A Fatal Case of Legionnaires’ Disease

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SUMMARY
A proven sporadic case of fatal Legionnaires’ disease, the first reported in South Africa to be diagnosed at autopsy, is described.


The extensive epidemiological studies that followed the outbreak of Legionnaires’ disease in Pennsylvania in 1976 indicated that similar cases were occurring in epidemic or sporadic form in other cities and countries. It was therefore expected that cases would occur in South Africa.

The pathology department of the National Centre for Occupational Health carries out approximately 600 autopsies and also receives for examination about 2 800 cardio-respiratory organs annually in accordance with the Occupational Diseases in Mines and Works Act No. 78 of 1973. The opportunity therefore occurred to investigate cases of pneumonic consolidation to determine whether Legionnaires’ disease was present. To date 1 case has been found.

CASE REPORT
The patient was a 55-year-old White male who became ill towards the end of July 1979. His widow stated that for the previous 2 weeks he had complained of pains in the hips and kidney region. He also had headaches, which was unusual for him, and took analgesic tablets as he suspected the onset of influenza.

On 28 July 1979 the pains became so severe that he could not complete his work shift and he went home at about 22h30 complaining of worsening, severe hip pains and pain in the chest with shortness of breath. He then vomited, after which he felt better. He took two aspirin tablets and black tea and slept well afterwards.

The next day his condition remained unchanged and he stayed in bed, but in the afternoon he became worse and a medical practitioner was telephoned. Doxycycline, prochlorperazine and other tablets were prescribed, but the next day he still had a high temperature and had shown no improvement. The practitioner, after examining him, gave him an injection and prescribed prednisone and a bronchodilator/expectorant. The patient had produced much sputum, he had a pale grey colour and his voice later became a whisper.

He had no control over his bladder and passed dark urine every few minutes. The practitioner at that stage suspected an acute urinary infection.

For the next few days his condition remained unchanged. He took liquid foods well and did not vomit again. At times he became confused and restless and complained of double vision. His sputum was now blood-stained. He was again seen by the practitioner and given another prescription.

On 2 August 1979 he appeared to have improved. He was not so restless and his temperature was not elevated for long periods. At 03h00, however, he woke up and started to cough persistently and his colour became blue. Oxygen was administered and it made the patient feel much better. The next day the practitioner was telephoned. He thought that the patient now had bronchopneumonia and that he should be admitted to hospital.

On admission the patient was seriously ill. He was conscious but confused and could not give a coherent history. The practitioner noted that he was breathless, with a cold, clammy skin. There was bronchial breathing over the right lung and rales were present in both lungs. The blood pressure was low. Chest radiographs showed extensive consolidation of the right lung. A diagnosis of pneumonia with endotoxic shock was made and treatment commenced with a combination of ampicillin and cloxacillin and gentamicin. The patient did not respond, however, and he died some 8 hours later. The total duration of the illness was therefore about 7 days.

During life the patient had worked on a gold mine. From 1942 until the time of his last illness he was in the reduction works as a mill learner, reduction worker, smelter and amalgamator. He was a non-drinker, but smoked 4 cigarettes per day, although in previous years he had smoked 10 - 12 cigarettes per day. He had a chronic cough, mainly at night and in the early morning, productive of about half a cupful of whitish-yellow sputum. For the past 10 - 12 years he had complained of quite marked exertional dyspnoea. He slept on two pillows and did not have nocturnal dyspnoea. His blood pressure was within normal limits and his general condition was good. His last routine chest radiograph read ‘0/0, em’, on the ILO/UICC Classification of Radiographs. His lung function tests in 1979 indicated markedly uneven distribution of inspired gas, mild hyperinflation with moderately severe obstruction of peripheral airways and a moderate diffusion defect. A degree of anoxaemia at rest was suggested, but the acid-base balance was normal.

Autopsy Findings
The body was that of a thin (59 kg) middle-aged male with slight clubbing of the fingers and toes. The peritoneal
and pleural sacs contained a slight excess of clear, straw-coloured fluid. The liver was slightly enlarged and microscopic examination showed slight fatty change and slight portal fibrosis. The other abdominal organs showed no significant macroscopic or microscopic changes. The right lung weighed 2.124 g, but the left lung was not weighed as it was inflated with formalin for preparation of Gough-Wentworth sections. The bronchi and pulmonary vessels showed no gross changes. The pleurae were slightly pigmented and thickened but there was no exudate. The cut surface of the right lung was moist and airless and there was extensive consolidation involving all three lobes, only small portions of lung tissue appearing to be aerated (Fig. 1). The left lung showed no consolidation but a moderate degree of panacinar and centrilobular emphysema was present in both lungs. The heart was enlarged (420 g) owing to right ventricular hypertrophy and the coronary arteries showed moderate atherosclerosis.

