Severe disseminated lung disease and bronchiectasis probably due to *Mycoplasma pneumoniae*

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Severe disseminated lung disease causing acute respiratory failure developed in a previously healthy 6½-year-old boy. *Mycoplasma pneumoniae* was implicated and a complement-fixing antibody titre of 1:1024 against this organism was detected. At autopsy bronchiectasis was found, affecting chiefly the right middle and lower lobes. The unusual radiologic and pathologic findings are discussed.

Les auteurs rapportent le cas d'un garçon de 6 ans et demi qui présente une maladie pulmonaire disséminée et sévère, ainsi qu'une défaillance respiratoire aiguë, avec des taux d'antîcorps fixant le complément de 1:1024 contre le *Mycoplasma pneumoniae*. L'autopsie révèle des bronchiectasies surtout aux deux lobes inférieurs ainsi qu'au lobe moyen droit. Les découvertes radiologiques et pathologiques inusitées sont discutées.

Pneumonia due to *Mycoplasma pneumoniae* is usually benign and self-limited. It is predominant in young people, the highest attack rate being among children aged 5 to 9 years.[1,2] The duration of the acute illness averages 8 to 10 days and the period of convalescence approximately 1 week. A specific diagnosis is made when the causative agent is recovered or an increase in titre of specific antibody is detected. A presumptive diagnosis is permissible if cold agglutinins are present in the blood.

Severe infections due to *M. pneumoniae* have rarely been reported in children and most of the few overwhelming cases have been described in patients with immunodeficiency syndrome[3] or sickle cell anemia.[4]

We report a case, in a previously healthy child, of pneumonia caused by *M. pneumoniae* presenting as severe disseminated lung disease leading to acute respiratory failure and bronchiectasis.

Case report

A 6½-year-old boy had a benign upper respiratory tract infection for 2 weeks before he started to suffer from an unproductive stubborn cough. Amoxicillin was prescribed by the family doctor and brought about slight improvement. However, 5 days later dyspnea developed. At this point the body temperature was 40°C and auscultation detected some degree of wheezing. The peripheral leukocyte count was 16.1 × 10^9/L with a predominance of polymorphonuclear cells. Chest roentgenogram demonstrated diffuse bilateral interstitial infiltration.

The patient was then admitted to a regional hospital and penicillin was given parenterally. Blood cultures were sterile and cultures from throat swabs produced a growth of *Staphylococcus aureus*. The tine tuberculin test gave a negative result.

On the 8th hospital day a chest roentgenogram showed an alarming degree of widespread alveolar infiltration. The same day ventilation deteriorated rapidly as the P_{CO_2} increased to 125 mm Hg just prior to intubation. While being ventilated artificially the patient was transferred to Sainte-Justine Hospital. On arrival he was unconscious. His temperature was 38°C, heart rate 120 beats/min and blood pressure 110/70 mm Hg. His nutritional status appeared excellent (weight and height were above the 75th percentile). He had bilateral otitis media, and fine crackling rales were heard over both lungs. The peripheral leukocyte count was 10.5 × 10^9/L with a shift to the left. Measurement of arterialized capillary blood gas tensions showed a P_{CO_2} of 88.9 mm Hg and a P_{O_2} of 158 mm Hg while the patient was breathing 100% oxygen. Protein immunoelectrophoresis showed normal findings. The chest roentgenogram was identical to the one taken at the referring hospital. Parenteral administration of wide-spectrum antibiotics (ampicillin, 200 mg/kg•d; nafcillin, 150 mg/kg•d; and gentamicin, 5 mg/kg•d) was started. Direct examination of tracheal aspirates discovered a few polymorphonuclear cells and no bacteria. Ziehl–Neelsen stains failed to reveal acid-fast organisms. The search for mycelia, siderophages and *Pneumocystis carinii* was unproductive. Cultures of blood and tracheal aspirate were repeatedly sterile.

Fourteen hours after the boy's admission he became conscious. He was weaned from the respirator on the 3rd day, but the pulmonary signs and the chest roentgenogram remained unchanged. A complement-fixing antibody titre of 1:1024 against *M. pneumoniae* and a cold agglutinins titre of 1:512 were demonstrated in a blood sample taken on the 1st day in our hospital (Table I). Viral cultures from blood, stool, urine and tracheal aspirate gave negative results. On the 4th day ampicillin, nafcillin and gentamicin were replaced by erythromycin administered orally at a dosage of 50 mg/kg•d.

On the 9th hospital day the findings on pulmonary auscultation were normal and the chest roentgenogram showed some clearing of the diffuse infiltration. A sweat test gave normal values and the patient was discharged. Six days later he was readmitted to the same regional hospital with severe bronchospasm. The chest roentgenogram showed mild hyperinflation. After 12 days of "difficult management" he was discharged. One week later he was allowed, for the first time, to go outside to play; shortly afterwards he was found dead.

At autopsy the pathologic changes were limited to the lungs. Histologic sections showed large- and medium-sized bronchi to contain gastric secretions. The small bronchi were filled diffusely with purulent material overlying an edematous purple mucosa; the lumen of each was extremely dilated, exceeding in general that of the main bronchi. These lesions predominated in the right middle and lower lobes.

