ARTICLE

Childhood Severe Acute Respiratory Syndrome in Taiwan and How to Differentiate It From Childhood Influenza Infection

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Objective: To investigate clinical features and outcomes of children in Taiwan with laboratory-confirmed severe acute respiratory syndrome (SARS) vs those of children with influenza to differentiate the 2 diseases.

Design, Setting, and Participants: Patients 20 years or younger with clinical, epidemiological, and laboratory evidence of SARS from March to July 2003 vs children with virus culture–confirmed influenza in a 1:1 age- and sex-matched control group.

Main Outcome Measures: Rates of symptoms, abnormal laboratory data, and outcomes of recovery, sequelae, or death.

Results: The 15 SARS patients (9 girls and 6 boys) had a median age of 17 years (age range, 4-20 years). Nine patients (60%) were infected through household contact, 4 (27%) nosocomially, 1 (7%) through contact with a neighbor, and 1 (7%) after returning from Hong Kong. All 15 patients had fever, 3 (20%) had chills, and 11 (73%) had cough. Only 1 patient (7%) had sputum production; 1 (7%) had rhinorrhea. At presentation, 5 patients (33%) had leukopenia, 6 (40%) had lymphopenia, and 5 (33%) had monocytopenia. All children recovered without sequelae. Children with SARS had significantly lower incidences of rhinorrhea (odds ratio [OR], 0.01; 95% confidence interval [CI], 0.00-0.09), sputum production (OR, 0.10; 95% CI, 0.02-0.63), and sore throat (OR, 0.17; 95% CI, 0.03-0.85) than children with influenza. Both groups had similar incidences of leukopenia or lymphopenia, but SARS patients had a significantly higher incidence of monocytopenia (33% vs 0%, $P = .04$).

Conclusions: Childhood SARS is usually not fatal. The absence of rhinorrhea and presence of monocytopenia in SARS may distinguish it from influenza.

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In November 2002, cases of a life-threatening pneumonia were found in Guangdong Province in China, followed by reports from Vietnam, Hong Kong, Singapore, Canada, the United States, Taiwan, and other countries.[1-9] This illness was identified as a new clinical entity and was designated as *severe acute respiratory syndrome* (SARS) in late February 2003, and SARS-associated coronavirus (SARS-CoV) was subsequently identified as its pathogen.[5-7]

In late February 2003, the first SARS patient, who had returned from travel to Guangdong Province, was identified in Taiwan.[8] At that time, Taiwan's Department of Health was notified of SARS being spread by persons recently returning to Taiwan from SARS-affected regions.[8] During that period, SARS was characterized as occurring sporadically among business travelers and being spread secondarily to identified contacts only. However, beginning in mid April 2003, unrecognized cases of SARS led to a large nosocomial cluster and subsequent SARS-CoV transmission to other health care facilities and community settings.[8] By July, 671 probable cases of SARS had been reported in Taiwan.[9] The highest percentages of persons diagnosed as having SARS were health care workers exposed to SARS patients (0.34%) and family members of SARS patients (0.33%).[8]

Since the SARS outbreak, many reports have been published. However, articles on pediatric SARS patients are limited, and many of the children described in those articles were not virologically confirmed to have the disease.[4,10-13] Only a small number of the SARS patients in Taiwan were pediatric patients. This report investigates the clinical findings of laboratory-confirmed pediatric SARS patients during the SARS outbreak in Taiwan. Because we are concerned about the reemergence of SARS or a concomitant

outbreak of SARS and influenza in the near future, the ability of physicians to distinguish between the 2 diseases is important. Therefore, we also compared the clinical features of SARS vs influenza among pediatric patients to determine which clinical variables might differentiate them.

METHODS

CASE ENROLLMENT

Institutional review board approval for this study was obtained from National Taiwan University Hospital. Of all the SARS cases reported to Taiwan's Department of Health from March to July 2003, we enrolled patients 20 years or younger who fulfilled the triad of the clinical criteria of SARS, an epidemiological link or contact history with SARS patients, and laboratory evidence of SARS infection by positive reverse transcription–polymerase chain reaction (RT-PCR) or antibody detection.

