the patient's syncopal attacks, but he had no further episodes after operation.

Treatement of malignant cardiac mesothelioma has been unsuccessful in all but two instances. Our patient enjoyed normal activities for more than a year after operation, and Sagerman and co-workers have reported complete sterilization of a cardiac sarcoma by radiation therapy. One must conclude that early operation seems mandatory in any patient with diagnostic features which are suggestive of cardiac neoplasm.

References


Fatal Diffuse Influenzal Pneumonia: Premortem Diagnosis by Lung Biopsy

Robert L. Noble, M.D.,** Glen A. Lillington, M.D., and Richard L. Kempson, M.D.

Primary viral pneumonia is an uncommon but serious complication of influenza infection. Pathologic changes in the lungs due to the virus per se are commonly obscured by secondary bacterial infection. An extensive disseminated influenza pneumonia in a 40-year-old woman was associated with intractable hypoxemia despite intensive supportive care, including continuous positive pressure breathing, hypothermia and adrenal corticosteroids. Open lung biopsy early in the course of the disease showed pathologic changes attributable to "pure" virus pneumonia free from bacterial superinfection at that time. Death eventually occurred from secondary bacterial and fungal pneumonia demonstrated at autopsy.

Secondary bacterial pneumonitis, usually streptococcal or staphylococcal, is a serious complication of pandemic and endemic influenza. A primary viral pneumonitis also may occur in influenza, usually as a patchy bronchopneumonia but occasionally manifesting itself as a bilateral diffuse process with high morbidity and mortality.1-4

We report a patient with unusually severe diffuse pneumonitis in which the nonbacterial and influenza etiology was proved by lung biopsy with cultures and in which the physiologic derangement was profound enough to be categorized as "adult respiratory distress syndrome."

Case Report

A 40-year-old white married woman was admitted to Stanford University Hospital after a five day illness with fever, cough, malaise and one episode of vomiting. Treatment at home had included three days of erythromycin and one day of tetracycline therapy, but her symptoms steadily worsened, and with the appearance of severe dyspnea and cyanosis, admission to hospital was advised. Her past history indicated that she consumed alcohol to excess and was a heavy cigarette smoker with a chronic cough. There was a history of recurrent cystitis and frequent upper respiratory infections. She had not received influenza vaccine.

On admission she was cyanotic and severely dyspneic. Her temperature was 41.0°C. Her blood pressure was 114/65 mmHg and her pulse rate was 180 per minute. Her respirations were rapid and shallow at a rate of 36 per minute; auscultation of the chest revealed bronchial breath sounds bilaterally and occasional fine inspiratory crepitant rales. The physical examination was otherwise unremarkable.

Laboratory tests gave the following results: hemoglobin 16.4 gm/100 ml; white blood cell count 3,800 per cu mm with 78 percent neutrophils, 7 percent bands, 6 percent lymphocytes and 2 percent monocytes. Abnormal values in the blood chemistry studies included: potassium 2.8 mEq/L; cholesterol 70 mg/100 ml; albumin 2.1 gm/100 ml; globulin 2.7 gm/100 ml; alkaline phosphatase 235 mg/100 ml (normal range 30-85); SLDH > 600 mg/100 ml (normal values 100-250); SGOT > 250 mg/100 ml (normal range 7-40); Cold agglutinins were absent. An immunoelectrophoresis revealed diffuse hypogammaglobulinemia. An arterial blood gas sample, taken on admission while she breathed 100 percent oxygen at 12 L/min via a face mask, gave the following results: PaO2 42.6 mm Hg, oxygen saturation 78.8 percent, PaCO2 29 mm Hg and pH 7.39. The admission chest roentgenogram (Fig 1) showed diffuse bilateral consolidation involving all areas of the lungs with an "alveolar-filling" pattern. There was no evidence of cardiac enlargement or pleural effusion. Subsequent chest roentgenograms showed no significant improvement. The central venous pressure measured 5 cm H2O.

