Original Contributions

COMPARATIVE STUDY OF PATIENTS WITH AND WITHOUT SARS WHO FULFILLED THE WHO SARS CASE DEFINITION

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□ Abstract—To differentiate severe acute respiratory syndrome (SARS) from non-SARS illness, we retrospectively compared 53 patients with probable SARS and 31 patients with non-SARS who were admitted to Mackay Memorial Hospital from April 27 to June 16, 2003. Fever (> 38°C) was the earliest symptom (50/53 SARS vs. 5/31 non-SARS, $p < 0.0001$), preceding cough by a mean of 4.5 days. The initial chest X-ray study was normal in 22/53 SARS cases versus 5/31 non-SARS cases. SARS patients with an initially normal chest X-ray study developed infiltrates at a mean of 5 ± 3.44 days after onset of fever (21/22 SARS vs. 0/5 non-SARS). Rapid radiographic progression of unifocal involvement to multifocal infiltrates was seen in 22 of 24 SARS vs. 0 of 26 non-SARS patients ($p < 0.0001$). Pleural effusion was not present in any SARS patients but was seen in 6 of 26 non-SARS cases ($p < 0.0001$). Initial lymphopenia, thrombocytopenia, and elevated lactate dehydrogenase were all more common in SARS than non-SARS ($p < 0.0001$). They may help differentiate SARS from non-SARS if a reliable and rapid diagnostic test is not available.   © 2005 Elsevier Inc.

□ Keywords—coronavirus; non-severe acute respiratory syndrome; nasopharyngeal swab; reverse-transcriptase polymerase chain reaction; severe acute respiratory syndrome

INTRODUCTION

Severe acute respiratory syndrome (SARS) is a rapidly progressive disease caused by a novel coronavirus. It spread to several continents in a very short time (1–3). Due to the apparent contagiousness and severity of the infection, prevention of further spread depended on isolation of patients and quarantine of contacts. A rapid, reliable diagnostic test was not widely available, so that early diagnosis had to be based on a clinical case definition established by the World Health Organization (WHO), resulting in many misdiagnoses (4).

At the end of April 2003, a major outbreak of SARS emerged in Taipei City. Any suspected patient was immediately isolated, using negative pressure rooms when available. The strain on health care facilities was tremendous. Suspected cases had to be reported promptly to the Health Department. Contacts of the index patient were quarantined by government order, resulting in widespread disruption of society and the economy. Had we been better able to distinguish SARS from non-SARS during the epidemic, this disruption could have been reduced. Should the infection reappear, we must be prepared with more precise diagnostic criteria to avoid a repeat of the serious health and societal consequences experienced in the recent outbreak.

We reported to the Health Department a total of 167 patients at our hospital who had either suspected or probable SARS according to the WHO case definition. In retrospect, a number of these patients did not have SARS. We retrospectively reviewed that experience to see if there were aspects of the presentation that would help differentiate between SARS and non-SARS illness.

METHODS

Patients

From 27 April to 16 June, 2003, 167 patients with probable (71) or suspected (96) SARS according to the modified WHO case definition (revised 1 May 2003) were seen at Mackay Memorial Hospital and reported to the Taipei City Health Department (4). We excluded 83 patients from the study because they were not admitted to our hospital. These included 9 who died in the emergency department (ED), 31 who were transferred to other hospitals, 1 who left, and 42 who were discharged from the ED and isolated at home due to resolution of symptoms within a few days in the ED. Of the remaining 84 patients who were admitted, 53 had convincing evidence of severe acute respiratory syndrome coronavirus (SARS-CoV) infection and 31 patients had no evidence of SARS-CoV infection. These 31 patients had an alternative diagnosis that fully explained their symptoms (Table 1) and all except one who died during hospitalization had two negative anti-SARS CoV. The evidence confirm-

Table 1. Alternative Diagnoses that Fully Explained the Symptoms in Non-SARS Group