The clinical criteria for suspected SARS cases included temperature higher than 38°C with or without the following respiratory symptoms: cough, sore throat, tachypnea, or dyspnea. The criteria for probable SARS cases are the presence of the aforementioned criteria plus radiographic evidence of pneumonia.

The epidemiological link or contact history included any of the following: (1) having contact with SARS patients within 10 days before illness, (2) visiting health care facilities with nosocomial SARS spreads within 10 days before illness, (3) traveling to the SARS-affected areas and returning within 10 days before illness, or (4) residing in an area with recent local transmission of SARS.

To compare the clinical features between patients with SARS and those with influenza, a control subject with virus culture–confirmed influenza infection was matched by age and sex for each SARS patient. The matched controls had visited or were hospitalized at National Taiwan University Hospital between January 2002 and July 2003, at which time they had received viral, blood, and radiographic examinations diagnosing them as having influenza.

DATA COLLECTION

For data collection, detailed histories were taken, symptoms were recorded, and physical examinations were performed. The detailed history included the patient's past health or underlying diseases, any affected family members, traveling, visits to medical facilities, and contact with health care workers. A complete workup of blood cell counts, renal and liver function tests, creatine kinase, and lactate dehydrogenase was done. Leukopenia was defined as a white blood cell count of less than $4\times10^3/\mu L$, lymphopenia as a lymphocyte count of less than $1\times10^3/\mu L$, monocytopenia as a monocyte count of less than $0.2\times10^3/\mu L$, thrombocytopenia as a platelet count of less than $100\times10^3/\mu L$, creatine kinase elevation as a level higher than 200 U/L, and lactate dehydrogenase elevation as a level higher than 400 U/L. Microbiological investigations included bacterial culture of blood and sputum, serologic testing for *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*, throat swab for virus isolation, and SARS-CoV virologic studies. Chest radiographs were taken for each patient and read by a pediatric radiologist.

LABORATORY METHODS

The SARS-CoV virologic studies included RT-PCR, neutralizing antibody, indirect fluorescence antibody, and indirect enzyme-linked immunosorbent assay against SARS-CoV.

SARS-CoV RT-PCR

RNA was extracted from the sputum or throat swabs by using a viral RNA kit (QIAamp; Qiagen Inc, Valencia, Calif). Reverse transcription–polymerase chain reaction for SARS-CoV was performed with 3 sets of primers (IN-6 and IN-7, Cor-p-F1 and Cor-p-R2, and BNIinS and BNIAs) developed by the Centers for Disease Control and Prevention and World Health Organization Network Laboratory. A PCR was considered positive when a specimen was confirmed positive in another reference laboratory or when a second specimen, from another site or collected at a different time, was confirmed as positive.

SARS-CoV NEUTRALIZING ANTIBODY

Serum samples were heat treated for 30 minutes at 56°C, serially diluted, mixed with 100 doses of 50% tissue culture infective SARS-CoV *Urbani* strain (GenBank accession No. AY278741), and then incubated for 2 hours at 37°C in microtiter plates seeded with Vero E6 cells. Each plate included a cell control, serum control, and virus back titration. Cytopathic effect was monitored from 2 to 7 days after incubation, and the serotiter was determined when the cytopathic effect was observed in a 50% tissue culture infective dose of the virus back titration. Seropositivity was defined as a serotiter of 16 or higher.

SARS INDIRECT FLUORESCENCE ANTIBODY

IgG antibody to the SARS-CoV was detected by a standard indirect fluorescence antibody assay with serial serum specimens. Spot slides for indirect fluorescence antibody were prepared by applying the suspension mixed with SARS-CoV–infected Vero E6 cells and uninfected cells onto 12-well Teflon-coated slides. Slides were dried and fixed in acetone. The conjugates we used were goat antihuman IgG conjugated to fluorescein isothiocyanate (Zymed Laboratories Inc, South San Francisco, Calif). The starting dilution of serum specimens was 1:100. A positive result was defined as a positive fluorescence staining at the titer of 1:100.

