PULMONARY RADIOGRAPHIC FINDINGS IN 118 LEPTOSPIROSIS PATIENTS

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Abstract. We retrospectively reviewed the medical records and chest radiographs of 118 patients who presented during January 1998 to October 2002 at Songklanagarin Hospital in Hat Yai, Songkhla Province, Thailand who had a high serum immunofluorescent assay titer for leptospirosis. Twenty-nine of 118 (24%) patients had abnormal chest films. Nearly all of these patients had respiratory symptoms and needed oxygen therapy (93% and 90%, respectively). Forty-eight of the 118 (40%) had respiratory symptoms, but only 27/48 (56%) had abnormal radiographs. Twenty-one of the 28 (75%) and 18/27 (67%) who had abnormal chest radiographs had coexisting impaired renal function or jaundice, respectively, whereas 21/69 (30%) of the patients who had impaired renal function and 18/55 (33%) of the patients with jaundice had abnormal radiographs. There were 6/27 (22%) patients who had abnormal chest radiographs without renal or liver impairment. The most common finding on the abnormal chest radiograph was bilateral diffuse air space disease, which resolved within 7 days. No permanent lung damage was seen. The patients who had an abnormal chest radiograph needed longer hospitalization, than those without an abnormal chest radiograph (average 12 days and 5 days, respectively).

INTRODUCTION

Leptospirosis is a systemic infectious disease caused by spirochetes of the genus *Leptospira*. Human infection typically results from exposure to infected animal urine, by either direct contact or indirect exposure through water or soil (Everard *et al*, 1989). Clinical features vary, and multiorgan involvement (mainly involving skeletal muscles, kidneys, adrenal glands, liver, stomach, spleen and lung) is common (Beeson and McDemott, 1987). Respiratory manifestations have been reported in 20-70% of patients, but such features of the disease are often overshadowed by other more serious expressions (O'Neil *et al*, 1991). Chest radiographic abnormalities have been observed in 11-64% of these patients (Im *et al*, 1989; O'Neil *et al*, 1991). Even though it has a world-wide distribution, it is more common in tropical countries. Reports of chest radiographic findings in leptospirosis patients in Asian countries are few. We review a large number of leptospirosis patients in Thailand who were infected and had chest radiographs between 1998 and 2002.

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PATIENTS AND METHODS

The names and hospital numbers of leptospirosis patients admitted to our hospital from January 1998 to October 2002, were collected from the seroloy unit. There were serum samples in 360 patients that had an immunofluorescent antibody (IFA) titer higher than 400. Two hundred and forty-two patients, whose medical records and chest radiographs were not available, were admitted to other hospitals. One hundred and eighteen patients were admitted to our hospital, all of them had medical records and chest radiographs. The medical records of these patients were reviewed, noting four particular features:

1. Respiratory system involvement, especially symptoms (dyspnea, cough and hemoptysis) and oxygen therapy, if any.

2. The renal function, especially the serum creatinine level and need for dialysis.

3. The hepatic function, especially the se-

rum bilirubin and transaminase enzyme levels.

4. The final patient outcome.

Chest radiographic abnormalities were analyzed with regard to any patterns of lung infiltration. The distribution of such infiltration and the extrapulmonary findings (adenopathy and pleural effusion) were also evaluated. The progression and resolution of the abnormalities were also studied.

RESULTS

There were 82 men and 36 women, with ages ranging from 2 to 82 years (mean = 42 years). One hundred and eight patients were hospitalized, including 4 to the intensive care unit. The length of hospitalization ranged from 2 to 36 days (mean = 8 days). Three died, 2 from adult respiratory distress syndrome with acute renal failure, and 1 due to a myocardial infarction with pulmonary edema.

Respiratory symptoms developed in 48/118 patients (40%); 35 of the 48 (72%) had cough, 22/48 (45%) had dyspnea and 5/48 (10%) had hemoptysis. A rising serum creatinine higher than 1.5 g% occurred in 69/118 (61%) patient; 55/107 (51%) patients had jaundice (serum bilirubin more than 2 g%). Of the 118 chest radiographs reviewed, there were 34 abnormal ones. Five of the abnormals were considered not to be related to leptospirosis; 2 had fibrosis and nodules in an upper lobe which was unchanged from previous films and consistent with tuberculosis, 1 had a large main pulmonary artery due to known pulmonary vulvular stenosis, 1 had thalassemia and cardiomegaly, and 1 had basal pleural thickening which was unchanged from a previous examination. Thus, in the end, there were 29/118 (24%) patients who had 30 chest radiograph abnormalities which were considered leptospirosis-related.

