Fatal Leptospirosis and *Escherichia coli* Co-infection in A Post-Partum Woman

by

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- Leptospirosis is known to be a zoonotic infections worldwide and is endemic in tropical and subtropical countries\(^1\)

Reference
• Co-infections in Leptospirosis have been reported with mixed survival outcomes

• Among organism that were reported before are Dengue virus, *Chikungunya* virus, *Burkholderia pseudomallei* and malaria\(^1,2,3,4\)

• To date with, this is the first report of *Escherichia coli* and Leptospirosis co-infection

Reference
Background History of Madamme

A

- 32 year old previously healthy Malay lady
- Delivered 23 days ago via spontaneous vaginal delivery
- Post-natal history was unremarkable as she was discharged home well the next day
- Home confinement in mother-in-law house since delivery (in a suburban area)
Complained of severe headache which was preceded by two days history of fever.

During the consultation, she developed GTC seizure.

Immediately Transferred to the nearest hospital via ambulance.
Arrival To Emergency Department 55 Minutes Later

She was comatose, hyperpyretic and in shock

Intubated immediately for Airway Protection and broad spectrum antibiotics IV Ceftriaxone 2 g stat was given after blood culture taken

Clinical examinations showed presence of neck stiffness but no hyporeflexia or hypertonia. Barbinski signs were equivocal and there was no clonus. Noted bleeding from oral cavity and venepuncture sites

GCS : E1V1M1
Pupils : 1/1 reactive to light
Temperature: 41.6 degree celcius
BP : 58/26 mmHg
PR: 100/Min
Spo2 : 100 % (on HFMO)
Resuscitation in Emergency Department

Bedside Cardiac Scan showed collapsed inferior vena cava
Bedside Abdomen and Pelvic scan were normal

Remained hypotensive and oliguric despite fluid resuscitations

BP stabilized being supported with IVI noradranaline
0.4 mcg/kg/min

Bleeding from venepuncture, branula and oral cavity persisted

Provisional diagnosis
Meningoencephalitis with dual septic and hypovolaemic shock

Hb 12.9 g/dL
WCC 7.1 x 10^3 u/L
PLT 217 x 10^3 u/L
Urea 4.1 mmol/L
Creat 152 umol/L
Na 138 mmol/L
K 4.5 mmol/L
AST 108 U/L
ALT 81 U/L
CK 724 U/L
PT 15 s
INR 1.18
APTT 33s
Transfer to Intensive Care Unit: 2 hours Later

- Pupils 2 mm bilaterally and sluggish to light stimulation
- Bedside cardiac scan: inferior vena cava diameter 1.09 cm with 50% collapsibility

- Fluid resuscitation continued and inotropic support maximised

- Blood oozing from venepuncture site and continuous per vaginal bleeding and oral cavity bleeding
  - Repeated blood parameters were consistent with consumptive coagulopathy

- Efforts were made to control her coagulopathy with DIVC regime transfusion, IV vitamin K, IV tranexamic acid
## Onset of Disseminated Intravascular Coagulopathy at 4th Hours of Presentation

<table>
<thead>
<tr>
<th>Hour(s) From Presentation To Our Facility</th>
<th>At Presentation</th>
<th>2 Hours</th>
<th>4 Hours</th>
<th>5 Hours</th>
<th>11 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full Blood Count</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>White Cell Count</td>
<td>7.1 x 10³ uL</td>
<td>Sample clotted</td>
<td>10 x 10³ uL</td>
<td></td>
<td>5.6 x 10³ uL</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>12.9 g/dL</td>
<td></td>
<td>12.4 g/dL</td>
<td></td>
<td>9.2 g/dL</td>
</tr>
<tr>
<td>Platelet</td>
<td>217 x 10³ uL</td>
<td></td>
<td>46 x 10³ uL</td>
<td></td>
<td>73 x 10³ uL</td>
</tr>
<tr>
<td><strong>Renal Profile</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Urea</td>
<td>4.1 mmol/L</td>
<td>4.6 mmol/L</td>
<td>Sample lysed</td>
<td>4.9 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>152 umol/L</td>
<td>175 umol/L</td>
<td></td>
<td>226 umol/L</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>138 mmol/L</td>
<td>141 mmol/L</td>
<td></td>
<td>150 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td>4.5 mmol/L</td>
<td>4.6 mmol/L</td>
<td></td>
<td>2.4 mmol/L</td>
<td></td>
</tr>
<tr>
<td><strong>Coagulation Profile</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PT</td>
<td>15 s</td>
<td>Sample clotted</td>
<td>&gt;120 s</td>
<td>&gt;120 s</td>
<td>50.1 s</td>
</tr>
<tr>
<td>INR</td>
<td>1.18</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>5.44</td>
</tr>
<tr>
<td>APTT</td>
<td>33 s</td>
<td>&gt;180 s</td>
<td>&gt;180 s</td>
<td>&gt;180 s</td>
<td>155 s</td>
</tr>
<tr>
<td><strong>Liver Function Test</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>108 U/L</td>
<td>209 U/L</td>
<td>Sample lysed</td>
<td>516 U/L</td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>81 U/L</td>
<td>78 U/L</td>
<td></td>
<td>234 U/L</td>
<td></td>
</tr>
<tr>
<td>Total Bil</td>
<td>13.2 umol/L</td>
<td>5.6 umol/L</td>
<td></td>
<td>9.8 umol/L</td>
<td></td>
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<tr>
<td>LDH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2480 U/L</td>
</tr>
<tr>
<td>CK</td>
<td>724 U/L</td>
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</table>
Onset of Pulmonary Haemorrhage Syndrome at the 5th Hours of Presentation