Shortly after admission, a cuffed nasotracheal tube was passed and subsequently, tracheotomy was performed. With assisted ventilation (100 percent oxygen, Bennett PR-2 respi-
FATAL DIFFUSE INFLUENZAL PNEUMONIA

FIGURE 1. Chest roentgenogram (AP, portable) taken shortly after admission to hospital. A diffuse "alveolar-filling" process causes almost complete opacification of both lungs. The left upper lobe is not quite so densely involved. Bilateral "air bronchograms" are present. Subsequent chest films during the course of her illness showed no improvement.

rator) her PaO2 initially rose to 59.5 mm Hg, but then fell below 40 mm Hg. On the fourth hospital day, open lung biopsy of the lingula was performed. The PaO2 varied between 23 and 36 mm Hg. Temperature varied between 38° and 41°C. Following a grand mal seizure on the sixth hospital day, hypothermia and respiratory paralysis with curare were instituted to lower the patient’s oxygen requirement. On the seventh day, a volume cycled respirator (Engstrom) was substituted for the Bennett, but only temporary improvement occurred, with PaO2 varying between 25.0 and 45.0 mm Hg. On the ninth day, a 5 cm H2O expiratory pressure was added and the PaO2 rose to 92 mm Hg. Thereafter the inspired oxygen concentration was gradually reduced to 70 percent, but the PaO2 on the 10th to 13th hospital days varied from 33.8 mm Hg to 44.5 mm Hg.

A number of microbiologic studies were performed. The tracheal aspirate on admission grew rare alpha Streptococcus on culture, and cultures of subsequent specimens gave similar results. Influenza A2 virus was isolated from a portion of the lung biopsy specimen, but no virus was recovered from throat washings or stool.* Bacterial and fungal cultures of the biopsied lung were negative. Serum specimens drawn on the 3rd and 12th hospital days demonstrated complement fixing antibody to influenza A at dilutions of 1:256 on both occasions. Multiple blood cultures were negative.

She was treated with Keflin (12 gm/day IV) for the first three days and with penicillin G (600,000 U/day IM) from the third to fifth day. Antibacterial therapy was then stopped because of the absence of bacterial pathogens on numerous cultures of the tracheal aspirate and a lung biopsy compatible with viral pneumonia. Aqueous hydrocortisone by IV drip was started on the first day because of hypotension and poor urinary output and was administered in massive doses (> 800 mg/day) from the fifth hospital day until her demise.

Throughout her hospital course she failed to show significant response to any therapeutic measures. Infarcts of the skin over the terminal portions of her digits were noted on the 12th day, and she expired on the 13th day.

Lung Biopsy Findings (Fig 2)

One of the most prominent features in the lung was a necrotizing bronchitis and bronchiolitis. This varied in severity with the more proximal larger bronchi demonstrating the greatest degree of necrosis. Acute inflammatory cells were present in the walls of the bronchi, in the peribronchial tissue and occasionally in the lumina of the bronchi. The bronchial epithelium, when present, was one cell thick and was partially or completely eroded in the most severely inflamed bronchi. Almost all alveoli contained prominent hyaline membranes and many contained edema fluid with red blood cells. Fibrin was present in only a few alveoli. The hyaline membrane could be seen extending out into the alveolar ducts. In most alveoli, the lining cells were not detectable. The alveolar wall contained scattered acute inflammatory cells and congested capillaries. No thrombosis or vasculitis was detected.

FIGURE 2. Lung biopsy. To the left is seen a bronchiole with acute inflammation, necrosis, and mucosal ulceration. Peribronchiolar inflammation is present. Hyaline membranes line the alveolar walls. See text (H and E, x 150).

FIGURE 3. Lung, autopsy specimen. The alveoli are filled with an acute inflammatory exudate. Remnants of hyaline membranes are still present in some areas. See text. (H and E, x 150).

*Virus cultures were performed by the California State Public Health Laboratory, Berkeley, California.
Post Mortem Findings

The lungs were diffusely consolidated with a confluent necrotizing pneumonia, epithelization of the air spaces and ulcerative bronchitis with squamous metaplasia (Fig 3). Hyaline membrane was focally present. An infarct was present in the left lower lobe and contained large numbers of Candida organisms and bacteria. The lung culture grew enterococci and Candida albicans. The heart showed recent thrombi on normal mitral, aortic and tricuspid valves. Cultures both of the blood and mitral valve vegetations yielded enterococci. The liver showed fatty changes, mainly centrilobular, associated with acute focal necrosis and an acute inflammatory reaction. Mallory's hyaline bodies were found in the hepatic cells. It was concluded that these findings represented early alcoholic hepatitis. The stomach contained a recent ulcer with Candida organisms in the base, and a Candida cystitis was noted. A large infarct was found in the frontal lobe of the left cerebrum. No organism was found in the infarct.