Illness	Number of patients
Mycoplasma pneumonia	7
Chlamydia pneumonia	4
Legionella pneumonia	1
Pneumocystis carinii pneumonia	1
Pulmonary tuberculosis	1
Nosocomial Staphylococcal pneumonia	1
Community-acquired pneumonia	2*
Acute myocardial infarction with pulmonary edema	1
Uremia with pulmonary edema	1
Alpha hemolytic streptococcal infective endocarditis with acute respiratory and heart failure	1
COPD with secondary infection	3*
COPD with acute respiratory failure	2
Acute bronchitis	2
Acute tonsillitis	1
Acute upper respiratory tract infection	2
Lower extremity cellulitis	1

* Responded to intravenous broad-spectrum antibiotics (ceftriaxone 500 mg q 12 h, or cefepime 500 mg q 12 h) and oral fluoroquinolones (levofloxacin 500 mg once daily, or moxifloxacin 400 mg once daily) and negative to RT-PCR test.

ing SARS consisted of either a positive polymerase chain reaction (PCR) and a typical clinical course or, in the absence of a positive PCR, a typical clinical course with a definite contact history or evidence that the patient transmitted the infection to someone else. On subsequent serologic testing for anti-SARS-CoV antibody, all 53 patients had positive results.

Clinical Data

Data collected from the medical records included symptoms, underlying diseases, physical findings, and radiologic and laboratory data. As a clear reference point for defining chronological progression, the first day of fever > 38°C was designated as fever day (FD) 1.

Radiological Data

Serial chest radiographs were obtained once the patient was isolated, on presentation to the ED and then throughout the hospital course.

Laboratory Data

Results of consecutive hematologic examinations including absolute lymphocyte and platelet counts and serum biochemistry assays including lactate dehydrogenase (LDH), creatine kinase (CK), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) performed during observation in the ED and during hospitalization were also recorded for all patients in whom they were done.

Microbiological Studies

To look for other possible infections, patients had blood cultures for bacteria and serologic tests for *Mycoplasma pneumoniae* IgM antibodies, Chlamydial IgA, IgM, and IgG antibodies, Widal test for *Salmonella typhosa* O and H antigen, *Salmonella paratyphosa* type A and B antigen, *Streptococcus pneumoniae* antigen, *Haemophilus influenzae* antigen, hepatitis B surface antigen (HBsAg), and antibody to hepatitis C (Anti-HCV).

Reverse-transcriptase PCR Specific for SARS-CoV

Early in the course of the outbreak, there were no specific diagnostic tests available. Once we had the reverse-transcriptase polymerase chain reaction (RT-PCR) test, either a throat or nasopharyngeal swab was obtained for

detection of SARS-CoV RNA in patients with suspected or probable SARS in the ED or the isolation ward after admission (2,5).

Detection of SARS Co-V Antibodies

Both indirect immunofluorescent test (IIFT) and enzyme immunoassay (EIA) were used for all samples to detect anti-SARS CoV antibodies.

Statistical Analysis

Categorical variables were analyzed by using Fisher's exact test or a chi-square test. Significance was defined as a p value of < 0.05.

RESULTS

Clinical Presentation and Confirmation of Diagnosis

Table 2 shows patients' demographic features. Forty SARS patients had a positive PCR and were accompanied by a typical clinical course. The remaining 13 had a typical clinical course and were clearly linked in a chain of transmission by a history of close contact with a SARS patient or evidence of transmission to other(s) subsequently diagnosed with SARS. These 13 included 7 with a negative PCR and 6 others in whom PCR was not done. The latter included both staff and patients from the hospital in which significant local transmission initially occurred in Taiwan (no PCR test was available at that time). On subsequent serologic testing for anti-SARS-CoV antibodies, all 53 patients had positive results, whereas non-SARS patients had negative results. There were 7 family clusters involving 17 patients.

