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Clinical Features of Pneumonia Caused by 2009 Influenza A(H1N1) Virus in Beijing, China

Lu Bai, MD; Li Gu, MD; Bin Cao, MD; Xiao-Li Zhai, MD; Min Lu, MD; Yong Lu, MD; Li-Rong Liang, MD; Lei Zhang, MD; Zi-Fen Gao, MD; Ke-Wu Huang, MD; Ying-Mei Liu, MD; Shu-Fan Song, MD; Lin Wu, MD; Yu-Dong Yin, MD; and Chen Wang, MD, FCCP

**Background:** Data on symptoms and radiographic changes in patients with pandemic 2009 influenza A(H1N1) pneumonia during convalescence have not been reported.

**Methods:** During October 26, 2009, and January 23, 2010, adult patients with pneumonia with laboratory-confirmed or clinically suspected A(H1N1) infections were observed for clinical characteristics, high-resolution chest CT scan, and lung function test changes during acute and 3-month convalescent phases.

**Results:** Of the 65 case subjects, the median age was 41 (interquartile range [IQR], 28-57) years, 60.0% were men, and 55.4% had at least one underlying medical condition. Sixty-two patients started oseltamivir therapy within a median of 5 (IQR, 4-6) days from the onset of illness, and 31 received IV corticosteroids. ARDS developed in 33 patients, and 24 were treated initially with noninvasive positive pressure ventilation (NPPV). In this group, NPPV was successful in 13 patients (54.2%). Nine patients died at a median of 16 (IQR, 10-24) days after onset of illness. Multivariate Cox regression identified two independent risk factors for death: progressive dyspnea after resolution of fever (relative risk, 5.852; 95% CI, 1.395-24.541; \( P = .016 \)) and a higher APACHE (Acute Physiology and Chronic Health Evaluation) II score on presentation (relative risk for each point, 1.312; 95% CI, 1.140-1.511; \( P < .001 \)). At 3-month follow-up of survivors with A(H1N1), ground-glass opacities were still present, although diminished, in 85.7%, and diffusing capacity for carbon monoxide was mildly reduced in 61.5%.

**Conclusions:** Ground-glass opacities and decreased diffusing capacity were the main abnormalities observed at 3-month follow-up of survivors of A(H1N1).

**Abbreviations:** A(H1N1) = pandemic 2009 influenza A(H1N1); APACHE = Acute Physiology and Chronic Health Evaluation; DLco = diffusing capacity for carbon monoxide; GGOs = ground-glass opacities; HRCT = high-resolution CT; IQR = interquartile range; LFT = lung function test; NPPV = noninvasive positive pressure ventilation; RT-PCR = reverse transcriptase polymerase chain reaction; SARS = severe acute respiratory syndrome

Outbreaks of novel 2009 influenza A(H1N1) (A[H1N1]) virus infection occurred in April 2009 in the United States and Mexico. The clinical spectrum of this disease has ranged from self-limited illness to respiratory failure and death. In our initial report of the A(H1N1) virus infection in China, the majority of patients had mild illness. Since the first report of pneumonia caused by the A(H1N1) virus in Mexico, severe cases have been documented throughout the world. As of March 7, 2010, ≥16,713 laboratory-confirmed cases of death have been reported by the six world regions. In mainland China, there were >127,000 confirmed cases up to February 28, 2010, including 793 deaths. Many studies have been published on the clinical manifestations of A(H1N1) pneumonia during the acute phase of illness, but no information has been reported on symptoms and radiographic and lung function changes in convalescence. We studied clinical manifestations during the acute phase, antiviral and corticosteroid therapy, noninvasive positive pressure ventilation (NPPV), and the histopathologic changes of a fatal case. Survivors were followed up after discharge for a period of 3 months. We believe...
our work can help optimize treatment, and also lead to a better understanding of the symptomatic, radiologic, and lung functional changes during the convalescent period.

**Materials and Methods**

**Study Patients and Case Definition**

Data were collected retrospectively and prospectively on all patients with confirmed A(H1N1)-related pneumonia treated at Beijing Chao-Yang Hospital between October 26, 2009, and January 23, 2010. The diagnosis of pneumonia was based on respiratory symptoms combined with a new infiltrate on chest radiograph. Real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay was used to confirm the diagnosis of A(H1N1) infection. Patients presenting with pneumonia with high clinical suspicion of A(H1N1) infection but negative RT-PCR test results for A(H1N1) were also included in this study. Children younger than 14 years of age were excluded. Most patients were hospitalized for treatment, whereas those who presented with less serious illness and did not need oxygen supplementation were treated as outpatients under home quarantine.