Discussion

The pathologic changes associated with primary influenzal pneumonia were described over 50 years ago1-2 and have been confirmed in subsequent reports, particularly since the influenza epidemic of 1957-1958.3-10 However, all of these studies were performed on autopsy material, and as most fatal influenzal pneumonias are complicated by bacterial superinfection, there has been some difficulty in distinguishing the pathologic changes due to the virus from those resulting from the secondary bacterial infection. Meticulous histologic studies in patients dying rapidly after the onset of influenzal pneumonia have disclosed pulmonary alterations considered to be characteristic of uncomplicated influenzal pneumonia. The findings in these autopsy cases included necrotizing bronchitis, hyaline membrane formation, intra-alveolar hemorrhagic edema and mild interstitial inflammation. These changes are identical to those demonstrated in our lung biopsy material, and undoubtedly represent the morphologic alterations associated with "pure" virus infection. It is emphasized that similar findings occur in primary pneumonias due to other viruses.

The pulmonary pathologic changes demonstrated at autopsy in our patient represent a combination of partially resolved viral pneumonitis and secondary bacterial and fungal pneumonia. Squamous metaplasia, as seen in our patient, has been found in autopsies of patients dying late in the course of influenzal pneumonia, and is assumed to represent a reparative process during resolution of the viral infection. This concept is supported by the work of Walsh and associates8 in which bronchial biopsies taken at various stages in the course of influenzal infection showed focal squamous metaplasia during the reparative process.

The case we are reporting is unique in that pathologic material was obtained during two different temporal and etiologic stages in the process: the lung biopsy shows the "pure" changes in the bronchi and alveoli resulting from uncomplicated influenza infection, while the autopsy material demonstrates the added effects of enterococcal and Candida secondary infections in the lungs and elsewhere.

Factors commonly associated with high mortality in influenzal pneumonia (advanced age, pregnancy, rheumatic heart disease, pre-existing lung disease) were not present in this case, yet the radiologic abnormalities and impairment of pulmonary oxygen transfer were of almost unprecedented severity. Possibly the depressed gamma globulin level and the presence of alcoholic hepatitis were contributory factors. Severe and even fatal influenzal pneumonia may occur in previously healthy young adults, however, particularly during epidemics.7

Radiologic changes attributable to diffuse influenzal pneumonia include a widespread "alveolar filling process" extending out from the perihilar areas in a pattern resembling acute pulmonary edema.11-14 The only reported cases with radiologic involvement as profound as in our patient were described by St. Geme and associates,14 and their patients had both been treated by pulmonary lavage which may have accentuated the abnormalities.

The derangement of pulmonary function in our patient was severe enough to categorize the case as an example of "adult respiratory distress syndrome."15 Supportive measures employed included continuous positive pressure breathing (CPAP) with 100 percent oxygen, hypothermia and high dose adrenal corticosteroids; yet, the arterial oxygen tension could not be maintained above 50 mm Hg. The experiences of St. Geme et al14 suggest that pulmonary lavage is ineffectual. A recent report16 suggests that hyperbaric oxygen therapy is helpful in maintaining life until spontaneous resolution of the pneumonia occurs.

References

2 Wintemitz MC, Wason IM, McNamara WG: The Pathology of Influenza. New Haven, Yale University Press, 1920
3 Parker F Jr, Jolliffe LS, Barnes MW, et al: Pathologic findings in the lungs of five cases from which influenza virus was isolated. Am J Path 22:797-832, 1946

CHEST, VOL. 63, NO. 4, APRIL, 1973
FATAL DIFFUSE INFLUENZAL PNEUMONIA


ANNOUNCEMENTS

11th Annual Workshop in Electrocardiography

The 11th Annual Workshop in Electrocardiography, sponsored by the Rogers Heart Foundation and St. Anthony's Hospital (St. Petersburg) will be held at the Tides Hotel and Bath Club, Redington Beach, Florida, April 26-30. Course director is Dr. Henry J. L. Marriott. For information, write: Rogers Heart Foundation, St. Anthony's Hospital, St. Petersburg, Florida 33705 (telephone 813/894-0790).

Cardiovascular Radiology Postgraduate Course

The Department of Radiology, Albert Einstein College of Medicine, will present a Cardiovascular Radiology Postgraduate Course May 14-18. Presentations will be made by guest faculty and members of the staff of the medical school. For information, contact Dr. Milton Elkin, Program Director, Radiology Postgraduate Course, Bronx, New York 10461.

Master Interpretation of Clinical Electrophysiology

The University of Miami School of Medicine and the Council on Clinical Cardiology, American Heart Association, will present a postgraduate seminar on "Master Interpretation of Clinical Electrophysiology." The program will be held at the Contemporary Hotel at Disney World, Lake Buena Vista, Florida, May 29-31. Address inquiries to Dr. Louis Lemberg, University of Miami School of Medicine, PO Box 875, Biscayne Annex, Miami 33152.