Table 2. Demographic Features in Patients with SARS and Non-SARS

Demographic Features	SARS (n = 53)	Non-SARS (n = 31)
Mean (SD) age (yr)	39.3 ± 18.1	42.8 ± 24.73
Sex (M/F ratio)	18/35†	16/15
Underlying diseases	12*	15**
Contact history		
Health care worker	13 (25)	3 (10)
Hospital visit	21 (42)	8 (26)
Community contact	11 (21)	6 (20)
Travel to SARS area	1 (2)	2 (6)
Unclear contact	7 (13)	12 (39)

* Diabetes mellitus (4 patients), essential hypertension (3), congestive heart failure (1), chronic obstructive pulmonary disease (1), rheumatoid arthritis (1), chronic hepatitis B (1), and end-stage renal disease with regular hemodialysis (1).
** Chronic obstructive pulmonary disease (5 patients), diabetes mellitus (3), essential hypertension (3), hepatoma (1), old pulmonary TB (1), schizophrenia (1) and end stage renal disease (1).
† Pregnancy (4).
Note: Number in parentheses is percentage.

Being a health care worker and visiting a hospital where SARS patients had been treated were risk factors for SARS. Lack of a clear contact history was more common in non-SARS patients than SARS patients. All of the latter had a typical clinical course and most had a positive PCR (Table 2).

Table 3 shows clinical features. SARS patients sought medical care at a mean of FD 3.1 ± 2.8, whereas non-SARS patients came at a mean of 4.2 ± 5.5 days after onset of their symptoms. In the SARS patients, fever ($> 38°C$) was both the most common (52/53, 98%) and the earliest symptom (50/53, 94%). The one patient without a fever initially was a 10-year-old girl who was part of a family cluster and had a positive PCR on throat swab. All of the patients presented with fever as their first symptom except for 2, of whom one had chronic

Table 3. Clinical Features of SARS and Non-SARS

Clinical Features	SARS (n = 53)	Non-SARS (n = 31)	p Value
First symptom			
Fever	50 (94)	5 (16)	< 0.0001
Cough/dyspnea	2 (4)	26 (84)	< 0.0001
Associated symptom			
Myalgia	30 (57)	6 (19)	
Headache	24 (45)	3 (10)	
Sore throat	13 (25)	4 (13)	
Diarrhea	35 (66)	4 (13)	< 0.0001
Abdominal pain	5 (9)	4 (13)	
Mean (SD) duration from symptom to admission (day)	3.1 ± 2.8	4.2 ± 5.5	
Mean (SD) admission temperature (C)	38.4 ± 0.96	37.9 ± 1.07	
Mean (SD) duration of fever (day)	10 ± 3.69	3 ± 2.57	< 0.0001

Note: Number in parentheses is the percentage.

obstructive pulmonary disease and the other congestive heart failure. Both had pre-existing respiratory symptoms related to these underlying chronic diseases, including productive cough and dyspnea on exertion. Of the non-SARS patients, only 5 of 31 (16%) presented with fever as the first symptom ($p < 0.0001$). The mean (SD) duration of fever was 10 ± 3.69 days in the SARS group and 3 ± 2.57 days in the non-SARS group ($p < 0.0001$).

As noted above, only two SARS patients (4%) with underlying illnesses had cough on the first day of fever. However, 75% (40/53) of patients with SARS eventually developed cough at a mean of FD 4.5 ± 1.9. By a mean of FD 9.3 ± 2.7, 35% (19/53) developed desaturation and dyspnea, and 8 (15%) needed mechanical ventilation. In non-SARS, 26 of 31 (84%) patients had cough or dyspnea preceding their fever ($p < 0.0001$).

Diarrhea was more common in SARS than in non-SARS patients (66% vs. 13%, respectively, $p < 0.0001$). Only 4 patients (8%) with SARS had diarrhea on FD 1. The onset of diarrhea varied considerably, at a mean (SD) of FD 6.0 ± 3.3. It lasted for a mean (SD) of 6.8 ± 5.1 days. In non-SARS, only 1 patient (3%) had diarrhea, developing 2 days before fever. Three other patients (10%) had diarrhea during their hospitalization.