SARS ENZYME-LINKED IMMUNOSORBENT ASSAY

An enzyme-linked immunosorbent assay antigen was prepared by detergent extraction of infected Vero E6 cells and subsequent γ irradiation. The optimal dilution (1:1000) for the use of this antigen was determined by checkerboard titration against serum from a patient with SARS in the convalescent phase. A control antigen, similarly prepared from uninfected Vero E6 cells, was used to control for specific reactivity of tested serum. The conjugates we used were goat antihuman IgG, IgA, and IgM conjugated to horseradish peroxidase for enzyme-linked immunosorbent assay (provided by the Centers for Disease Control and Prevention, Atlanta, Ga).

STATISTICAL ANALYSIS

The clinical and laboratory data were expressed as number (percentage), median (range), or mean±SE. Data were analyzed with the SAS statistical package (version 8.2; SAS Institute, Cary, NC). Univariate analysis was performed to compare patients with SARS infection and those with influenza infection using *t* test, Mantel-Haenszel χ^2 test, or Fisher exact test. The mean difference or odds ratios (ORs) and 95% confidence intervals (CIs) were provided. Probabilities

Table 1. Demographics, Source of Infection, Positive Severe Acute Respiratory Syndrome (SARS) Virus or Antibody Detection, and Specific Treatment for Children With SARS in Taiwan

Case No./Sex/Age, y	Source of Infection	Positive SARS Virus or Antibody Detection	Specific Treatment
1/F/4	Household contact	IFA, NT, ELISA	None
2/F/16	Travel to Hong Kong	IFA, NT, ELISA	Ribavirin
3/M/18	Nosocomial	RT-PCR	Ribavirin
4/M/16	Household contact	RT-PCR, IFA, NT, ELISA	Ribavirin, corticosteroid, IV Ig, elective ventilator support
5/F/14	Nosocomial	RT-PCR	None
6/M/15	Household contact	RT-PCR	Ribavirin, corticosteroid, IV Ig, oxygen
7/M/13	Household contact	IFA, NT, ELISA	Ribavirin, corticosteroid, IV Ig, oxygen
8/F/18	Household contact	IFA, ELISA	None
9/F/17	Nosocomial	ELISA	Ribavirin
10/M/17	Household contact	RT-PCR	Ribavirin, corticosteroid
11/F/20	Nosocomial	RT-PCR, IFA, ELISA	Ribavirin, corticosteroid, IV Ig
12/F/18	Household contact	IFA, NT, ELISA	Ribavirin, corticosteroid, oxygen
13/F/20	Household contact	RT-PCR, IFA, ELISA	Ribavirin, corticosteroid, IV Ig
14/F/9	Household contact	RT-PCR	Ribavirin
15/M/17	Neighbor contact	IFA, NT, ELISA	Ribavirin, corticosteroid, IV Ig, oxygen

Abbreviations: ELISA, enzyme-linked immunosorbent assay; IFA, indirect fluorescence antibody; IV Ig, intravenous immunoglobulin; NT, neutralizing test; RT-PCR, reverse transcription–polymerase chain reaction.

were 2 tailed, and $P<.05$ was considered statistically significant.

RESULTS

DEMOGRAPHICS AND SOURCE OF INFECTION

Of the 671 SARS patients reported to Taiwan's Department of Health, 48 (7.2%) were 20 years or younger. Of the 48 patients, 15 (31%) had laboratory confirmation of SARS-CoV infection in addition to clinical evidence and an epidemiological link. These 15 patients were enrolled in this study, and their data were further analyzed. Their demographics, source of infection, positive SARS-CoV or antibody detection, and specific treatment are given in **Table 1**. They did not have other significantly positive viral or bacterial culture results. The patients consisted of 6 boys and 9 girls with a mean age of 15.5 years (median age, 17 years [range, 4-20 years]). A 17-year-old boy had epilepsy controlled by regular carbamazepine therapy, a 17-year-old girl had a history of spontaneous pneumothorax, and the other 13 were previously healthy. The 15 SARS patients had been hospitalized for a mean duration of 14 days (median, 12 days [range, 2-30 days]).