These abnormalities could be categorized into 6 groups:

1. Twelve of the 29 (41%) patients presented with multiple tiny ill-defined nodules in both lungs, which, in 8 of the 12 (66%), subsequently became bilateral diffuse patchy infiltrates (Fig 1). One patient had a right pleural effusion.

2. Seven of the 29 (24%) had bilateral diffuse patchy infiltration.

3. Four of the 29 showed bilateral haziness of the hili with congested pulmonary vessels and Kerley's lines which were consistent with pulmonary edema.

4. Small but thick plates in the basal lungs, so-called plate atelectasis, were the main feature in 3/29 (10%) patients.

5. Small pleural effusions were present in

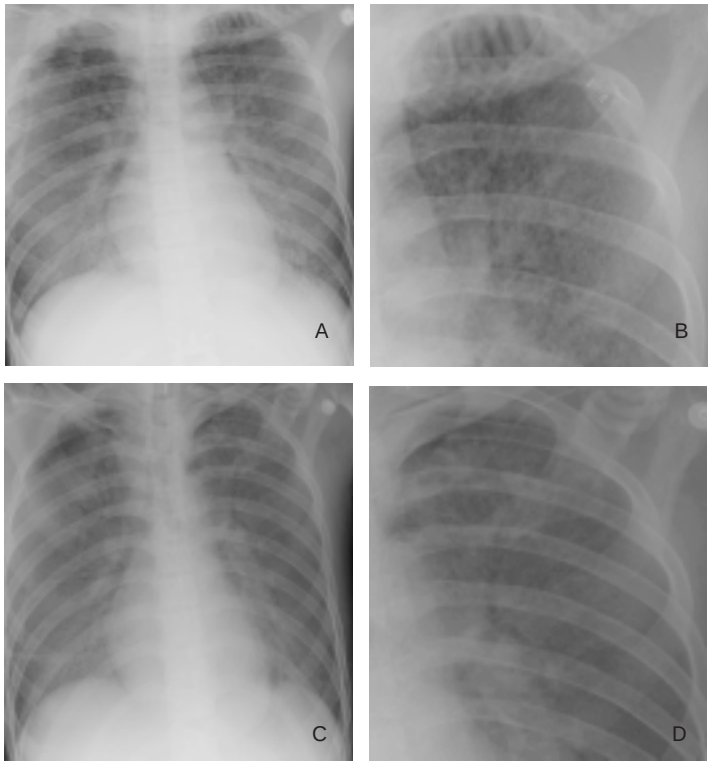

Fig 1–The most common abnormal chest radiographs found in our leptospirosis patients (A) showed multiple ill-defined nodules in both lungs (A, with a magnified view of a left upper lobe, B) that subsequently became confluent and turned to bilateral patchy infiltration (C, with a magnified view of the left upper lobe, D).

3/29 (10%) patients.

6. There was one patient (3%) who had perihilar reticular infiltration in both lungs. Because this patient also had HIV, he therefore received treatment for both leptospirosis and *Pneumocystis carinii* pneumonia.

All 29 of the patients who had abnormal chest radiographs related to leptospirosis were hospitalized, 12 (41%) of them in the intensive care unit. The average length of hospitalization was 12 days, versus 5 days for those who had a normal chest radiograph. Of the patients with abnormal chest radiographs, 27/29 (93%) had chest symptoms, 26/29 (90%) needed oxygen therapy (including 12 with endotracheal intubation and artificial ventilation support), 21/28 (75%) had a rising serum creatinine, including 9 patients who needed dialysis, and 18/27 (67%) who had a rising serum bilirubin and liver enzymes. Six of 27 (22%) patients had an abnormal chest radiograph without renal or liver impairment. All five hemoptysis patients had abnormal chest radiographs. Four patients were in the first and one patient was in the second radiographic group, respectively). In patients who had rising serum creatinine and bilirubin, 21/69 (30%) and 18/55 (33%), respectively, had abnormal chest radiographs.

There were 17 patients who had follow-up chest radiographs. Complete resolution occurred within 3 days, 3-7 days and more than 7 days in 5/17 (29%), 10/17 (59%) and 2/17 (12%) patients, respectively. No permanent damage was seen.

DISCUSSION

The definitive diagnosis of leptospirosis depends mainly on serologic tests. The microscopic agglutination (MA) method is the reference standard serodiagnostic test (Adler *et al*, 1980). However, it is time-consuming and increases the risk of laboratory- acquired infection which decreases the specificity (Sundharakiati *et al*, 1966; Silpapojakul *et al*, 1988). The immunofluorescent antibody (IFA) test is more practical for initial diagnosis and initial management of leptospirosis. The most sensitive and specific IFA test is a fourfold or greater increase in titers of acute and subsequent sera. However, this is often not possible in our hospital, where most patients are lost to follow-up once they are discharged. In addition, since it is the only tertiary unit in southern Thailand, our serology unit receives specimens, most of which are single, from many other hospitals. We chose a cut-off titer for single sera of 1:400 based on a study done at our hospital showing that such a titer was the most specific and moderately sensitive (Appassakij *et al*, 1995).