Radiologic Changes

Initial chest X-ray studies were normal in 22 of 53 SARS patients (41%) and 5 of 31 non-SARS patients (16%) (Table 4). Conversely, 31 SARS patients (59%) and 26 non-SARS patients (84%) had abnormal films on presentation ($p = 0.0001$). At initial presentation, air-space opacity was commonly found in SARS patients (25/31, 80% in SARS vs. 13/26, 50% in non-SARS, $p < 0.0001$). No pleural effusion was found in SARS (0 vs. 6/26, 23% in non-SARS, $p < 0.0001$). No patient in either group had hilar lymphadenopathy or cavitation.

All but 1 (52/53, 98%) SARS patient eventually had an abnormal chest X-ray. On presentation, 14 patients already had multifocal involvement. Of the remaining 38, two-thirds (24/38, 63%) initially (either on admission or once the chest X-ray became abnormal) had a unifocal lesion. All but 2 of these patients progressed to multifocal involvement. The remaining one-third (14/38, 37%) had multifocal infiltrates as the first chest X-ray abnormality observed after admission. The infiltrates remained unilateral (either uni- or multifocal) in 13 patients (25%) and were bilateral (either initially or on progression) in 39 patients (75%). Pneumothorax or pneumomediastinum developed in 5 of the 53 SARS patients (9%), 3 of whom were mechanically ventilated and eventually died.

In the non-SARS patients, 26 of 31 had X-ray abnormalities on admission. The lesions were unifocal in 11 (42%) and multifocal in 15 (58%). Among the latter 15, 3 had unilateral and 12 bilateral lung involvement. In contrast to the SARS patients, the non-SARS patients' serial X-ray studies did not have progression of unifocal to multifocal infiltrates. No non-SARS patient had a pneumothorax or pneumomediastinum.

Table 4. Radiographic Findings in SARS and Non-SARS

Radiographic findings	SARS (n = 53)	Non-SARS (n = 31)	p Value
Initial CXR			
Negative	22 (41)	5 (16)	0.0001
Positive	31 (59)	26 (84)	
Air-space opacity	25/31 (80)	13/26 (50)	< 0.0001
Interstitial infiltrate	6/31 (20)	13/26 (50)	
Pleural effusion	0	6/26 (23)	< 0.0001
Hilar lymphadenopathy	0	0	
Cavitation	0	0	
Serial CXR			
Pneumothorax or pneumomediastinum	5/53 (9)	0	0.0016
No. of lesions			
Static unifocal	2/52 (4)	11/26 (42)	
Uni- to multifocal	22/52 (42)	0	< 0.0001
Static multifocal	28/52 (54)	15/26 (58)	
Location			
Unilateral infiltrate	13/52 (25)	14/26 (54)	
Bilateral infiltrates	39/52 (75)	12/26 (46)	
Mean (SD) duration in days			
From negative to abnormal CXR	5 ± 3.44	0	
From first symptom to progression of CXR	6.55 ± 2.95	2.88 ± 2.3	< 0.0001
From first symptom to resolution of CXR	19.25 ± 9.03	11.09 ± 8.04	0.0001

Note: Number in parentheses is the percentage.

Table 5. Laboratory Changes in SARS and Non-SARS

Laboratory findings	Initial Laboratory Findings			During Hospitalization		
	SARS (n = 53)	Non-SARS (n = 31)	p Value	SARS (n = 53)	Non-SARS (n = 31)	p Value
Hematology						
Mean (SD) total Leukocyte count (× 10^9/L)	6.68 ± 3.26	10.16 ± 4.59	0.0008			
Leukopenia*	10/53 (19)	2/31 (6)	0.0057			
Leukocytosis**	6/53 (11)	12/31 (39)	< 0.0001			
Normal leukocyte Counts†	37/53 (70)	17/31 (55)	0.0298			
Mean (SD) Lymphocyte count (× 10^9/L)	0.8 ± 0.47	1.82 ± 1.69	0.0026			
Lymphopenia‡	30/43 (70)	9/31(29)	< 0.0001	38/40 (95)	6/25 (24)	< 0.0001
Thrombocytopenia§	12/43 (28)	0	< 0.0001	16/40 (40)	0	< 0.0001
Biochemistry						
Elevated LDH‖	23/40 (58)	8/27(30)	< 0.0001	35/40 (88)	10/24 (43)	< 0.0001
Elevated CK ¶	7/39 (18)	2/30 (7)	< 0.02	12/37 (32)	4/27 (15)	0.0072
Elevated AST#	11/41 (27)	6/30 (20)	< 0.3170	19/39 (49)	9/27 (33)	0.0308