Treatment decisions for all patients were made by their attending physicians. Hospitalized patients were discharged when their temperatures had returned to normal for at least 3 days, most influenza-like symptoms had disappeared, and they were clinically stable.

**Data Collection During Hospitalization and Follow-up**

Information recorded included demographic data, underlying medical conditions, symptoms, signs, laboratory and chest radiograph findings before therapy and during follow-up, and the clinical course, treatment, and adverse events during hospital stay. APACHE (Acute Physiology and Chronic Health Evaluation) II scores were determined in all patients to assess the severity of illness. During hospitalization, clinical data were collected retrospectively from medical records.

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Results

From October 26, 2009, to January 23, 2010, a total of 2,415 cases of influenza-like illness were reported in our hospital, of which 516 were laboratory-confirmed A(H1N1) cases. During the epidemic, a total of 65 patients were eligible for this study, including 62 patients with laboratory-confirmed A(H1N1) and three patients with high clinical suspicion for A(H1N1) infection. Among the 65 patients, 50 were hospitalized, and 15 were treated as outpatients.

**Clinical Characteristics**

Median age was 41 years, 60.0% were men, and 55.4% had at least one underlying medical condition (Table 1). Dyspnea persisted in 13.8% of patients after resolution of fever. Smokers were more common in the ARDS group (P = .067), and moist rales and wheezing were significantly more frequent in this group. Although leukocyte counts were similar in the two
Table 1—Characteristics, Symptoms and Signs, Laboratory and Radiographic Findings on Admission, Clinical Course, and Outcome of Patients Who Developed ARDS Compared With Those Who Did Not

