Fever with hemorrhagic manifestations

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Case with a tick bite

- A 70-year old British man
- Recent trip to Bulgaria
- He was bitten by a tick while outdoors
- He removed the tick that evening without difficulty
- Approximately five days previously, he had removed a tick from a cat and crushed it between his fingers
Clinical features

- Fever, sweats, cough, sore throat, myalgia, headache, diarrhea and two episodes of collapse
- A petechial rash on his legs and bilateral crepitations on chest auscultation
- Blood count and chemistry
  - Platelet count of $26 \times 10^9$/L (norm: $150–400 \times 10^9$ /L)
  - Neutrophils of $1.1 \times 10^9$/L (norm: $2.0–7.5 \times 10^9$/L)
  - ALT, at 64 units (U)/L (norm: 10–40 U/L)
Petecheie
What is your diagnosis?

- Malaria
- Dengue
- Rickettsial infection
- Ebola Virus Disease
- Crimean Congo Hemorrhagic Fever
Fever with hemorrhage

- Viral hemorrhagic fevers
  - Lassa, Ebola, Marburg, Yellow fever, Crimean–Congo, Dengue, Hantaan
- Rickettsial infections
- Typhoid fever
- Leptospirosis
- Severe sepsis (DIC)
- Infective endocarditis
- Meningococcal septicemia
Non infectious diseases

- Acute leukemia
- Hemolytic uremic syndrome
- Collagen-vascular diseases
- Vasculitis including Henoch–Schönlein purpura
- Idiopathic or thrombotic thrombocytopenic purpura
- Drug rashes
- Snakebite
Travel history

- Destination
- Prophylaxis
- Immunization
- Exposures
- Time
- Activities
- Returning traveller
Geographical distribution of diseases

Ebola

Dengue

CCHF

Malaria
International Alerts

Most Recent Alert

Published Date: 2015-04-07 21:26:41
Subject: PROIAHEDRl> Avian influenza (70); Netherlands (Noord Brabant) poultry, LPAI H5N2, OIE
Archive Number: 20150407.3262420

AVIAN INFLUENZA (70); NETHERLANDS (NOORD BRABANT) POULTRY, LPAI H5N2, OIE

A ProMED-mail post
http://www.promedmail.org
Promed-mail is a program of the
International Society for Infectious Diseases
http://www.isid.org

Date: Tue 7 Apr 2016
Source: OIE, WAHID (World Animal Health Information Database), weekly disease information 2015; 26(19) [EID 17]

Low pathogenic avian influenza (poultry), Netherlands

Information received on [and dated] 7 Apr 2015 from Dr Christianne Draaisma, Chief Veterinary Officer, Ministry of Agriculture, Nature and Food Quality, The Hague, Netherlands

Summary
Report type: Immediate notification
Date of start of the event: 1 Apr 2015
Date of pre-confirmation of the event: 3 Apr 2015
Rationale for notification: Reoccurrence of a listed disease
Date of previous occurrence: Mar 2015
Manifestation of disease: Sub-clinical disease
Causal agent: Low pathogenic avian influenza virus
Serotype: H5N2
Nature of diagnosis: Laboratory (advanced)

This event pertains to a defined zone within the country

New outbreaks (1)
Summary of outbreaks: Total outbreaks: 1

Follow us on:
### Viral Hemorrhagic Fevers

<table>
<thead>
<tr>
<th>Virus/Condition</th>
<th>Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lassa fever</td>
<td>West Africa</td>
</tr>
<tr>
<td>Junin (Argentina HF)</td>
<td>South America</td>
</tr>
<tr>
<td>Machupa (Bolivian HF)</td>
<td>South America</td>
</tr>
<tr>
<td>Hantavirus</td>
<td>Diverse</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Tropical Africa, Latin America</td>
</tr>
<tr>
<td>Dengue fever</td>
<td>Tropical areas</td>
</tr>
<tr>
<td>Rift Valley fever</td>
<td>Africa</td>
</tr>
<tr>
<td>CCHF</td>
<td>Africa, Eurasia</td>
</tr>
<tr>
<td>Omsk HF</td>
<td>Siberia</td>
</tr>
<tr>
<td>Kyasanurs Forest Disease</td>
<td>India</td>
</tr>
<tr>
<td>Alkhurma HF</td>
<td>Saudi Arabia</td>
</tr>
<tr>
<td>Severe fever with thrombocytopenia syndrome</td>
<td>Japan</td>
</tr>
</tbody>
</table>
VHF: Human to human transmission

- Ebola
- Marburg
- CCHF
- Lassa Fever

- Close contact with the blood secretions, organs or other body fluids of patients
- Needle stick injury
- Aerosol generating procedures
Typical incubation period for travel-related IDs

- Chikungunya
- CCHF
- Dengue
- Tick typhus
- Typhoid fever
- Malaria
- Leishmaniasis
- Tuberculosis
- HIV
- Echinococcosis
- Hepatitis B

Time periods:
- 1 week
- 1 month
- 6 months
- 1 year
- 10 years
### Physical examination

- CNS status
- Bleeding
- Murmur, cardiac rhythm
- Pulmonary
- Abdomen
- Lymphadenopathy
- Rash, other skin symptoms
- Temperature
- Pain
- Pulse, regular?
- Blood pressure
- O2 Saturation (respiratory rate)
Hemorrhagic signs
## Associated symptoms