* Total leukocyte count is < 4 x 10^9/L.
** Total leukocyte count is > 10 x 10^9/L.
† Total leukocyte count is 4–10 x 10^9/L.
§ Platelet count is less than 130 x 10^9/L.
‖ LDH (Lactase dehydrogenase) level is > 200 U/L.
¶ CK (Creatine Kinase) level is > 232 U/L.
# AST (Aspartase aminotransferase) level is > 45 U/L.
‡ Lymphocyte count is less than 1.0 x 10^9/L.
Note: Number in parentheses is the percentage.

All except 1 of the 22 SARS patients with an initially normal chest X-ray study eventually developed abnormalities (mean FD 5 ± 3.44). No non-SARS patient with an initially negative chest X-ray developed abnormalities on follow-up films.

Laboratory Findings (Table 5)

Two-thirds of the SARS patients for whom we had data (30/43, 70%) had lymphopenia on the first day of hospitalization. The absolute lymphocyte count decreased, as the disease progressed, to less than 1.0×10^9/L after FD 4. Ninety-five percent of hospitalized SARS patients were initially or became lymphopenic during hospitalization. Nearly one-third of the non-SARS patients (9/31, 29%) had lymphopenia initially and (6/25, 24%) developed lymphopenia during hospitalization (p < 0.0001 comparing SARS with non-SARS initially and during the hospital course).

One-third of the SARS patients for whom data were available (12/43, 28%) had thrombocytopenia on presentation, and a total of 16 of 40 had thrombocytopenia during hospitalization. In most cases, the low platelet counts were near the lower limit of normal and usually returned to normal during the course of the disease. None of the non-SARS patients had thrombocytopenia either initially or during their hospital course (p < 0.0001

comparing SARS with non-SARS initially and during the hospital course).

LDH elevation was found in half of the SARS patients tested (23/40, 58%) on presentation and in most (35/40, 88%) at some point in the hospital course. It increased to a mean (SD) highest value of 445 ± 184 IU/L as the disease progressed at an average of FD 5. Among non-SARS patients, about one-third of patients (8/27, 30%) tested initially and half eventually (10/24, 43%) had LDH elevation (p < 0.0001 comparing SARS with non-SARS initially and during the hospital course).

In the SARS group, 40 of 47 patients tested (85%) had a positive SARS-CoV RT-PCR and Q-PCR compared with none of the non-SARS patients (29 negative of 29 tested) (p < 0.0001).

Feasibility Analysis of Additional Parameters

In our series, the WHO case definition had a positive predictive value (PPV) for SARS of only 63% (4). Tables 6 and 7 show how the PPV changes with exclusion of various other factors.

DISCUSSION

We have described the clinical course and findings in a set of patients in whom the diagnosis of SARS is

Table 6. Positive Predictive Values and False Negative Changes with Exclusions of Various Factors