| Variable | Total (N = 65) | Without ARDS (n = 32) | With ARDS (n = 33) | P Value |
|----------|---------------|------------------------|--------------------|---------|
| Male sex | 39 (60.0)     | 19 (59.4)              | 20 (60.6)          | .919    |
| Age, y   | 41 (28-57)    | 36 (28-53)             | 46 (34-60)         | .069    |
| Range    | 14-75         | 18-67                  | 14-75              | ...     |
| BMI ≥ 30 kg/m² | 15 (23.1) | 6 (18.8)              | 9 (27.3)          | .415    |
| Underlying medical condition | 36 (55.4) | 13 (40.6)             | 23 (69.7)         | .018    |
| Asthma   | 3 (4.6)       | 2 (6.3)                | 1 (3.0)           | .613    |
| COPD     | 2 (3.1)       | 1 (3.1)                | 1 (3.0)           | .100    |
| Chronic bronchitis | 3 (4.6) | 1 (3.1)              | 2 (6.1)          | 1.000    |
| Bronchiectasis | 2 (3.1) | 1 (3.1)            | 1 (3.0)          | .100    |
| Obstructive sleep apnea syndrome | 4 (6.2) | 1 (3.1)             | 3 (9.1)         | .613    |
| Hypertension | 17 (26.2) | 5 (15.6)           | 12 (36.4)        | .090    |
| Coronary heart disease | 3 (4.6) | 1 (3.1)             | 2 (6.1)         | 1.000    |
| Chronic heart failure | 3 (4.6) | 1 (3.1)          | 2 (6.1)        | 1.000    |
| Cerebrovascular disease | 2 (3.1) | 0                 | 2 (6.1)       | .492    |
| Diabetes mellitus | 10 (15.4) | 3 (9.4)            | 7 (21.2)        | .303    |
| Chronic renal disease | 3 (4.6) | 0                 | 3 (9.1)        | .238    |
| Cirrhosis | 1 (1.5)       | 1 (3.1)                | 0                 | .492    |
| Mental disorder b | 2 (3.1) | 1 (3.1)            | 1 (3.0)       | 1.000    |
| Immune suppression c | 4 (6.2) | 0                 | 4 (12.1)       | .114    |
| Pregnancy | 2 (3.1)       | 0                      | 2 (6.1)         | .492    |
| Postpartum | 1 (1.5)       | 0                      | 1 (3.0)         | 1.000    |
| Current smoker | 19 (29.2) | 6 (18.8)        | 13 (39.4)       | .067    |
| Symptoms and signs (on presentation) | | | | |
| Fever d | 65 (100)       | 32 (100)                | 33 (100)         | ...     |
| Body temperature, °C | 39.5 (39.1-39.7) | 39.5 (39.2-39.7) | 39.5 (38.9-39.8) | .664     |
| Cough and sputum production | 56 (86.2) | 27 (84.4)          | 29 (87.9)       | .733    |
| Blood in sputum | 30 (46.2) | 12 (37.5)         | 18 (54.5)       | .168    |
| Dyspnea | 57 (87.7)      | 24 (75.0)               | 33 (100)         | .002    |
| Progressive dyspnea after resolution of fever | 9 (13.8) | 1 (3.1)           | 8 (24.2)      | .027    |
| Sore throat or rhinorrhea | 36 (55.4) | 19 (59.4)         | 17 (51.5)      | .524    |
| Myalgia  | 37 (56.9)      | 22 (68.8)               | 15 (45.5)        | .058    |
| Fatigue  | 60 (92.3)      | 30 (93.8)               | 30 (90.9)        | 1.000    |
| Diarrhea | 18 (27.7)      | 8 (25.0)                | 10 (30.3)        | .633    |
| Moist rales | 52 (80.0) | 21 (65.6)         | 31 (93.9)       | .005    |
| Wheezing | 19 (29.2)      | 4 (12.5)                | 15 (45.5)        | .006    |
| Laboratory findings (on presentation) | | | | |
| Leukocyte count, mm³ | 5,000 (3,400-7,600) | 5,700 (3,500-8,600) | 5,000 (3,300-7,200) | .189     |
| < 4000/mm³ | 21 (32.3) | 10 (31.3)         | 11 (33.3)       | .857    |
| Lymphocyte count, mm³ | 750 (500-1,150) | 920 (700-1,300) | 560 (360-840) | < .001     |
| < 1000/mm³ | 47 (72.3) | 18 (56.3)        | 29 (87.9)       | .006    |
| PaO₂/FiO₂ | 295 (242-374) | 375 (321-412) | 244 (211-290) | < .001     |
| Serum albumin, g/L | 31.9 (27.0-35.2) | 35.2 (31.5-38.2) | 29.7 (24.0-33.0) | < .001     |
| Creatine kinase, U/L | 180 (74-544) | 155 (75-644) | 221 (73-520) | .857    |
| Lactate dehydrogenase, U/L | 345 (272-501) | 290 (201-411) | 404 (314-548) | .004    |
| Alanine aminotransferase, U/L | 30 (22-44) | 30 (27-53) | 29 (20-42) | .164    |
| Aspartate aminotransferase, U/L | 55 (34-99) | 45 (27-86) | 57 (40-106) | .245    |
| Potassium, mmol/L | 3.8 (3.5-4.0) | 3.5 (3.2-4.0) | 3.8 (3.6-4.2) | .033    |
| < 3.5 mmol/L | 14 (21.5) | 10 (31.3)       | 4 (12.1)       | .028    |
| Sodium, mmol/L | 133.5 (130.9-136.3) | 133.6 (131.5-135.6) | 133.4 (129.1-136.5) | .572     |
| Procalcitonin, ng/mL | 0.29 (0.05-0.99) | 0.09 (0.05-0.73) | 0.46 (0.15-1.01) | .170    |
| APACHE II score | 8 (4-11) | 4 (2-6)         | 11 (9-13)       | < .001   |

Initial radiographic findings

| Chest radiograph | No. of involved zones ≥ 3 | 38/57 (66.7) | 13/29 (44.8) | 25/28 (89.3) | .001 |
| Bilateral infiltrate | 41/57 (71.9) | 14/29 (48.3) | 27/28 (96.4) | < .001 |

High-resolution chest CT scan

| No. of involved zones | 6 (4-6) | 4 (4-5) | 6 (5-6) | < .001 |
| Ground-glass opacities | 31/35 (88.6) | 11/14 (75.6) | 20/21 (95.2) | .279 |