Of these 15 SARS patients, 9 (60%) were infected through household contact, 4 (27%) got nosocomial infections after visiting certain SARS-affected health care facilities, 1 (7%) was infected through contact with a neighbor who was proven to have SARS infection, and 1 (7%) was found to be infected after returning from Hong Kong in late April 2003. All 15 pediatric patients came from different families.

CLINICAL SYMPTOMS

Between April and May 2003, after an incubation period of 2 to 10 days, the SARS patients developed symptoms. All 15 patients had fever, 3 (20%) also had chills, 11 (73%) had cough, but only 1 (7%) had sputum production (**Table 2**). Two (13%) experienced shortness of breath, but none had chest pain. Only 1 (7%) had rhinorrhea, 3 (20%) had sore throat, 1 (7%) had abdominal pain, 3 (20%) had diarrhea, 1 (7%) had myalgia, 4 (27%) had headache, and 2 (13%) had general malaise. On physical examination, only 4 (27%) had rales.

LABORATORY DATA

The patients' laboratory findings are given in **Table 3**. At presentation, 5 (33%) had leukopenia (white blood cell count, $<4\times10^3/\mu L$), 6 (40%) had lymphopenia (lymphocyte count, $<1\times10^3/\mu L$), 5 (33%) had monocytopenia (monocyte count, $<0.2\times10^3/\mu L$), and 1 (7%) had thrombocytopenia (platelet count, $<100\times10^3/\mu L$). During the whole clinical course, 7 (47%) had leukopenia, 10 (67%) had lymphopenia, 7 (47%) had monocytopenia, and 4 (27%) had thrombocytopenia.

RADIOGRAPHIC FINDINGS

Radiographic findings demonstrated that only 1 patient did not have lung infiltrates. The radiographic findings for the other 14 patients are listed in **Table 4**. Multifocal involvement was found in 8 patients (57%), with the right lower lobe being the most common focus (9 patients [64%]) of SARS pneumonia. Ten patients (71%) had peripheral and central consolidation. No pleural effusion was found.

TREATMENT AND OUTCOME

Of the 15 SARS patients, 14 received antibiotics (usually cephalosporin, macrolides, or both), 12 received oral ribavirin, 8 received oral or intravenous corticosteroids, and 6 received intravenous immunoglobulin (Table 1). Four received oxygen therapy, and only 1 received elective intubation with ventilator support (2 days). All 15 recovered without sequelae.

Table 2. Clinical Symptoms of 15 Pediatric Severe Acute Respiratory Syndrome Cases*

Feature	Value
Male-female ratio	6:9
Age, mean ± SE (range), y	15.5 ± 1.1 (4-20)
Fever	15 (100)
Chills	3 (20)
General malaise	2 (13)
Headache	4 (27)
Cough	11 (73)
Sputum production	1 (7)
Rhinorrhea	1 (7)
Sore throat	3 (20)
Shortness of breath	2 (13)
Chest pain	0
Myalgia	1 (7)
Nausea	1 (7)
Vomiting	1 (7)
Abdominal pain	1 (7)
Diarrhea	3 (20)

*Data are given as number (percentage) unless otherwise indicated.

