Severe Acute Respiratory Syndrome: Lessons from Singapore

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An outbreak of severe acute respiratory syndrome (SARS) occurred in Singapore in March 2003. To illustrate the problems in diagnosing and containing SARS in the hospital, we describe a case series and highlight changes in triage and infection control practices that have resulted. By implementing these changes, we have stopped the nosocomial transmission of the virus.

A n outbreak of severe acute respiratory syndrome (SARS) was first recognized in Singapore on March 12, 2003. The index patient was hospitalized at Tan Tock Seng Hospital, which has since become the country’s designated SARS hospital. The patient infected 20 other people (including patients and healthcare workers), who subsequently became the sources for secondary spread of the infection (1). As of June 12, 2003, a total of 206 cases and 31 deaths attributed to SARS had been reported in Singapore.

We describe the important lessons learned during the triage and containment of SARS at the National University Hospital, Singapore. Both involved expanding isolation criteria to include all patients with undifferentiated fever (even in the absence of respiratory symptoms or chest x-ray changes), improving contact-tracing methods, enforcing the use of fit-tested personal protective equipment in all patient-care areas, avoiding aerosol-generating procedures, and carefully monitoring all healthcare workers for fever or respiratory symptoms. We also highlight the impact of these measures on preventing the entry and nosocomial spread of infection.

The Study

From March 13 to May 5, 2003, we identified all epidemiologically linked patients whose disease met the Centers for Disease Control and Prevention’s case definition of SARS issued on April 29, 2003 (2). Initial investigations included a complete blood count (with a differential count), serum biochemical measurements (including electrolytes, renal and liver function values, creatine kinase, and lactate dehydrogenase), and a chest x-ray. Since the cause of the virus was not known at the onset of the outbreak, routine microbiologic cultures of sputum, urine, and blood were done to rule out common bacterial causes of pneumonia. In addition, mycoplasma serology and urine Legionella antigen testing were carried out. When reverse transcriptase–polymerase chain reaction (RT-PCR) kits for coronavirus detection became available, later patients also provided samples for RT-PCR.

Probable SARS was diagnosed in 14 patients and healthcare workers at National University Hospital. The median age of the patients (five men and nine women) was 58 years (range 21–84). Detailed patient characteristics, including background, medical histories, symptoms, and signs, are shown in Tables 1 and 2.

Case Histories

Case 2

A woman 43 years of age was admitted to the hospital on March 23; she had had fever, headache, vomiting, and coughing for 7 days and diarrhea on the first day of her illness, which spontaneously resolved. She reported no SARS contacts. The patient was admitted to an isolation room with the diagnosis of community-acquired pneumonia, but her condition rapidly deteriorated. She was transferred to the intensive care unit (ICU), where she died on March 31. On day 3 of her hospital stay, healthcare workers discovered that she had previously visited a friend with hepatitis at the Tan Tock Seng Hospital. Two unidentified SARS patients had been on that hospital ward.

Case 3

Case-patient 3 was an ICU physician who performed a bronchoscopy on case-patient 2 on March 26. This procedure was performed in a negative-pressure room with gloves, gown, and an N95 mask. He became ill with fever, headache, and myalgia on March 29. His initial chest x-ray was clear, and his fever resolved transiently for 30 hours before recurring. Subsequent chest x-rays showed right lower-lobe infiltrates that went on to involve both lung fields. He eventually required intubation and ventilatory support in the ICU. He was successfully extubated and has since been discharged.

Case 6

A man 63 years of age with coronary artery disease was admitted to the hospital on April 8 after he reported dizziness and shortness of breath. He had seen his general practitioner 2 days earlier with complaints of rhinorrhea, cough,
and myalgia. He had a documented temperature of 37.7°C at the physician’s office. On admission he was afebrile, and his chest x-ray showed cardiomegaly with bilateral lung infiltrates. He was admitted to the general medical ward with probable congestive heart failure. However, a transthoracic echocardiogram showed a normal ejection fraction. Within 12 hours, he became critically ill and was transferred to the ICU, where he was intubated. His repeat chest x-ray showed worsening bilateral infiltrates consistent with acute respiratory distress syndrome. The patient had visited an ill brother at the Singapore General Hospital (hitherto a SARS-free hospital). The brother had previously been in Tan Tock Seng Hospital, on March 9–31, and was subsequently identified as the index case-patient for the outbreak at the Singapore General Hospital (3). Case-patient 6 went on to infect 15 other people.