(Continued)
groups, lymphocyte counts were significantly lower and serum potassium levels significantly higher in the ARDS group. Patients with ARDS also required more frequent use of higher doses of oseltamivir, longer duration of oseltamivir treatment, and more frequent use of corticosteroids and vasopressors, and more frequently had positive bacterial and fungal cultures. The most common initial radiologic findings on HRCT scan were bilateral GGOs involving several zones with or without associated multifocal areas of consolidation. Centrilobular nodules were also common, and small pleural effusions were present in 25.7% of patients (Fig 1). In patients without ARDS, those who were hospitalized more frequently had diarrhea ($P = .003$), moist rales ($P = .001$), a lower serum albumin level ($P = .011$), and more involved lung zones on chest radiograph ($P = .002$) than did those who were outpatients.

### Medication Treatment

Sixty-two of 65 patients started oseltamivir therapy within a median of 5 (IQR, 4-6) days from the onset of illness. Dosages and duration of antiviral therapy are listed in Table 1. Thirty-one patients received IV corticosteroids for a median duration of 3 (IQR, 3-6) days, with a dose of methylprednisolone, 1-3 mg/kg/d.

Adverse effects involving hallucinations and disorientation occurred in three male hospitalized patients 24 to 36 h after beginning corticosteroids or oseltamivir. Two of the three patients received both drugs, and the other one received only oseltamivir. Symptoms

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**Table 1—(Continued)**

| Variable | Total (N = 65)$^a$ | Without ARDS (n = 32)$^a$ | With ARDS (n = 33)$^a$ | $P$ Value |
|----------|--------------------|---------------------------|----------------------|----------|
| Consolidation | 27/35 (77.1) | 8/14 (57.1) | 19/21 (90.5) | .039 |
| Centrilobular nodules | 15/35 (42.9) | 5/14 (35.7) | 10/21 (47.6) | .728 |
| Pleural effusion | 9/35 (25.7) | 3/14 (21.4) | 6/21 (28.6) | .712 |
| **Clinical course** | | | | |
| Days from onset of symptoms to ED | 5 (4-6) | 5 (4-6) | 5 (4-7) | .383 |
| Duration of fever, d | 6.0 (4.0-7.0) | 6.0 (4.5-6.8) | 6.0 (4.0-7.3) | .665 |
| Antiviral therapy (oseltamivir) | 62 (95.4) | 29 (90.6) | 33 (100) | .114 |
| 150 mg bid po | 23 (37.1) | 6 (20.7) | 17 (51.5) | .012 |
| Duration of antiviral, d | 5 (5-7) | 5 (5-5) | 6 (5-8) | .<.001 |
| Duration of antiviral > 5 d | 21 (33.9) | 0 | 21 (63.6) | .<.001 |
| Interval from onset to antiviral ≤ 48 h | 6 (9.7) | 4 (13.8) | 2 (6.1) | .405 |
| Use of antibiotics | 49 (75.4) | 20 (62.5) | 29 (87.9) | .023 |
| Use of corticosteroids | 31 (47.7) | 5 (15.6) | 26 (78.8) | .<.001 |
| Mechanical ventilation | 25 (38.5) | 1 (3.1) | 24 (72.7) | .<.001 |
| Invasive | 10 (15.4) | 0 | 10 (30.3) | .001 |
| Noninvasive | 15 (23.1) | 1 (3.1) | 14 (42.4) | .<.001 |
| Extracorporeal membrane oxygenation | 2 (3.1) | 0 | 2 (6.1) | .492 |
| Renal replacement therapy | 3 (4.6) | 0 | 3 (9.1) | .238 |
| Acute liver function failure | 1 (1.5) | 0 | 1 (3.0) | 1.000 |
| Hypotension needed vasopressor | 7 (10.8) | 0 | 7 (21.2) | .011 |
| Positive culture on presentation or during hospitalization | 13 (20.0) | 1 (3.1) | 12 (36.4) | .001 |
| Bacterial | 7 (10.8) | 1 (3.1) | 6 (18.2) | .105 |
| Fungal | 2 (3.1) | 0 | 2 (6.1) | .492 |
| Bacterial and fungal | 4 (6.2) | 0 | 4 (12.1) | .114 |
| Length of stay in hospital for survivors | 7.0 (5.3-11.0) | 5.0 (4.0-6.5) | 11.0 (7.0-13.0) | .<.001 |
| (n = 41), d | | | | |
| Death | 9 (13.8) | 0 | 9 (27.3) | .002 |
| Days from onset of symptoms to death | 16 (10-24) | ... | 16 (10-24) | ... |
| Days from admission to death | 9 (4-16) | ... | 9 (4-16) | ... |

Data are presented as No. (%) or median (interquartile range). APACHE = Acute Physiology and Chronic Health Evaluation.