Table 3. Clinical Laboratory Data of 15 Pediatric Severe Acute Respiratory Syndrome Cases

Laboratory Parameter	Median (Range) or No. (%)
Initial white blood cell count, cells/μL	5060 (3060-13 100)
Initial leukopenia, $<4 \times 10^3$ cells/μL	5 (33)
Leukopenia during the whole course	7 (47)
Initial PMN %	69 (26.1-87.2)
Initial PMN count, cells/μL	3182 (966-10 350)
Initial lymphocyte %	18.6 (7-68.9)
Initial lymphocyte count, cells/μL	1339 (371-2892)
Initial lymphopenia, $<1 \times 10^3$ cells/μL	6 (40)
Lymphopenia during the whole course	10 (67)
Initial monocyte %	5.7 (2-15)
Initial monocyte count, cells/μL	359 (106-1485)
Initial monocytopenia, $<0.2 \times 10^3$ cells/μL	5 (33)
Monocytopenia during the whole course	7 (47)
Initial platelet count, $\times 10^3$ cells/μL	160 (89-392)
Initial thrombocytopenia, $<100 \times 10^3$ cells/μL	1 (7)
Thrombocytopenia during the whole course	4 (27)
Initial hemoglobin, g/dL	13.6 (11.6-15.9)
Initial serum urea nitrogen, mg/dL*	8.0 (5.0-16.3)
Initial CK, U/L	76 (37-474)
Elevation of CPK, >200 U/L	3 (20)
Initial LDH, U/L	370 (109-1201)
Initial elevation of LDH, >400 U/L	7 (47)
C-reactive protein, mg/L	14.8 (0.0-36.2)
Initial aspartate aminotransferase, U/L	27 (17-82)
Initial alanine aminotransferase, U/L	17 (8-43)

Abbreviations: CK, creatine kinase; LDH, lactate dehydrogenase; PMN, polymorphonuclear leukocyte.
*To convert to millimoles per liter, multiply by 0.357.

Table 4. Radiographic Findings in 14 Children With Severe Acute Respiratory Syndrome

Characteristic	No. (%)
Focus	
Unifocal	6 (43)
Multifocal	8 (57)
Location	
Left upper lobe	4 (29)
Left lower lobe	3 (21)
Right upper lobe	4 (29)
Right lower lobe	9 (64)
Right middle zone	4 (29)
Left middle zone	2 (14)
Central or peripheral	
Central only	3 (21)
Peripheral only	1 (7)
Both	10 (71)
Other characteristics	
Consolidation	7 (50)
Patch	5 (36)
Infiltration	2 (14)

COMPARISON OF CLINICAL FEATURES BETWEEN PATIENTS WITH SARS AND INFLUENZA

Among the 15 age- and sex-matched controls, 9 had influenza B infection and 6 had influenza A infection. Nine had upper respiratory tract infection, 2 had bronchitis, 1 had bronchitis plus acute otitis media, and 3 had pneumonia. Eight influenza patients had been hospitalized for a mean duration of 4 days (range, 2-8 days).

Comparing the patients with SARS vs those with influenza, we found similar incidences of fever, cough, chills, myalgia, and diarrhea between the 2 groups at presentation (**Table 5**). Patients with SARS had less rhinorrhea (7% vs 93%; OR, 0.01; 95% CI, 0.00-0.09), less sputum production (7% vs 53%; OR, 0.10; 95% CI, 0.02-0.63), and less sore throat (20% vs 60%; OR, 0.17; 95% CI, 0.03-0.85) than influenza patients. Both groups had similar incidences of leukopenia or lymphopenia. Patients with SARS had a significantly higher incidence of monocytopenia, whereas monocytopenia was not found in any patients with influenza (33% vs 0%, $P=.04$).

Among the 15 patients with influenza, 13 had chest radiographic examinations: 8 had negative results and 5 had positive findings, including 2 with peribronchial infiltration, 2 with multiple patches, and 1 with single consolidation. Patients with SARS had a higher incidence of positive radiographic examinations than influenza patients (93% vs 38%; OR, 22.4; 95% CI, 2.2-227.0). Among patients with positive radiographic findings, 1 SARS patient had isolated peripheral consolidation, but no patient with influenza had such characteristic peripheral consolidation. Otherwise, no significant difference was found between the 2 groups.