Abnormal chest radiographs related to leptospirosis were found in 24% of our patients. Similar to other studies, the characteristic and most common chest radiographic abnormality in our patients was multiple, tiny, ill-defined nodules in both lungs, some of which subsequently became confluent and turned into patchy infiltration (Lee *et al*, 1981; Courtin *et al*, 1998). These nodules might have been acinar or alveolar nodules representing fluid in the terminal airspaces (Ziskind *et al*, 1963; Felson, 1967; Recavarren *et al*, 1967). They typically had rapid progression and resolution. No pathological study was done in our patients, but these nodules might have been hemorrhagic spots and the bilateral patchy infiltration could have been pulmonary hemorrhage as mentioned in some reports (Antonio *et al*, 1997; Du Couedic *et al*, 1998; Yersin *et al*, 2000). Du Couedic *et al* (1998) found evidence of pulmonary hemorrhage from bronchoalveolar lavage in 100% (13/13) of patients who had respiratory symptoms and 70% (7/10) of patients who had no chest symptoms. Immunohistochemistry studies performed by Nicodemo *et al* (1997) following autopsies on 12 patients were positive for leptospiral antigen, and fibrin aggregation on the lumen/vascular endothelium and/or alveolar surfaces in most cases. The ultrastructural findings were uniform with consistent capillary lesions in hemorrhagic areas. They suggested leptospirosis caused hemorrhagic pneumopathy and septal capillary lesions. However, this chest radiographic finding is not pathognomonic for leptospirosis since it can be seen in other diseases, such as aspiration, bronchioloalveolar cell carcinoma, or pulmonary hemorrhage due to many entities. Correct determination of these diseases needs clini-

cal correlation. The second most common chest radiographic abnormality was bilateral patchy infiltration, which may have simply been a late manifestation of the first group. These cases were unlikely to have been adult respiratory distress syndrome as mentioned in one report since they had rapid resolution (Kiatboonsri *et al*, 1995; Niwattayakul *et al*, 2002). In adult respiratory distress syndrome, complete resolution of chest radiographic abnormalities often needs a much longer time (Felson, 1973; Dailey *et al*, 1993; Milne and Pistolesi, 1993). They were also unlikely to have been pulmonary edema due to their peripheral distribution and lack of other supportive evidence, such as Kerley's lines or pleural effusion.

We also observed that most patients who had abnormal chest radiographs had higher morbidity. They had longer hospitalization and usually had renal and liver involvement. A small number of patients with renal or liver involvement had abnormal chest radiographs. This may indicate that pulmonary involvement could be either a late manifestation of the disease or correlate with disease severity. Dupont *et al* (1977) used alveolar infiltration seen on chest radiographs as one of the significant prognostic factors associated with mortality.

We believe that the patients in the third group who had chest radiographic abnormalities consistent with pulmonary edema were likely to have had impaired renal excretion and received excessive fluid replacement rather than having real pulmonary involvement from leptospirosis. Other nonspecific abnormal findings including subsegmental atelectasis (group 4) and pleural effusions (group 5), which occurred in a small number of patients. We could not make any firm conclusions concerning bilateral reticular infiltrations in one patient (group 6), since he was also diagnosed as being HIV-positive, and he improved after receiving treatment for *Pneumocystis carinii* pneumonia.

Even though leptospirosis is prevalent in tropical regions, reports from Asia are few, and all large studies to date of radiographic findings from leptospirosis are from South America (Trevejo *et al*, 1995; Lomar *et al*, 2000). The largest known Asian studies are from China (Research Laboratory of Sino-Soviet Friendship Hospital, 1959; Wang *et al*, 1965), Korea (Im *et al*, 1989), and India (Sehgal *et al*, 1995). Our current study is the largest radiological study to date from Southeast Asia (Silverstien *et al*, 1953; McCrumb *et al*, 1957; Poh and Soh, 1970; Berman *et al*, 1973; Kiatboonsri *et al*, 1995; Niwattayakul *et al*, 2002). It confirms what is currently known. From 1953 to now, in various regions of the world, patterns of lung involvement in leptospirosis do not seem to be have changed; most commonly pulmonary hemorrhage and much less common ARDS. Pulmonary hemorrhage is usually mild in the course of disease, with spontaneous resolution and no permanent damage to the lungs. However, pulmonary hemorrhage and ARDS are two of the most fatal conditions in leptospirosis.

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