*Unless otherwise indicated.

$^a$One patient had schizophrinia, and the other had alcohol withdrawal syndrome.

$^b$Two patients were taking oral corticosteroids equal to prednisolone 15 mg per day for >2 mo; one patient was receiving immunosuppressant after kidney transplant; one patient had aplastic anemia.

$^c$The highest temperature before presentation.

$^d$Total (N = 59); without ARDS group (n = 26), with ARDS group (n = 33).

$^e$Total (N = 58); without ARDS group (n = 25); with ARDS group (n = 33).

$^f$Chest radiograph was performed within 1 wk after onset of symptoms. Total (N = 57); without ARDS group (n = 29); with ARDS group (n = 28).

$^g$High-resolution chest CT scanning was performed at a median 6 (interquartile range, 4-9) days after onset of symptoms. Total (N = 35); without ARDS group (n = 14); with ARDS group (n = 21).
disappeared 1 to 2 days after stopping corticosteroids and oseltamivir or lowering the dose of oseltamivir.

**Ventilation Support**

Among 33 patients with ARDS, 24 required ventilation support, all of whom were initially treated with NPPV. In this group, NPPV succeeded in 13 (54.2%) (duration 5.1 ± 2.5 days) and 10 (41.7%) failed and were intubated at a median of 16 (IQR, 10-84) h after admission; the last one refused intubation and died. Among the 10 patients who were intubated, eight died. Patients who failed NPPV treatment had higher APACHE II scores on presentation (median 13 [IQR, 11-14]) compared with those who succeeded (median 10 [IQR, 9-11]; P = .020). Barotrauma occurred in two patients, one during extracorporeal membrane oxygenation therapy.

**Coinfections**

Sputum or transtracheal aspirate specimens obtained for bacterial culture were positive in 13 patients (Table 1), including Acinetobacter baumannii, four; Klebsiella pneumoniae, four; Pseudomonas aeruginosa, two; Enterobacter aerogenes, one; Escherichia coli, one; Staphylococcus aureus, one; and Aspergillus spp, six. Only one patient had a positive sputum culture within the first 48 h of hospitalization (Klebsiella pneumoniae). All other positive bacterial or fungal cultures were obtained ≥48 h after hospitalization.

**Postmortem Findings**

An autopsy was performed on a 44-year-old previously healthy man who was admitted 7 days after onset of symptoms and died of severe ARDS on day 18 of hospitalization (Fig 2). Gross examination of lung tissue revealed prominent congestion and consolidation, with increased weight (left, 860 g; right, 1,178 g). An abscess was seen in the right lower lobe that...
contained a large number of *Aspergillus* spp hyphae on microscopic examination. Microscopically, the lungs showed diffuse alveolar damage with hyaline membrane formation, intralveolar edema and/or fibrin, necrotizing bronchiolitis, hemorrhage, secondary infection, focal alveolar necrosis, multifocal proliferation of pneumocytes, and fibrosis of the interstitium. Bacterial culture of lung tissue was positive for *E coli*, *K pneumoniae*, and *Aspergillus* spp. Lung tissue was also positive for A(H1N1) virus by real-time RT-PCR. No significant lesions were seen in other organs.

**Outcome and Predictors of Mortality**

Among the 65 patients, nine died, of whom eight had hemorrhagic respiratory secretions. One 19-year-old man died of severe hemoptysis within 24 h of admission. The death rate among patients with ARDS was 27.3% (9/33). The main cause of death was refractory hypoxemia. Two factors were found to be independently associated with death: progressive dyspnea after resolution of fever (relative risk, 5.852; 95% CI, 1.395-24.541; *P* = .016) and a higher APACHE II score on presentation (relative risk, 1.312; 95% CI, 1.140-1.511; *P* < .001) (Table 2).