COMMENT

This study first investigated laboratory-confirmed pediatric SARS patients and then compared their clinical features with those of influenza patients. The SARS-infected children were found to have usually become infected with the disease through household contact and to have less severe clinical manifestations than adults. All of the SARS-infected children in this study recovered with-

Table 5. Comparison of Clinical Features at Presentation Between Patients With Severe Acute Respiratory Syndrome (SARS) and Influenza*

Feature	SARS (n = 15)	Influenza (n = 15)	Odds Ratio or Mean Difference† (95% Confidence Interval)
Fever	15 (100)	15 (100)	NA
Chills	3 (20)	5 (33)	0.5 (0.10 to 2.63)
Cough	11 (73)	15 (100)	NA
Sputum production	1 (7)	8 (53)	0.10 (0.02 to 0.63)
Rhinorrhea	1 (7)	14 (93)	0.01 (0.00 to 0.09)
Myalgia	1 (7)	4 (27)	0.20 (0.03 to 2.02)
Sore throat	3 (20)	9 (60)	0.17 (0.03 to 0.85)
Diarrhea	3 (20)	2 (13)	1.63 (0.23 to 11.46)
White blood cell count, cells/μL	5799 ± 681	6415 ± 842	−616 (−2834 to 1602)†
Initial leukopenia, $<4\times10^3$ cells/μL	5 (33)	4 (27)	1.83 (0.39 to 8.57)
PMN %	65.9 ± 4.4	64.1± 5.0	1.8 (−11.8 to 15.3)†
PMN count, cells/μL	3961 ± 621	4493 ± 716	−531 (−2476 to 1414)†
Lymphocyte %	24.5 ± 4.4	22.4 ± 4.2	2.1 (−10.3 to 14.5)†
Lymphocyte count, cells/μL	1275 ± 193	1042 ± 126	233 (−239 to 706)†
Initial lymphopenia, $<1\times10^3$ cells/μL	6 (40)	6 (40)	1.0 (0.2 to 4.3)
Monocyte %	7.0 ± 1.0	10.5 ± 1.0	−3.5 (−6.4 to −0.6)†
Monocyte count, cells/μL	420 ± 85	585 ± 63	−165 (−382 to 53)†
Initial monocytopenia, $<0.2\times10^3$ cells/μL	5 (33)	0	NA‡
Platelet count, $\times10^3$ cells/μL	189 ± 24	203 ± 16	−14 (−74 to 47)†
Initial thrombocytopenia, $<100\times10^3$ cells/μL	1 (7)	1 (7)	1.0 (0.1 to 17.6)
Hemoglobin, g/dL	13.5 ± 0.4	12.8 ± 0.4	0.7 (−0.4 to 1.9)†
C-reactive protein, mg/L	16.4 ± 3.2	33.8 ± 14.3	−17.3 (−52.4 to 17.8)†
Aspartate aminotransferase, U/L	29.9 ± 4.1	22.2 ± 1.9	7.7 (−1.4 to 16.8)†

Abbreviations: NA, not applicable; PMN, polymorphonuclear leukocyte.
*Data are given as number (percentage) or mean ± SE unless otherwise indicated.
†Values indicate mean difference (95% confidence interval).
‡P = .04, Fisher exact test.

out sequelae. Our comparison of patients with SARS vs influenza found that the SARS patients at presentation had lower incidences of rhinorrhea, sputum production, and sore throat. Although the 2 groups of patients had similar incidences of leukopenia and lymphopenia, SARS patients had a significantly higher incidence of monocytopenia.

All of the SARS patients in this series not only met the clinical and epidemiological criteria for SARS but also were laboratory confirmed to have the disease, thereby avoiding the possibility of other pathogen-induced pneumonia diluting our results. Most patients in other series were diagnosed as having SARS based on clinical criteria and epidemiological link rather than virologically proven laboratory evidence,[4,10-13] making it possible that inclusion of patients with pneumonia of other etiologies might dilute the results and mask important SARS-related information.