<table>
<thead>
<tr>
<th>Physical finding</th>
<th>Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>Dengue, typhoid, rickettsial infections, syphilis, gonorrhoea, ebola virus, brucellosis</td>
</tr>
<tr>
<td>Jaunice</td>
<td>Hepatitis, malaria, yellow fever, leptospirosis, relapsing fever</td>
</tr>
<tr>
<td>LAP</td>
<td>Rickettsial infections, brucellosis, dengue, HIV, Lassa fever, visceral leishmaniasis</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>Hepatitis, leptospirosis, typhoid, amoebiasis, malaria</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>Malaria, relapsing fever, tyrpanasomiasis, typhoid, brucellosis, kala azar, typhus, dengue</td>
</tr>
<tr>
<td>Eschar</td>
<td>Rickettsial infections, borrelia</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>HFVs, Rocky Mountain spotted fever, epidemic louse borne typhus</td>
</tr>
<tr>
<td>Organ System</td>
<td>Clinical Manifestation</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>General</td>
<td>Fever (87%), fatigue (76%), arthralgia (39%), myalgia (39%)</td>
</tr>
<tr>
<td>Neurological</td>
<td>Headache (53%), confusion (13%), eye pain (8%), coma (6%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Chest pain (37%),</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Cough (30%), dyspnea (23%), sore throat (22%), hiccups (11%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Vomiting (68%), diarrhea (66%), anorexia (65%), abdominal pain (44%), dysphagia (33%), jaundice (10%)</td>
</tr>
<tr>
<td>Hematological</td>
<td>Any unexplained bleeding (18%), melena/hematochezia (6%), hematemesis (4%), vaginal bleeding (3%), gingival bleeding (2%), hemoptysis (2%), epistaxis (2%), bleeding at injection site (2%), hematuria (1%), petechiae/ecchymoses (1%)</td>
</tr>
<tr>
<td>Integumentary</td>
<td>Conjunctivitis (21%), rash (6%)</td>
</tr>
</tbody>
</table>

WHO Ebola Response team. NEJM 2014
Special investigations

- Thick & thin smear (repeat)
- CBC with differential
- Coagulation (PT, aPTT)
- Biochemistry & Transaminases
- Cultures Blood/Fecal/Urine
- Malaria Ag test
- Imaging - CXR & Liver Ultrasound
- Save serum sample for acute serology
Diagnosis of VHF

Critical information: Date of onset of fever/symptoms

- **viremia**
- **IgM**: up to 3 – 6 months
- **IgG**: 3 – 5 years or more (life-long persistence?)

RT-PCR, ELISA IgM, ELISA IgG

Fever
CCHF: Poor prognostic factors
Warning signs

- Thrombocytopenia
- Leukocytosis
- Prolonged aPTT
- Decreased fibrinogen
- Elevated ALT, AST, LDH
- Hematemesis
- Melena
- Hematuria
- Diarrhoea
- Somnolence
- Splenomegaly

Independent predictors of mortality

Viral load is predictor of outcome

Differential diagnosis

- Other HFVs
- Leptospirosis
- Meningococcemia
- Rickettsial diseases
- Malaria
- Sepsis
- Influenza
- Viral hepatitis
- Toxic shock syndrome

- Idiopathic or thrombotic thrombocytopenic purpura
- Hemolytic uremic syndrome
- Acute leukemia
- Collagen-vascular diseases

68% of cases have an initial misdiagnosis of various diseases

Consider geographic distribution of diseases

Farrar J et al. Manson’s Tropical Disease 2015
Ebola vs Malaria

Bottom line – always exclude malaria first
Beyond malaria: causes of fever in outpatient Tanzanian children

VHFs: Treatment

- **Standard treatment is supportive therapy**
- Early aggressive intensive care support
- Support of coagulation system
- Careful monitoring
  - Oxygenisation
  - Fluid & electrolyte balance
  - Blood pressure
- Early use of inotropic agents (dobutamine)
- Ventilation support for severe cases
- Renal replacement therapy
- Pain management
- Parenteral nutrition

Early recognition is critical

- Initiate
- Identify
- Diagnose
- Isolate
- Treat
- Inform
VHF risk assessment

Modified from
Public Health England

Moore LSP et al. British J Hospital Medicine 2014;75:515-22
Isolation

- Standard
- Contact
- Droplet

Royal Free London
NHS Foundation Trust
Cohorting
Personal protective equipment (PPE)
Conclusion

- Common causes of fever with hemorrhage are VHF, rickettsia infections, meningococcemia & malaria.
- Careful assessment of travelers involves:
  - Obtaining detailed travel history
  - Determine risk factors for infection
- Early clinical assessment of the severity of infection is crucial.
- Early diagnosis, early management and isolation of patient.
- Inform ID & CM and public health.
ESCMID Study Group for Infections in Travellers and Migrants - ESGITM

News & Activities

ESGITM @ ECCMID 2015 in Copenhagen, Denmark

- **ESGITM Educational Workshop EW11**: Final destination ICU - cases of severely ill travelers. Organized jointly with the Critically Ill Patients Group (ESGCP).
- **ESGITM Meet-the-Expert Session ME01**: Screening and prophylaxis of migrants. 18:15 - 19:15 (Room 17)
- **ESGITM Business Meeting**: All interested persons are cordially invited to join the meeting and plan future Study Group activities.
- **ESGITM Symposium SY30**: Refugees, migrants and infections.

For more details, please check the ECCMID programme.

European national websites with Ebola guidelines

Members of ESGITM and the UEMS Section of Infectious Diseases (ESGIDM) have compiled a list of national Ebola guideline websites from round Europe.

Find the list on the ESCMID Ebola news page.