Case 11

Case-patient 11 was the on-call physician who assessed case-patient 6 and transferred him to the ICU. She had worn a gown, gloves, and N95 mask, despite no requirement to do so on the general ward at that time. She had fever, headache, and myalgia 3 days later. Her chest x-ray on admission was clear. Respiratory and chest x-ray changes occurred on day 5 of illness; the patient was discharged after 12 days.

Course of Illness

Most of the patients had a prodrome of fevers and myalgias with no respiratory or chest x-ray changes until several days later. Their illnesses ran a steady course, lasting a median of 11 days. In case-patient 3, the illness exhibited a biphasic pattern with a brief resolution of fever, followed by the return of high temperature and progression of respiratory and chest x-ray changes. A subset of these patients had a fulminant course with rapidly progressing respiratory failure requiring intubation and mechanical ventilation.

Hematologic and Biochemical Findings

The hematologic and biochemical findings of the case-patients on admission are summarized in Tables 3 and 4. Leukocyte count was normal in nine case-patients. Mild leukopenia was observed in one case-patient, and leukocytosis was observed in another. Lymphopenia (defined as <1.50 X 10⁹/L) was observed in another. C-reactive protein was elevated in 7 of 11 case-patients, and the procalcitonin was raised in four of five case-patients.

Radiologic Changes

We saw a variety of chest x-ray changes in these patients (Tables 3 and 4). The primary abnormalities were
patchy unilateral or bilateral consolidation. Opacities were predominantly in the lower lung zones in most patients. Three patients had upper lobe infiltrates. However, five of the patients were admitted to the hospital with normal chest x-ray results.

Conclusions
On March 18, 2003, our emergency department began screening all febrile patients with respiratory complaints for possible SARS (2). All suspected SARS patients were admitted to a negative-pressure isolation room for monitoring. Probable SARS case-patients were transferred to Tan Tock Seng Hospital for further management to keep the hospital free of the SARS virus.

The varied clinical signs and symptoms of SARS have limited the success of such a triage system (4–8). We have observed that current diagnostic guidelines may not be sufficiently sensitive for assessing patients before admission to hospital. For example, although a temperature of >38°C is part of the diagnostic criteria (2), this symptom was notably absent in two patients. The lack of a fever in case-patient 6 may have been the result of long-term steroid use. However, the hospital confirmed a probable SARS case based on significant thoracic symptoms and chest x-ray findings that were consistent with SARS.

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infection, but fecal-oral transmission has also been report-
sleeve gowns. Virus transmission is likely due to droplet
which included an N95 mask, disposable gloves, and long-
rooms to wear full personal protection equipment (PPE),
working in the emergency department, ICU, and isolation
investigation.

Suspected case-patients are then
monitors and investigates any clusters of pneumonias
also used to perform more exhaustive contact tracing and
lished to assist with this process. An epidemiology team is
base of SARS patients and their contacts has been estab-
clinical suspicion is high. A national computerized data-
whether any family members are ill or hospitalized.
Seng Hospital or other healthcare facilities and to inquire
elicit a history of visits or previous admissions to Tan Tock

changes until later (cases 3 and 11). Booth et al., in a ret-
orsions of this illness often require
The nonspecific symptoms of this illness often require
a critical clue to the diagnosis (2). However, a contact histo-
ary may not be forthcoming at the initial interview. In
Singapore, SARS is an imported infection in which the
epidemiology remains well defined with clear lines of sec-
performed in a negative-pressure room (with an anteroom)
tory secretions (13). Therefore, these procedures are now
now examined with the use of dedicated equipment.

Despite the use of PPE, two of our physicians were
infected with the virus. The first physician performed an
invasive procedure (bronchoscopy) on case-patient 2. The
outlet port of the patient’s ventilator was later discovered
to have malfunctioned during the procedure, exposing the
physician to a large jet of exhaled air. Reports of protected
healthcare workers becoming infected during intubation of
SARS patients have also emerged from Canada (12). The
recommendations on the use of PPE are likely insufficient
for procedures that may promote aerosolization of respira-
tory secretions (13). Therefore, these procedures are now
performed in a negative-pressure room (with an anteroom)
using a positive air–purifying respirator suit.