	Positive Predictive Value			False Negative		
Exclusion factors	Before (%)	After (%)	p	Before (%)	After (%)	p
No fever on the first day of symptoms.	63	91	< 0.0001	0	1	0.5000
Cough/dyspnea on the first day of symptoms.	63	91	< 0.0001	0	2	0.2487
Patients with preexisting cardiopulmonary disease who had cough/dyspnoea on the first day of symptoms.	63	80	0.0082	0	2	0.2487
Patients without preexisting cardiopulmonary disease who had cough/dyspnoea on the first day of symptoms.	63	83	0.0015	0	0	1
Initial leukocytosis	63	71	0.2341	0	7	0.0070
Initial leukopenia	63	60	0.6663	0	12	0.0002
Initial lymphopenia	63	42	0.0031	0	44	< 0.0001
Initial thrombocytopenia	63	55	0.2549	0	18	< 0.0001
Initial elevated LDH	63	50	0.0661	0	37	< 0.0001
Initial elevated CK	63	60	0.6663	0	12	0.0002
Initial elevated AST	63	61	0.7732	0	17	< 0.0001
Initial negative CXR	63	54	0.2010	0	26	< 0.0001
Airspace opacity on initial CXR	63	42	0.0031	0	50	< 0.0001
Pleural effusion on initial CXR	63	68	0.4621	0	0	1

fairly certain and a group of non-SARS patients who had other diagnoses sufficient to account for their symptoms. Case series published during the outbreak most likely included some patients with diseases other than SARS, but it was difficult to separate the diagnoses at that point in the epidemic (6). The disease pattern we have delineated for SARS and non-SARS

should be useful for comparison with other series of patients with confirmed diagnoses.

Other respiratory viral infections (such as influenza) are known to manifest with the abrupt onset of systemic symptoms including fever, chills, myalgia, headache or malaise. Respiratory complaints often become more prominent as systemic symptoms subside (7). In our

Table 7. Positive Predictive Values and False Negative Rates for SARS with Exclusion of Various Factors

Increased PPV Decreased FN	Decreased PPV Increased FN	No significant change in PPV No FN
No fever on first day of symptoms.	Initial lymphopenia	Pleural effusion (initial CXR)
Cough/dyspnea on first day of symptoms.	Initial leukopenia* Initial leukocytosis **	
Patients with pre-existing cardiopulmonary disease	Initial thrombocytopenia Initial elevated LDH	
	Initial elevated CK who had cough/dyspnea Initial elevated GOT on first day of symptoms. Airspace opacity (initial CXR)**	
Patients without pre-existing cardiopulmonary disease	Negative initial CXR	
who had cough/dyspnea on the first day of Symptoms.[†]		

* No significantly increase in PPV but significantly increased FN for SARS.
** Very significantly decreased PPV and increased FN for SARS.
† Increased PPV but no false positives.
PPV = Positive Predictive Value; FN = False Negative.

series, fever was the sole initial symptom in SARS patients with 3 exceptions. Two patients also had cough and dyspnea at fever onset, but they both had already had those symptoms for years, related to underlying disease. The other exception was the 10-year-old girl who was part of a family cluster. It will be important to look at the course of the disease in other children to see if fever is less prominent in that age group than we found it to be in our adults with SARS. Others have also reported fever as an early sign in almost all patients with SARS (8–13). Although it has been noted that fever may be absent in elderly patients, we did not observe this in any of our patients (10). Among the non-SARS patients, only 5 (16%) complained of fever as the earliest symptom.

Although cough and dyspnea were very common in SARS patients, they did not appear as early as did the high fever, with the exception of the 2 patients noted above. By contrast, 84% of non-SARS patients had cough or dyspnea preceding their fever. This suggests that, in the absence of an underlying cardiopulmonary disease, patients presenting with a cough that precedes or is concurrent with a high fever are less likely to have SARS.

Diarrhea was more common in SARS patients than in those with non-SARS illnesses, and it started in the former only after the onset of high fever. Fever to this degree is less common in other viral infections that cause similar abdominal symptoms. Coronaviruses are known to cause both respiratory and enteric diseases of humans and domestic animals (14,15). However, abdominal symptoms alone do not seem to be sufficient to discriminate between SARS and non-SARS.

In a series reported from Hong Kong, 20% of patients with SARS had normal chest X-ray studies on initial presentation, compared with 41% in our series (16,17). This discrepancy may be because in most cases we did not perform conventional or high-resolution computed tomography (HRCT) imaging. However, all but 1 patient eventually had abnormal X-rays. (This patient contracted the disease from her husband who died of SARS. Serial X-rays and an HRCT of the thorax were all negative.) An initially negative chest radiograph thus cannot exclude SARS. Serial films should be done if SARS is suspected. We found that abnormalities appeared by a mean of FD 5, with a range of 2 to 8 days.

