • Most central distribution (May spare face)
  • “RMSP- Peripheral eruptions: start in wrists and ankles and spread centripetally”: rarely observed
  • Sometimes confined to one body area
  • Erythematos maculopapular, vesicular etc

Rash

Discrete, erythematous, maculopapular
Prominent with fever
Mostly trunk arms palms soles

• Commoner in SFG than ST
Mediterranean spotted fever

Rossio R et al. IJD 2015; 35: 34-36

Malignant Mediterranean spotted fever in the setting of diabetes mellitus: An uncommon cutaneous entity


Rocky mountain spotted fever


Rickettsialpox

A case of rickettsialpox in Northern Europe

Renvoisé A et al. IJD 2012 (16) : e221-e222

Rash: Chikungunya

Tick-borne lymphadenopathy (TIBOLA)


Reg Sot et al. BMC Infectious Diseases 2011; 11:167
Approach based on the regional epidemiology

Tick borne rickettsiosis: A returning traveler from Americas…

Reported incidence rate of spotted fever rickettsiosis, by county — United States, 2000-2013

2013: Tick-borne rickettsiae (TBR) in North America (except Mexico)
Pathogenic rickettsiae (Coloured): possible pathogenicity and unknown pathogenicity (White)

2013: TBR in Mexico and Central America
Pathogenic rickettsiae (Coloured): possible pathogenicity and unknown pathogenicity (White)
Main rickettsial pathogens circulate in the Americas

- *R. rickettsii*
- *R. parkeri*
- *R. massiliae*

At least four in Africa

- *R. africae*
- *R. conorii*
- *R. massiliae*
- *R. aeschlimanni*
TBR: A returning traveler from Australia

Pathogenic rickettsiae (Coloured) possible pathogenicity and unknown pathogenicity (White)

Four in Australia

- *R. australis*
- *R. honei*
- *R. honei* subsp. *marmionii*
- *R. gravesii*

Typhus group: *R. prowazekii*: Body louse / *Amblyomma* ticks

Typhus group: *R. typhi*: Flea borne

Transitional Group: *Rickettsia felis* (Flea borne)
Treatment

• In vitro susceptibility:
  • doxycycline, thiamphenicol and fluoroquinolone.
  • Not susceptible to
  • Beta-lactams, aminoglycosides and cotrimoxazole

• R. massiliæ, R. aeschlimanii and R. raoultii are resistant to rifampicin
• All SFG Rickettsiae are resistant to erythromycin
• Susceptibility in vitro of Rickettsiae to other macrolides is variable
• Josamycin seems to be the most active compared to clarithromycin
  and pristinamycin

Fluoroquinolone are also used for treatment of spotted fever group Rickettsiosis:

• Fluoroquinolone are significantly associated with more severe spotted fever infection, particularly for patients presenting MSF:

• Using fluoroquinolone for Rickettsioses treatment is not recommended.