**Follow-up in Survivors**

Of the 56 survivors, 39 had one or more follow-up visits. Among 14 who completed the 3-month visits, symptoms reported at the last visit included exertional dyspnea (four), hair loss (two), and cough (one). The duration of symptoms was as follows: sputum 19.6 ± 6.6 days, bloody sputum 11.0 ± 4.1 days, fatigue 16.0 ± 7.7 days. A 31-year-old female patient who was previously healthy still had a low platelet count of 34,000 per mm³ at 75 days after the onset of illness.

Changes in lung abnormalities from initial to follow-up HRCT scan examinations are shown in Table 3. Among the 14 patients who completed their 3-month visit, 12 still showed lesser degrees of GGOs (Fig 1). In those who had ARDS (n = 9), “involved zones” were significantly (*P* = .002) more frequent than in those without ARDS (n = 5).

LFTs were performed at visit 3 for 13 patients (Table 4). All 13 had been hospitalized, and there was no statistical difference in clinical and laboratory characteristics between these patients and those in whom LFTs were not obtained. Impairment of DLCO was the most common (8/13 [61.5%]) abnormality detected.

### Table 2—Analysis of Predictors for Fatal A(H1N1) Viral Pneumonia by Univariate and Multivariate Cox Regression

| Variable                          | Patients Who Survived (n = 56) | Patients Who Died (n = 9) | Univariate Analysis | Multivariate Analysis |
|-----------------------------------|-------------------------------|--------------------------|---------------------|----------------------|
| Hemoptysis, No. (%)               | 22 (39.3)                     | 8 (88.9)                 | 10.288 (1.286-82.309) | .028                 |
| Progressive dyspnea after resolution of fever, No. (%) | 5 (8.9) | 4 (44.4) | 5.173 (1.386-19.304) | .014 |
| Lymphocyte count, mm³             | 800 (605-1,300)               | 330 (300-640)            | 0.028 (0.002-0.328)  | .004                 |
| PaO₂/FiO₂                          | 302 (246-382)                 | 215 (164-277)            | 0.990 (0.982-0.997)  | .006                 |
| Serum albumin, g/L                | 32.3 (29.9-33.6)              | 25.7 (20.9-27.1)         | 0.850 (0.774-0.933)  | .001                 |
| Lactate dehydrogenase, U/L        | 325 (246-474)                 | 546 (454-637)            | 1.005 (1.002-1.009)  | .001                 |
| Imaging finding involved all      | 16 (28.6)                     | 7 (77.8)                 | 7.548 (1.506-36.388) | .012                 |
| six zones, No. (%)                | 7 (3-10)                      | 13 (11-14)               | 1.276 (1.130-1.441)  | <.001                |
| Days from onset of symptoms to ED | 5 (4-6)                       | 6 (5-8)                  | 1.319 (1.103-1.578)  | .002                 |

Data are presented as median (interquartile range) unless otherwise indicated. A(H1N1) = 2009 influenza A(H1N1). See Table 1 for expansion of the other abbreviation.

### Table 3—Analysis of HRCT Scanning During Follow-up

| Follow-up Number | Days From Onset of Illness, mean ± SD | Involved Zones, mean ± SD | GGOs | Consolidation | Interlobular Septal Thickening | Reticular Nodules Pattern |
|------------------|---------------------------------------|---------------------------|------|--------------|-------------------------------|---------------------------|
| Initial (n = 20) | 6.6 ± 2.8                             | 5.1 ± 1.2                 | 20 (100) | 16 (80.0)  | 0                             | 9 (45.0)                  |
| Visit 1 (n = 12) | 24.4 ± 3.8                             | 5.3 ± 1.4                 | 12 (100) | 4 (33.3)    | 9 (75.0)                      | 6 (50.0)                  |
| Visit 2 (n = 9)  | 49.8 ± 6.3                             | 4.6 ± 1.7                 | 9 (100)  | 1 (11.1)    | 5 (55.6)                      | 3 (33.3)                  |
| Visit 3 (n = 14) | 93.9 ± 14.0                            | 3.4 ± 2.2                 | 12 (85.7)| 0           | 3 (21.4)                      | 2 (14.3)                  |

Data are presented as No. (%) of patients, unless otherwise indicated. Of the 20 patients who had ≥1 follow-up visits, four made all three visits, one made visits one and two, four made visits one and three, and two made visits two and three. The other 9 patients made only one visit (visit one for three of them, visit two for two of them, and visit three for four of them). GGOs = ground-glass opacities; HRCT = high-resolution CT.
Our series of 65 cases of A(H1N1) identified two independent risk factors associated with fatal pneumonia: progressive dyspnea after resolution of fever and a higher APACHE II score on presentation. Three months later, GGOs of less severity were still present on chest radiographs in 85.7% of patients (12/14). LFTs revealed decreased DLCO (<80% predicted) in eight (61.5%) of the 13 patients tested.