Overall, SARS patients were more likely than non-SARS patients to have air-space opacities (80% vs. 50%, respectively, $p < 0.0001$) on the initial chest X-ray study. A series in Hong Kong also reported airspace infiltrates in 78% of SARS patients (15). However, the appearance of the initial film alone cannot differentiate SARS from non-SARS. None of our SARS patients had pleural effusion, cavitation or hilar lymphadenopathy, in agreement with other series (8,16,17). In contrast, 23% of our non-SARS patients did have pleural effusion, a statistically significant difference.

Of perhaps greater use as a discriminatory feature is the relatively common pattern in SARS of progression of air-space opacities from unifocal to multifocal, found in our series as well as others (8,16). This contrasted with a lack of such progression in non-SARS ($p < 0.0001$). This particular factor will not help to discriminate between SARS and non-SARS on admission, but rapid progression of the radiographic abnormalities over several days may help confirm the diagnosis of SARS. Although pneumothorax or pneumomediastinum occurred in 5 of 53 SARS patients, none of the non-SARS patients had these complications ($p = 0.0016$). A possible explanation for this is that SARS-affected lungs may be less compliant and therefore more subject to barotrauma.

Many SARS patients had prominent pulmonary function impairment and residual pulmonary fibrosis at discharge from hospital. However, after 2 months of follow-up, their pulmonary function and pulmonary fibrosis had improved (data not shown). This implies that SARS-induced radiographic features suggested by early publication as fibrosis could in fact be viral pneumonitis and may resolve completely without leaving permanent damage (18).

Leukopenia (34%), lymphopenia (70%), and thrombocytopenia (45%) are non-specific but may suggest SARS (8). In our series, we found that SARS patients were more likely to have a normal or decreased leukocyte count on presentation, along with lymphocytopenia and thrombocytopenia, whereas those with non-SARS generally had normal or elevated white cell counts and normal lymphocyte and platelet counts (Table 5). There is quite a bit of overlap in these findings, but results at one end of the extreme or the other may add to the evidence for or against SARS.

Lymphopenia in SARS may be due to apoptosis or the use of glucocorticoids or stimulation of the hypothalamic-pituitary-adrenal axis (19,20). In our series, on admission, 70% of SARS patients tested had lymphopenia, at a time when they had not yet received any steroid therapy. At some point in their illness, 95% of our patients who were tested were lymphopenic, but a number had received glucocorticoids. It is therefore unclear if the development or persistence of lymphopenia in our patients was a result of the disease or of the treatment.

Although elevations of LDH and CK were statistically more common in SARS than non-SARS, these are unlikely by themselves to provide adequate discrimination, given the degree of overlap. However, they may be helpful in combination with other findings.

In our series, RT-PCR for SARS-CoV was positive

in 85% of the patients tested. We believe the 7 negative results were false negatives. However, the possibility of false positives and negatives with the tests used in the recent epidemic implies that we still need better means for differentiating SARS from non-SARS.

CONCLUSION

According to our findings in SARS and non-SARS, a high fever ($> 38°C$) that precedes the onset of cough by several days; an initially normal or decreased leukocyte count; lymphopenia and thrombocytopenia; elevated LDH; and air space opacities on initial chest X-rays are suggestive of SARS. If these features are present along with a positive PCR for SARS-CoV, we can be fairly confident of the diagnosis of SARS. For patients whose initial presentation is not so clear, rapid progression of chest X-ray abnormalities, particularly with changes from uni- to multifocal or uni- to bilateral infiltrates is also strong evidence of SARS. These clinical patterns are particularly important if PCR testing is not available. However, further comparison with other series of patients with confirmed SARS and non-SARS is necessary to ascertain important discriminatory features.

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