Histological sections from the right lung showed a confluent bronchopneumonia (Fig. 2). The air spaces were filled in varying degrees with neutrophils, macrophages, erythrocytes and fibrinous exudate and the proportion of these cells varied in different parts of the sections (Fig. 3). In parts the alveolar septa were destroyed. The larger bronchioles and bronchi were not involved, but the smaller blood vessels and capillaries were congested. There was fibrous thickening of the pleura with congested, dilated vessels, but surface exudate was not present. Dieterle staining showed short, rod-shaped organisms lying free in the air spaces or within phagocytic cells, but they could not be positively identified morphologically (Fig. 4). Sections of the left lung showed early silicotic lesions, but there was no evidence of pneumonia.

**Bacteriological Examination**

A piece of the unfixed consolidated lung tissue was examined bacteriologically in the Department of Microbiology of the South African Institute for Medical Research.

Lung tissue showing consolidation was selected for microscopy, guinea-pig inoculation and culture on Mueller-Hinton agar supplemented with Isovitalex (BBL) and haemoglobin powder, agar containing casein hydrolysate, l-cysteine, ferric pyrophosphate and starch, and on cysteine-yeast extract agar containing activated charcoal. The 4 guinea-pigs inoculated intraperitoneally were observed daily for 10 days for signs of disease and were bled for

**Fig. 1.** Cut surface of right lung showing extensive consolidation.

**Fig. 2.** Histological section showing a confluent bronchopneumonia (H and E ×30).

**Fig. 3.** Air spaces filled with neutrophils, macrophages, erythrocytes and fibrinous exudate (H and E ×500).
serum samples and sacrificed after 6 weeks. None of the animals became ill and the indirect fluorescent antibody test for Legionella pneumophila was negative in all 4 guinea-pigs. Cultures incubated in 5% CO₂ at 36°C were negative after 2 weeks. The microscopic examination was performed on scrapings from consolidated lung tissue fixed in formalin as well as on imprints of tissue fluid from the cut surface of appropriate tissue. The preparations were stained by Gram’s method and the direct fluorescent antibody technique. The conjugated serum prepared from the Knoxville strain of L. pneumophila was obtained from the Center for Disease Control, Atlanta, Georgia (CDC). Only Gram-positive cocci were seen in Gram-stained preparations. The direct fluorescent antibody test was strongly positive, showing 2 - 50 strongly fluorescing bacteria per oil immersion field (× 100 objective). This result was confirmed when smears submitted to the CDC were reported as positive.

Fig. 4. Short rod-shaped intra- and extracellular organisms (Dieterle × 1,250).

To establish a possible source of infection, serum samples were obtained from the patient’s wife and from 19 close contacts in the reduction works section of the mine where he had been employed. Indirect fluorescent antibody tests using the Philadelphia 1 antigen (lot No. 78/0296) obtained from the CDC were performed on the sera of these contacts, using the method recommended by the CDC. The patient’s wife had a titre of 32 while 3 of the other contacts gave a history of a recent illness consistent with legionellosis. The indirect fluorescent antibody test was strongly positive, showing 2 - 50 strongly fluorescing bacteria per oil immersion field (× 100 objective). This result was confirmed when smears submitted to the CDC were reported as positive.

DISCUSSION

The pathological findings in this case of Legionnaires’ disease are essentially the same as those described by other workers. In this case, however, the disease was confined to the right lung, while bilateral involvement is commoner. The demonstration of L. pneumophila bacilli by the direct fluorescent antibody test was regarded as definite confirmation of the diagnosis. The reliability and specificity of the technique were amply substantiated when pure cultures of 25 appropriately chosen genera and 59 species of different bacteria were shown by workers from the CDC not to fluoresce with the diagnostic dilution of the Knoxville conjugate of L. pneumophila. As regards the possibility that the patient acquired his infection at work, it is worth mentioning that 28% of serum samples submitted to the South African Institute for Medical Research have titres between 32 and 128, compared with 25% (5 out of 19) of the contacts. The fact that one contact had a titre which was within the diagnostic range of 256 suggests that this miner had probably suffered from legionellosis in the past, but the source of that infection need not have been associated with his work. There is therefore no convincing evidence that the patient acquired his infection at work and the source of infection remains unknown.

The disease tends to occur in compromised patients and in this case there was clinical evidence of chronic obstructive Airways disease and autopsy evidence of emphysema.

Hepatic fatty change was described in a number of the previously reported cases, and this case also demonstrated it. The finding of endotoxic shock on admission to hospital is interesting, since Wong et al., in chemical studies and biological assays on the causative organism, did not find the usual endotoxin-producing substances that occur in Gram-negative organisms. They did find evidence of an endotoxin-like substance, but in general the organisms were weak in ‘endotoxicity’. Shock before death is however not unusual in legionellosis, and 12 of the 26 patients that died in the Philadelphia epidemic suffered from shock. It was not apparently associated with respiratory failure but clinically resembled shock after bacteraemia.

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REFERENCES