Chest X-Ray at Arrival to ED

Chest X-Ray at ICU after Clinical Diagnosis of Pulmonary Haemorrhage
Remained in decompensated shock despite early institution of broad spectrum antibiotics and intensive care

Patient succumbed at 12th hours
Post-Mortem Examination

- Conducted by state forensic pathologist next morning
- The only clue we had was blood culture showed gram negative bacilli
- There was no structural abnormality or obvious inflammation detected in the genitourinary system

Figure 1. Gram negative bacilli
The brain was oedematous with the weight of 1452 g

There was also Duret hemorrhage at the midbrain confirming presence of raised ICP that complicated with uncal herniation

Confirming the lethal insult to the brain

Figure 2. Duret haemorrhage of the midbrain
Other Post-Mortem Examination Findings

There were evidence of
• DIVC
• Pulmonary haemorrhage

Photomicrograph 1: Mixture of microfibrin thrombi and inflammatory cells within the blood vessels. (with H&E stain, 40x)
Microbial Confirmation of *Leptospirosis* and *Escherichia coli* Co-infection

- Blood C & S: *Escherichia coli*
- Leptospirosis Ig M antibody: Positive (Leptorapidae test kit with sensitivity 88%; specificity 93%)
- Microscopic agglutination test: 1:400
  - Leptospirosis serovar Sarawak (Sensitivity 92%; specificity 98%)

* Dengue NS1 antigen: Negative
* CSF fluid PCR for Leptospirosis: Negative
* Urine C & S, HVS C & S, CSF C & S: NG
Discussion

Acute Neurological Presentation In *Escherichia coli* and Leptospirosis Dual infection

- Synergism between *Escherichia coli* and Leptospirosis resulted in acute neurological deterioration due to widespread endothelial damage

- Swift increase in intracranial pressure due to generalized cerebral edema caused transtentorial herniation complicated with Duret haemorrhage

- Duret haemorrhage is almost always associated with fatal outcome

Henry Duret, a nineteenth century French surgeon who first described Duret Haemorrhage
Increased Susceptibility Among Puerperal Populations In This Fatal Dual Infection

Puerperal populations from Leptospirosis endemic countries are at increased risk of such fatal dual infections.
## Escherichia coli

### Intermediate Susceptibility To Empiric Antibiotic

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Susceptibility Profiles</th>
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</thead>
<tbody>
<tr>
<td><strong>Cephalosporins</strong></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>Resistance</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>Resistance</td>
</tr>
<tr>
<td><strong>Quinolones</strong></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Susceptible</td>
</tr>
<tr>
<td><strong>Aminoglycoside</strong></td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Susceptible</td>
</tr>
<tr>
<td><strong>B-lactam</strong></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Resistance</td>
</tr>
<tr>
<td>Amoxicillin/clavulinic acid</td>
<td>Resistance</td>
</tr>
<tr>
<td>Ampicillin/Sulbactam</td>
<td>Resistance</td>
</tr>
<tr>
<td>Pipercillin / Taz</td>
<td>Susceptible</td>
</tr>
<tr>
<td><strong>Carbapenem</strong></td>
<td></td>
</tr>
<tr>
<td>Imipenem</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>
Clinical Implications of this Novel Case

- Underscores the importance of considering Leptospirosis co-infections in patients from tropical countries presented with similar rapid deterioration.

- A missed diagnosis will happen when only either blood culture or Leptospirosis serology is considered.
Clinical Implications of this Novel Case

- Home environment advice be given to puerperal populations who are at risk of Leptospirosis infection and to seek health care advice at the earliest sign of illness

- This advice should be emphasized during post-natal home visit care
Conclusion

- This is a novel case of fatal Leptospirosis and *Escherichia coli* co-infection which took a fulminant course once it happened

- Puerperal populations has increased susceptibility to this dual infections

- High index of suspicion in subjects presented with fever and rapid neurological deterioration

- Effort to prevent Leptospirosis and *Escherichia coli* infections among puerperal population
Acknowledgement

We would like to acknowledge the following members for their permission to publish this case report and contributions

- Deceased family
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- Dr Siti Zanariah, Forensic Pathologist, Hospital Raja Permaisuri Bainun