Hantavirus Case at Wrexham

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The case

• A 28 year old man presented in November 2012 with a 4-day history of fever, vomiting and headache.

• Known type two diabetic receiving sitagliptin and metformin

• He had travelled to Turkey for a resort holiday in September 2012

• No contact with animals or animal products when on holiday
Contacts

• His girlfriend did kept two pet brown rats (*Rattus norvegicus*) at home in Wales
• They were kept in the bedroom in a cage
• Patient cleared the cage periodically
Examination

- Febrile, tachypnoeic, diaphoretic, tachycardic and hypotensive
- Urine analysis revealed the presence of protein, blood, glucose and ketones
- Haemoglobin 20.3g/dl
- WBC 15.0 (12.3 neutrophils)
Investigations

- Platelet count 19 x10^9/l.
- Clotting was disturbed
  - INR 1.6
  - PTT 57 seconds
  - Thrombin time 66 seconds
- Liver function was abnormal
  - ALT of 511u/l
  - Bilirubin 87umol/l
  - Albumin 32g/l
- Hyponatraemic
- Raised serum creatinine (169umol/l)
- Blood glucose (20.3mmol/l)
- LDH (1993u/l) and lactic acid (7.5mmol/l).
- Blood cultures were sterile
- Legionella, Coxiella leptospirosis negative
Impression

Overwhelming infection with lactic and keto-acidosis
Treatment

• ITU
• Aggressive fluid replacement
• Antibiotics:
  – tazocin, meropenem, vancomycin, coamox........
• Platelets, FFP, cryoprecipitate
• Ventilation needed for 21d
  • Complicated by Pseudomonas superinfection
Diagnosis

• Sample taken 30d after admission:
  • Serology for Seoul hantavirus strongly positive 1:10000 by IFA
• PCR for hantavirus negative
• An earlier sample sent by his GP for mild transaminasemia in October 2012 was retrieved:
  • Negative for hantavirus by serology and RT-PCR.
• After 52 days in hospital, his renal function made a full recovery, rehabilitated, and discharged
Overview of hantavirus infections

- Family Bunyaviridae.
- Enveloped negative-stranded RNA viruses with a tripartite genome.
- Genetic diversity generated by genetic drift, reassortment of genome RNA segments, and recombination.
Overview of hantavirus infections

• Rodent reservoir
• Each hantavirus spp carried by a specific rodent
• Seoul hantaviruses carried by *Rattus norvegicus*
• 23 distinct hantaviruses species have been recognized
• Provisional species includes 30 viruses.
• ‘explosion’ in a number of newly discovered hantaviruses
# Characteristics of Some Known Hantaviruses

<table>
<thead>
<tr>
<th>Hantaviruses</th>
<th>Region</th>
<th>Reservoir</th>
<th>Pathology</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hantaan</strong></td>
<td>Asia</td>
<td>Field mouse</td>
<td>Renal</td>
<td>5-15%</td>
</tr>
<tr>
<td><strong>Seoul</strong></td>
<td>Worldwide</td>
<td>Domestic rat</td>
<td>Renal</td>
<td>1%</td>
</tr>
<tr>
<td><strong>Puumala</strong></td>
<td>N Europe</td>
<td>Bank vole</td>
<td>Renal</td>
<td>1%</td>
</tr>
<tr>
<td><strong>Prospect Hill</strong></td>
<td>United States</td>
<td>Meadow vole</td>
<td>No known human disease</td>
<td></td>
</tr>
<tr>
<td><strong>Sin Nombre</strong></td>
<td>North America</td>
<td>Deer mouse</td>
<td>Pulmonary</td>
<td>50%</td>
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</tbody>
</table>
Overview of hantavirus infections

- Clinical presentation: hantavirus pulmonary syndrome (HPS) to haemorrhagic fever with renal syndrome (HFRS)
- Seoul hantaviruses are believed to present as HFRS
  - Range from a benign undifferentiated febrile illness without renal failure to diffuse haemorrhage, intractable shock and multi-organ failure
- History of contact with rats should be elicited
- Hantavirus as a differential diagnosis even in the absence of a history of foreign travel
- Diagnosis can be made by serology or RT-PCR to demonstrate viral RNA. Supportive therapy is the mainstay of care for patients with HFRS.
Figure 71.4 Schema of clinical course of severe hemorrhagic fever with renal syndrome (HFRS).