Radiographic results demonstrated multifocal involvement, including peripheral and central consolidation, to be common in SARS pneumonia, but not pleural effusion. Other studies[4,10-14] reported that multifocal consolidation was the most common radiographic feature of pediatric SARS patientss, and only 1 patient had pleural effusion.[14] Therefore, consolidation plus pleural effusion is likely to be caused by bacterial or other pyogenic infections, rather than SARS.

Clinical severity and the case-fatality rate in our children were different from those reported for adults.[1-3] This difference may be related to host factors and virus load. For example, most of the SARS-infected children had no underlying disease, they might have had less overwhelming immune response, and their virus loads may not have been as high as the virus loads of SARS patients who are health care workers. We also propose that the upper respiratory tract infection so frequently found in children may have helped them develop cross-protection against SARS-CoV, although further clinical studies would be necessary to prove these hypotheses.

The antiviral drug ribavirin has been used extensively to treat SARS, but no data have shown it to be effective. Concern over its adverse effects and lack of in vitro efficacy may not justify its routine use for SARS infection. Three of our patients who did not receive ribavirin therapy did not develop respiratory failure and recovered without any sequelae. We believe that further clinical evidence is needed to determine whether children with SARS need ribavirin therapy.

About one half of our patients received corticosteroids. In fact, the benefit of corticosteroid treatment for SARS has not been well established. Adverse effects of corticosteroid use, such as secondary pyogenic infection, acne, or hypertension, have been reported.[12,15,16] Prolonged viral shedding after use of corticosteroids has also been a concern. In addition, because children with SARS may have less severe clinical manifestations than adults with SARS, they may not need the same treatment guidelines suggested for adults. We need further consensus before treating children with SARS infection with corticosteroids.

What This Study Adds

It is a challenge to differentiate childhood SARS from influenza. We thus compared the clinical features of childhood SARS with those of influenza to differentiate the 2 diseases. The absence of rhinorrhea, less sore throat, less sputum production, and the presence of monocytopenia in SARS patients may distinguish them from influenza patients.

In differentiating influenza from SARS, we found rhinorrhea to be the most useful symptom. According to other reports, rhinorrhea only occurred in 3% to 22.5% of SARS adult patients[1-3,17] and in 25% (4/16) of virologically confirmed children with SARS,[4,11,18,19] while rhinorrhea occurred frequently (62%-93%) in patients with influenza in our series and others.[20,21]

Laboratory findings on leukopenia or lymphopenia did not produce any result that would allow us to differentiate influenza and SARS. Patients with influenza and SARS had similar incidences of leukopenia and lymphopenia. It was thought that leukopenia or lymphopenia was characteristic or unique for SARS infection, but from this study, we conclude that leukopenia and lymphopenia were not unique for SARS.

In contrast, SARS patients had a significantly higher incidence of monocytopenia and lower monocyte counts than patients with influenza. This finding is considered new, because previous reports have not described the status of circulating monocytes in SARS patients.[1-14] The monocytopenia may be due to the migration of monocytes to the lung tissue, an idea supported by the evidence that histopathologic examination of lung tissue from SARS patients has revealed abundant foamy macrophage and giant multinucleated syncytial cells.[5] Another possible reason may involve monocyte lysis or damage when a monocyte or phagocyte ingests the SARS virus and subsequently lyses itself. Because SARS is an emerging infectious disease, the innate immune response of monocytes or macrophages should play a critical role in controlling SARS infection before the initiation of an adaptive immune response. Such monocyte or macrophage activation will subsequently release inflammatory cytokines systemically or locally in the lung, which may be associated with further development of respiratory distress or alveolar damage.

In conclusion, although this study was a retrospective controlled study rather than a prospective controlled study, we found some useful variables to help us differentiate influenza from SARS. The results of our study should help physicians worldwide differentiate SARS from influenza, based on these simple clinical features.

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