Microscopic examination showed infiltration of alveolar septa by lymphocytes, plasma cells and macrophages, desquamation of alveolar lining cells and intra-alveolar fibrinous exudate. Hyaline membranes, fibrosis and edema were also present. The bronchial mucosa was ulcerated and covered in some areas with a fibrinous exudate. The bronchial walls showed infiltration of their superficial layers by histiocytes and macrophages. Lymphocytes and plasma cells were more prominent in the deeper portions of the bronchial structures. In many areas the cartilage was destroyed and replaced by fibrosis (Fig. 1). Most of the bronchioles showed similar changes — that is, ulceration, fibrosis and infiltration of their walls by lymphocytes and plasma cells. Ectasis was present both in small bronchi and in bronchioles.

Discussion

Neither the clinical course nor the roentgenologic manifestations in this case were usual for pneumonia due to *M. pneumoniae*. A recent survey by Putman and colleagues[5] of 100 patients confirmed the previous findings that

Table I—Complement-fixing antibody titres

Organism	Titre
Influenza A virus	1:8
Adenovirus	1:8
Parainfluenza virus	
1	1:16
2	1:64
3	1:16
Respiratory syncytial virus	1:16
Influenza B virus	0
Chlamydia psittaci	0
Coxiella burneti	0
Measles virus	0
Cytomegalovirus	0
Mycoplasma pneumoniae	1:1024

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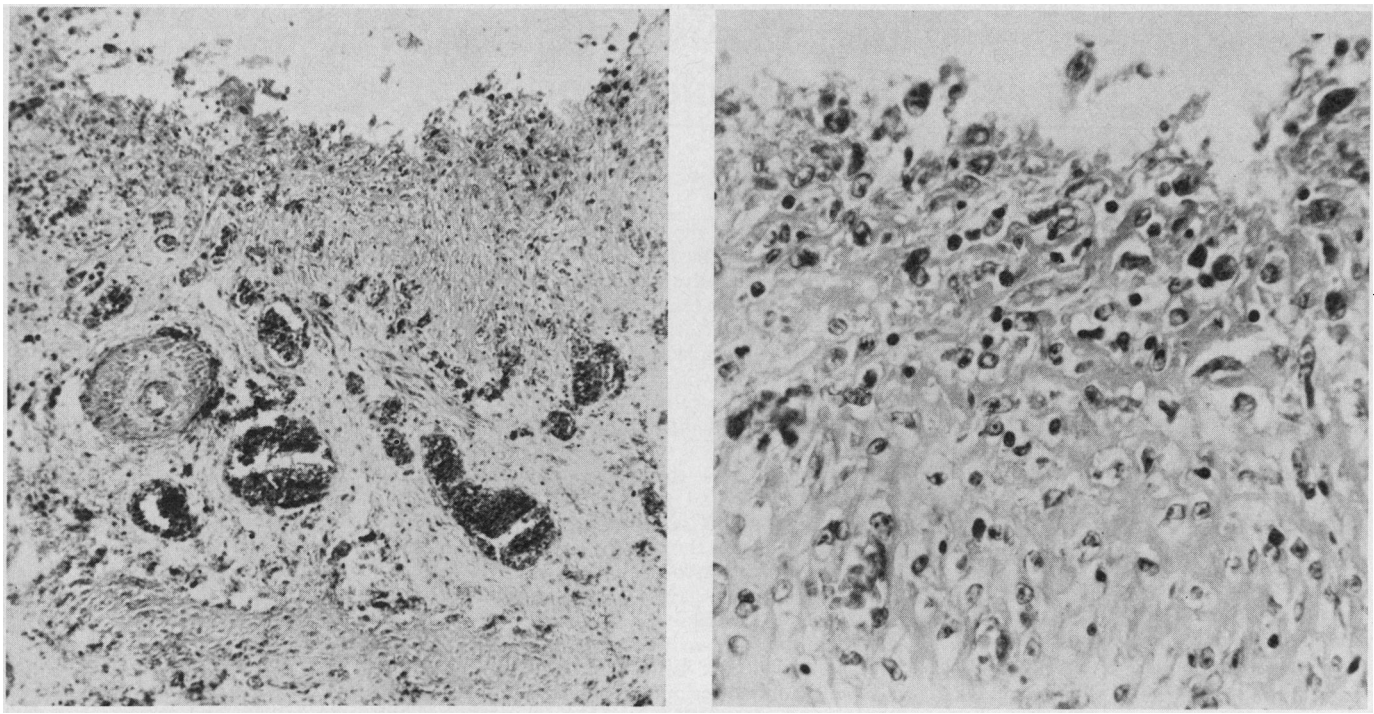

FIG. 1—Postmortem lung tissue: dilated bronchus showing ulceration of mucosa, inflammatory cells, destruction and fibrosis of bronchial wall (hematoxylin–phloxine–saffron; ×125 (left), ×500 (right).

this disease may present with either segmental consolidation or a diffuse reticulonodular pattern. Massive pulmonary involvement is rare, and when it occurs it is most often unilateral.[4,6] Only 1 of 180 patients studied over a 6-year period by George and associates[7] in military recruits aged 18 to 21 years had widespread lobular consolidation.

