Mycoplasma pneumonia with fulminant evolution into diffuse interstitial fibrosis

J M KAUFMAN, C A CUVELIER, AND M VAN DER STRAETEN

From the Departments of Medicine and Pathology, State University Hospital, Gent, Belgium

ABSTRACT A fatal case of interstitial pneumonia caused by Mycoplasma pneumoniae with fulminant evolution into diffuse interstitial fibrosis is reported. Treatment with tetracycline and corticosteroids failed to arrest the progress of the disease. Fatal Mycoplasma pneumoniae infections have been reported previously and some degree of pulmonary fibrosis has been described in a few cases but as far as could be ascertained there are no other well-documented cases of diffuse interstitial fibrosis with proved Mycoplasma pneumoniae infection.

Mycoplasma pneumoniae is a well-documented and recognised cause of pneumonia, although in most cases infection remains subclinical or limited to upper respiratory tract involvement.1-4 Clinical and radiographic features are inconstant and do not allow for differentiation from pneumonias caused by other micro-organisms.5-6 Mycoplasma pneumoniae usually has a rather benign, self-limiting course. However, besides important extrapulmonary complications such as haemolytic anaemia,7 8 myopericarditis,8-10 and neurological manifestations,3 4 severe and even fatal respiratory disease from Mycoplasma pneumoniae has been reported. The pulmonary complications include unilateral and bilateral massive pneumonia,11 12 large unilateral and bilateral pleural effusions,3 11 13 lung abscess,3 12 Swyer-James syndrome,13 and extensive interstitial pneumonia with severe hypoxaemia.15-17 Although exceptional, persistence of respiratory symptoms after Mycoplasma pneumoniae infection has been reported,1 8 and on a few occasions some degree of fibrosis has been demonstrated at necropsy17-19 but this condition has not yet been well documented.

Case report

Sixteen days postpartum, a previously healthy 31-year-old woman complained of rhinitis and general malaise followed the next day by chills, fatigue, and non-productive cough. On the third night she woke up with mild dyspnoea which became more pronounced during the morning. She also complained of vertigo and anorexia, and vomited once. The next morning she became severely dyspnoic and was admitted to a local hospital. Arterial blood gas analysis revealed a carbon dioxide tension (PCO₂) of 35 mmHg and an oxygen tension (PO₂) of 75 mmHg while breathing 4 litres of oxygen per minute. The chest radiograph showed patchy lobular shadows involving both lower zones (fig 1). The patient was transferred to the intensive care unit of the University Hospital, with tachypnoea (36 to 40/min), a temperature of 37.5°C, and slightly diminished breath.

Address for reprint requests: Dr JM Kaufman, Department of Medicine, State University Hospital, Gent, Belgium.

Fig 1 Chest radiograph (PA) on admission to hospital shows patchy lobular infiltration involving both lower zones.
day 15 000 between changes, progressive infiltrates to ing and two immediately intubated and cline breathing mmHg. The patient showed respiratory distress.ated dose area, diac area, temperature chest radiograph increased two days, of 25 dose doxycycline intravenously, 200mg 70% neutrophils. of P02 rate at sounds air ambient hospital shows Mycoplasma pneumoniae associated with respiratory distress. The lung film was clear. There were no signs of alveolar opacities or consolidation. The patient's temperature was 39°C, and pulse was 100 beats/min. She was tachypneic with a respiratory rate of 30 breaths/min. Arterial blood gas analysis revealed a pH of 7.45, P02 of 60 mmHg, and Pco2 of 40 mmHg. The patient was given oxygen supplementation via nasal cannula to maintain a P02 of 80 mmHg and Pco2 of 35 mmHg. The patient was referred to the intensive care unit (ICU) for further management.

The patient's condition deteriorated further. She developed progressive respiratory failure, requiring mechanical ventilation. A chest radiograph showed diffuse infiltrates throughout both lungs, with no evidence of air bronchograms. A computed tomography (CT) scan of the chest confirmed the presence of diffuse interstitial infiltrates. The patient was started on broad-spectrum antibiotics, including azithromycin and ceftazidime, and was given high-dose corticosteroids (prednisolone 100 mg daily). The patient's respiratory rate increased to 40 breaths/min, and her oxygen saturation decreased to 92% on 100% oxygen supplementation. A fiberoptic bronchoscopy was performed, which showed no evidence of endobronchial lesions or evidence of Mycoplasma pneumoniae infection. The patient's condition continued to deteriorate, and she died on the eighteenth day in hospital.

The necropsy revealed diffuse interstitial fibrosis involving both lungs. The lungs were firm and heavy, weighing 800 g each. There were no signs of alveolar consolidation or airspace disease. Microscopically, the lungs showed diffuse interstitial fibrosis with increased collagen deposition and decreased lung compliance. The fibrosis was associated with infiltration of lymphocytes, macrophages, and neutrophils. The bronchioles were dilated and contained mucus, occasional giant cells, histocytes, polymorph leucocytes, and monocytes. The patient had a history of asthma, which may have contributed to the development of interstitial fibrosis.

No cold agglutinin titre could be demonstrated. Further studies on paired sera were negative for Coxsackie 1–6, Varicella, influenza A–B, para-influenza 1–3, adenovirus, psittacosis, ornithosis, and respiratory syncytial virus.
nuclei. Some had desquamated into the lumen. The alveoli were filled with a homogenous exudate, haemosiderin laden macrophages, polymorph leucocytes, erythrocytes, and giant cells (fig 4). Fibrin was seen only occasionally. The pleura was thickened by bundles of collagen fibres.

**Discussion**

*Mycoplasma pneumoniae* has been mentioned as a possible cause of interstitial fibrosis but only in a few cases has some degree of fibrosis been reported. There are no well-documented cases in which evolution of a *Mycoplasma pneumoniae* pneumonia into diffuse interstitial fibrosis has been described. The mechanisms leading to the pathological changes in diffuse interstitial fibrosis are well known but not specific. The alterations can be the result either of direct interstitial involvement or, as in this case, of a primary intra-alveolar process. The pneumocytes are desquamated into the alveolar lumen. This is followed by exudation and incorporation of the exudate into the alveolar walls. Afterwards, fibroblast proliferation starts between the sixth and ninth day and gives rise to more organised and mature fibrous tissue. The alveolar lining epithelium is changed into type 2 pneumocytes and the bronchiolar lining epithelium grows into the respiratory bronchiole which causes squamous metaplasia.

Numerous different agents are known to cause diffuse interstitial fibrosis. It may follow radiation therapy, oxygen toxicity, anti-neoplastic drugs, paraquat poisoning, inhalation of organic or mineral dust and toxic fumes. It is also seen as a terminal phase of sarcoidosis, collagen diseases, miscellaneous occupational diseases and other interstitial pneumonias. Infectious diseases have also been implicated including bacterial, viral, fungal and parasitic infections. In our case, there was a significant rise in *M pneumoniae* complement fixation titre from 1/4 to 1/128 and most of the other possible aetiological agents could easily be excluded.

Oxygen toxicity may have been a factor in our
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Fig 4  Alveoli covered by cuboidal pneumocytes. The alveolar lumen is filled with macrophages, polymorph leucocytes, erythrocytes, and giant cells. Masson's trichrome stain, original magnification ×360.

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References