The clinical characteristics of A(H1N1) pneumonia we described during the acute phase were similar to those reported by others. In this report, most patients complained of dyspnea, which usually occurred within 1 week after illness onset. Dyspnea continued to progress after resolution of fever in 13.8% of the patients, a finding that has not been reported by others.

In this report, the success rate for NPPV was 54.2%, which is much higher than that reported by others (14.5%-27.3%). Although the death rate (8/10 [80%]) in patients who received invasive ventilation in our study was higher than that reported in another study, among patients with ARDS, the death rate was 27.3%, similar to other reports. Moreover, although NPPV was used widely in the ward specifically set aside for patients infected with A(H1N1), none of the 28 doctors and nurses who were in direct contact with these patients developed respiratory symptoms or influenza-like illnesses. Therefore, we believe that with proper infection-control procedures, NPPV can be used successfully and safely for treating patients with A(H1N1) pneumonia complicated by ARDS.

It has been reported that 29% to 55% of autopsied patients with A(H1N1) had evidence of bacterial coinfection. Streptococcus pneumoniae, Streptococcus pyogenes, and S aureus were the most predominant pathogens. However, in our study, community-acquired bacterial infection (defined as sputum collected within 48 h of hospitalization) was detected in only one of 50 patients (K pneumoniae). The low yield of gram-positive bacteria before or within 48 h of hospitalization may be due to the widespread use of prophylactic antibiotic therapy. In contrast, nosocomial infection was common in the patients (12/50 [24.0%]), and gram-negative bacilli were the predominant causative pathogens. Aspergillus spp was also seen. Progressive A(H1N1) infection, intubation, a prolonged hospital stay, IV antibiotic use, and use of oral or IV corticosteroids may be risk factors for nosocomial infection caused by gram-negative bacilli and Aspergillus spp.

We showed that symptoms and laboratory abnormalities in survivors of A(H1N1) virus infection returned to normal within 1 month of the onset of illness.

### Table 4: LFT Results and HRCT Scanning Patterns for 13 Discharged Patients With A(H1N1) Pneumonia, Performed at Visit Three (3 Mo After Onset of Illness)

| Patient No. | Age | Sex | Underlying Condition | ARDS/NPPV | FEV1/FVC, % DLCO, % | TLC, % Dlco/VA, % | HRCT Scan Findings | LFTs Were Performed (Involved Zones) |
|-------------|-----|-----|----------------------|-----------|---------------------|-------------------|-------------------|-------------------------------------|
| 1           | 65  | M   | Chronic bronchitis, diabetes mellitus, hypertension, smoke (35 pack-y) | Yes/No    | 76.5                | 97.6              | 98.0              | GGOs (6)                           |
| 2           | 30  | F   | Asthma, smoke (5 pack-y) | No/No     | 50.9                | 92.4              | 129.8             | Normal                             |
| 3           | 40  | M   | Diabetes mellitus, hypertension, OSAS | Yes/Yes   | 78.1                | 95.6              | 99.6              | GGOs (6)                           |
| 4           | 40  | M   | Emphysema, diabetes mellitus, hypertension, OSAS | Yes/Yes   | 91.3                | 97.9              | 116.6             | GGOs (6)                           |
| 5           | 55  | M   | Emphysema, diabetes mellitus, hypertension, OSAS | Yes/Yes   | 97.6                | 97.9              | 123.3             | GGOs (6)                           |
| 6           | 50  | F   | Emphysema, diabetes mellitus, hypertension, OSAS | Yes/Yes   | 90.2                | 97.9              | 114.7             | GGOs (6)                           |
| 7           | 30  | M   | Emphysema, diabetes mellitus, hypertension, OSAS | Yes/Yes   | 100.1               | 102.4             | 127.2             | GGOs (6)                           |
| 8           | 55  | M   | Diabetes mellitus, hypertension, OSAS | Yes/Yes   | 95.6                | 97.9              | 123.3             | GGOs (6)                           |
| 9           | 25  | M   | Emphysema, diabetes mellitus, hypertension, OSAS | Yes/Yes   | 91.3                | 97.9              | 116.6             | GGOs (6)                           |
| 10          | 60  | M   | Diabetes mellitus, hypertension, OSAS | Yes/Yes   | 89.1                | 97.9              | 114.7             | GGOs (6)                           |
| 11          | 50  | F   | Emphysema, diabetes mellitus, hypertension, OSAS | Yes/Yes   | 95.6                | 97.9              | 116.6             | GGOs (6)                           |
| 12          | 30  | M   | Diabetes mellitus, hypertension, OSAS | Yes/Yes   | 91.3                | 97.9              | 116.6             | GGOs (6)                           |
| 13          | 50  | F   | Diabetes mellitus, hypertension, OSAS | Yes/Yes   | 95.6                | 97.9              | 116.6             | GGOs (6)                           |