Although bronchiectasis was mentioned by Rytel[8] as a possible complication of pneumonia caused by *M. pneumoniae* it has rarely, if ever, been reported in children. Abnormal pathologic findings in the few fatal cases have generally been limited to the alveoli, bronchioles and small blood vessels. The interstitial infiltration, swelling and desquamation of the alveolar lining cells, hyaline membranes, intra-alveolar fibrinous exudate and bronchiolitis in our patient have been described previously.[9-11] However, significant changes in the bronchi such as those seen in our patient have not been reported since 1944, when Golden[12] studied the autopsy findings in 21 patients with "atypical pneumonia".

Since the occurrence of severe bronchiectasis in children with this type of pneumonia is unusual, one could argue its possible existence prior to the acute episode reported in our patient. But in a child whose nutritional status was excellent and in the absence of a chronic cough, of clubbing of the fingers, or of any significant history of pulmonary disease, this hypothesis seems unlikely.

Antibody titres of 1:256 or higher for *M. pneumoniae* are considered suggestive of recent infection.[13] Convincing evidence of infection with *M. pneumoniae* (a complement-fixing antibody titre of 1:1024) was present in the serum from the first blood sample obtained in our hospital but no attempt was made to examine a second specimen or to isolate the organism. An antibody titre of 1:64 against parainfluenza 2 virus is considered significant, and a possible concomitant infection with this organism cannot definitely be excluded. However, the negative viral cultures and the usual association of parainfluenza 2 virus with upper respiratory tract infections plead against this possibility.

References

1. FOY HM, KENNY GE, MCMAHAN R, et al: *Mycoplasma pneumoniae* pneumonia in an urban area. *JAMA* 214: 1666, 1970
2. NOAH ND: Mycoplasma pneumoniae infection in the United Kingdom, 1967-73. *Br Med J* 2: 544, 1974
3. FOY HM, OCHS A, DAVIS SD, et al: *Mycoplasma pneumoniae* infections in patients with immunodeficiency syndrome: report of 4 cases. *J Infect Dis* 127: 388, 1973
4. SHULMAN ST, BARTLETT J, CLYDE WA, et al: The unusual severity of mycoplasmal pneumonia in children with sickle-cell disease. *N Engl J Med* 287: 164, 1972
5. PUTMAN CE, CURTIS AM, SIMEONE JF, et al: *Mycoplasma* pneumonia: clinical and roentgenographic patterns. *Am J Roentgenol Radium Ther Nucl Med* 124: 417, 1975
6. DECANCQ HG, LEE FA: *Mycoplasma pneumoniae* pneumonia. Massive pulmonary involvement and pleural effusion. *JAMA* 194: 1010, 1965
7. GEORGE RB, WEILL H, RASCH JR, et al: Roentgenographic appearance of viral and mycoplasmal pneumonias. *Am Rev Respir Dis* 96: 1144, 1967
8. RYTEL MW: Primary atypical pneumonia: current concepts. *Am J Med Sci* 247: 84, 1964
9. BENISCH BM, FAYEMI A, GERBER MA, et al: Mycoplasma pneumonia in a patient with rheumatic heart disease. *Am J Clin Pathol* 58: 343, 1972
10. MAISEL JC, BABBITT LH, JOHN TJ: Fatal *Mycoplasma pneumoniae* infection with isolation of organisms from lung. *JAMA* 202: 287, 1967
11. MEYERS BR, HIRSCHMAN SZ: Fatal infections associated with Mycoplasma pneumoniae: discussion of three cases with necropsy findings. *Mt Sinai J Med NY* 39: 258, 1972
12. GOLDEN A: Pathological anatomy of "atypical pneumonia, etiology undetermined"; acute interstitial pneumonitis. *Arch Pathol* 38: 187, 1944
13. ROSE NR, FRIEDMAN H (eds): Serology of mycoplasmic infections, in *Manual of Clinical Immunology*, Washington, American Society for Microbiology, 1976, pp 357-62

BOOKS

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AN INTRODUCTION TO THE STUDY OF DISEASE. 7th ed. William Boyd and Huntington Sheldon. 492 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1977. $15.95. ISBN 0-8121-0600-8

LUNG CANCER. Clinical Diagnosis and Treatment. Edited by Marc J. Straus. 295 pp. Illust. Grune & Stratton, Inc., New York; Longman Canada Limited, Don Mills, 1977. $32.75. ISBN 0-8089-0998-3

MONOGRAPHS IN PAEDIATRICS. Vol. 9. Fundamentals of Mortality Risks during the Perinatal Period and Infancy. Illustration by A Comparative Study between Götenborg and Palermo. F. Falkner. Edited by F. Falkner, N. Kretchmer and E. Rossi. 203 pp. Illust. S. Karger AG, Basel, 1977, $34, paperbound. ISBN 3-8055-2651-2

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