### HPS

<table>
<thead>
<tr>
<th>Phase</th>
<th>Prodrome</th>
<th>Cardiopulmonary</th>
<th>Convalescent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Shock</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Diuresis</td>
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</tbody>
</table>

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<tr>
<th>Parameter</th>
<th>Prodrome</th>
<th>Cardiopulmonary</th>
<th>Convalescent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoblasts</td>
<td>±</td>
<td>+ +</td>
<td>± ±</td>
</tr>
<tr>
<td>Bands/Meta</td>
<td>±</td>
<td>+ + +</td>
<td>± + + + + +</td>
</tr>
<tr>
<td>Platelets</td>
<td>±</td>
<td>+ + + +</td>
<td>± + + + + +</td>
</tr>
<tr>
<td>HCT</td>
<td>±</td>
<td>+ +</td>
<td>± + + + + +</td>
</tr>
<tr>
<td>AST</td>
<td>±</td>
<td>+ + + + +</td>
<td>± + + + + + + +</td>
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<tr>
<td>LDH</td>
<td>±</td>
<td>+ + + + +</td>
<td>± + + + + + + +</td>
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<tr>
<td>PTT</td>
<td></td>
<td>+ + + + +</td>
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<table>
<thead>
<tr>
<th>Phase</th>
<th>3–6 days</th>
<th>7–10 days</th>
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</thead>
<tbody>
<tr>
<td>Fever</td>
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**Figure 71.5** Schema of clinical course of severe hantavirus pulmonary syndrome. Meta, metamyelocytes; HCT, hematocrit; AST, aspartate transaminase; LDH, lactate dehydrogenase; PTT, partial thromboplastin time.

(Prepared by Li Lien Yang.)
Epidemiological investigations

- RNA similar to Seoul hantavirus detected in the 2 pet rats
- Acquired from a larger pack owned by a couple in England
- Retrospective inquiry -> November 2011 one of the owners admitted to hospital with fever, renal impairment, splenomegaly and thrombocytopenia -> secondary to an unidentified viral illness.
- Retrospective testing -> samples retrieved from November 2011 and January 2013 hantavirus titre 1:1000 and 1:10000
- The second owner had a low titre IgG titre of 1:100 in samples from August 2012 and January 2013, also suggesting a hantavirus infection in the past. No recollection of any significant illness.
- Seoul-like hantavirus was detected in seven rats owned by the couple.
- All 21 rats had antibodies to Seoul-like hantavirus
Implications

• Hantavirus infection has long been considered an imported infection not indigenous to the UK
• The first hantavirus isolated from an infection acquired in the UK was reported in 2012 and was traced to wild rats in the Yorkshire area
• The occurrence of these two further cases, very strong evidence of local transmission within mainland UK
• Molecular analysis indicates that there are at least two separate Seoul-like hantaviruses circulating in the UK.
IMPLICATIONS

- Owners of pet rats
- Visitors to owners of pet rats
- Farmers
- Areas with rat infestation
- Undiagnosed cases of a viral-like illness? hantavirus
- Unexplained renal failure? hantavirus
Dilemmas

Should they be tested?
Unanswered questions

• Extend of infection in rats in the UK
• Risk of transmission to owners/visitors
• Risk of overt infection
• Any role for testing owners/rats?
• Should PCR positive rats be culled?
• Does sero-positivity indicate immunity?
Further studies

- Large multicentre seroprevalence study to determine seropositivity in owners of pet rats. Pet rats to be tested simultaneously
  - Blood collection from rats difficult
  - Urine testing not very sensitive
- Blood donor study to determine seroprevalence in general population
- Rat blood collection
acknowledgements

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NFRs