DLCO = diffusing capacity for carbon monoxide; Dlco/VA = DLCO adjusted for alveolar volume; F = female; LFT = lung function test; M = male; NPPV = noninvasive positive pressure ventilation; OSAS = obstructive sleep apnea syndrome; TLC = total lung capacity; VA = ventilatory area; V/Q = ventilation/perfusion ratio; X-ray = chest radiograph; DLCO = diffusing capacity for carbon monoxide; OSAS = obstructive sleep apnea syndrome; V/Q = ventilation/perfusion ratio; X-ray = chest radiograph; DLCO = diffusing capacity for carbon monoxide; OSAS = obstructive sleep apnea syndrome; V/Q = ventilation/perfusion ratio; X-ray = chest radiograph.
illness. Nonetheless, GGOs were still found at 3 months, although no fibrotic changes were seen. In survivors of A(H5N1) virus infection, persistent radiologic abnormalities including GGOs, often with a reticular pattern, have been seen as long as 1 year after illness onset. In survivors of severe acute respiratory syndrome (SARS) followed for 1 year, marked improvements in pulmonary fibrosis have been seen, but some patients still had residual changes. Because this kind of fibrosis was reversible, it has been suggested that these findings were partially caused by postinflammatory atelectasis rather than by genuine fibrosis alone. The resolution of lung abnormalities in patients with A(H1N1) viral pneumonia seemed better than that seen in patients with SARS and influenza A(H5N1) infection.

Impairment of DLCO was the most common (8/13 [61.5%]) abnormality in lung function testing 3 months after the onset of illness, followed by restrictive defects (2/13 [15.4%]). The DLCO findings were similar to the findings of one study of patients with SARS at 3-month follow-up visits. The impairment of DLCO in survivors of SARS persisted for 1 year in 23.7% of patients reported by other investigators. Although the number of cases with LFTs in our series is limited (only 13 cases, of whom eight had a reduction of DLCO), it seemed that patients who had bilateral GGOs on HRCT scan were more likely to have an impaired DLCO. During the convalescent period of ARDS, GGOs, may consist of partially caused by postinflammatory atelectasis rather than by genuine fibrosis alone. The resolution of HRCT scanning. A longer follow-up study intralobular fibrosis that is below the limits of resolution of GGOs, often with a reticular pattern, have been seen as long as 1 year after illness onset. In survivors of severe acute respiratory syndrome (SARS) followed for 1 year, marked improvements in pulmonary fibrosis have been seen, but some patients still had residual changes. Because this kind of fibrosis was reversible, it has been suggested that these findings were partially caused by postinflammatory atelectasis rather than by genuine fibrosis alone. The resolution of lung abnormalities in patients with A(H1N1) viral pneumonia seemed better than that seen in patients with SARS and influenza A(H5N1) infection.

In conclusion, we found that progressive dyspnea after resolution of fever and a higher APACHE II score on presentation were independent risk factors associated with death in patients with A(H1N1) viral pneumonia. At the 3-month follow-up visit of survivors of A(H1N1) pneumonia, some degree of GGOs persisted in most patients and decreased DLCO was common.

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