The second physician (case-patient 11) may haveecome infected because the N95 mask was poorly fitting.
Alternatively, transmission may have occurred through the
conjunctival mucosa. All healthcare workers are now
required to use eye protection when examining patients.
Fit-testing of N95 masks is also mandatory, in addition to
training on the correct use and disposal of PPE.

SARS has demonstrated remarkably efficient transmis-
sion in the hospital environment (76% of Singapore cases
were nosocomially acquired) (3). At our hospital, nosoco-
mial transmission occurred in nine persons. Our hospital
structure of open wards with large numbers of beds sepa-
rated by curtains may have been a contributory factor to
the spread of the virus. These wards are subdivided into
cubes of four to eight beds and have open windows and
celing fans with no controlled airflow patterns. Another
likely factor was the failure to implement a policy of uni-
versal PPE use early in the outbreak. Where such measures
were implemented (i.e., isolation rooms), no nosocomial
transmission occurred.

Table 4. Laboratory data for patients 8 through 14 admitted with severe acute respiratory syndrome

<table>
<thead>
<tr>
<th>Patient</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>15.0</td>
<td>8.4</td>
<td>11.2</td>
<td>12.5</td>
<td>14.3</td>
<td>13.2</td>
<td>13.5</td>
</tr>
<tr>
<td>Leukocyte count (X10³/µL)</td>
<td>3.73</td>
<td>7.2</td>
<td>4.94</td>
<td>6.3</td>
<td>3.6</td>
<td>6.2</td>
<td>6.76</td>
</tr>
<tr>
<td>Lymphocyte count (X10³/µL)</td>
<td>0.83</td>
<td>1.34</td>
<td>1.04</td>
<td>0.30</td>
<td>0.84</td>
<td>1.13</td>
<td>0.97</td>
</tr>
<tr>
<td>Platelet count (X10³/µL)</td>
<td>121</td>
<td>163</td>
<td>167</td>
<td>231</td>
<td>176</td>
<td>184</td>
<td>240</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>51</td>
<td>31</td>
<td>20</td>
<td>10</td>
<td>15</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>68</td>
<td>52</td>
<td>19</td>
<td>21</td>
<td>21</td>
<td>21</td>
<td>25</td>
</tr>
<tr>
<td>CK</td>
<td>35</td>
<td>192</td>
<td>73</td>
<td>68</td>
<td>85</td>
<td>88</td>
<td>56</td>
</tr>
<tr>
<td>LDH</td>
<td>685</td>
<td>1,034</td>
<td>390</td>
<td>280</td>
<td>275</td>
<td>319</td>
<td>696</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>3.1</td>
<td>4.3</td>
<td>0.9</td>
<td>&lt;0.7</td>
<td>&lt;0.7</td>
<td>&lt;0.7</td>
<td>&lt;0.7</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>ND</td>
<td>1.27</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

*ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; LDH, lactate dehydrogenase; ND, not done.*
In addition, because hospital staff are a recognized source of secondary transmission (3,4,6), all healthcare workers are now required to monitor their temperatures three times a day. Anyone with a respiratory illness or a temperature >37.5ºC is removed from duty, pending further evaluation. This policy has successfully prevented the secondary transmission of SARS from affected healthcare workers.

The lessons gathered from our hospital outbreak have resulted in dramatic changes to our triage and infection-control policies. All patients with undifferentiated febrile illness, respiratory complaints, or chest x-ray infiltrates are isolated, screened for SARS contacts, and nursed with full PPE. Despite continued community transmission of SARS in Singapore (the last community case was identified on May 10, 2003), the measures implemented since April 8, 2003, enabled us to identify and contain eight additional SARS cases and prevent the nosocomial transmission of the virus.

Dr. Singh is an associate consultant in infectious diseases and microbiology at the National University Hospital. His research interests include serologic assays for the diagnosis of severe acute respiratory syndrome, and molecular epidemiology, and polymerase chain reaction for the rapid diagnosis of dengue virus.

References

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