CASE STUDY: PATIENT WITH ALVEOLAR PROTEINOSIS

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SUMMARY

Alveolar proteinosis is a rare disease of unknown etiology in which the alveoli are filled with lipid-proteinaceous material. The diagnosis is usually made on an open lung biopsy. The main symptoms are chest pain, tiredness, persistent pyrexia and a productive cough with purulent, bloodstained sputum. Exertion dyspnoea, however, is regarded as the most important symptom. Chest X-rays demonstrate a picture similar to severe pulmonary oedema. The lung functions and the blood gases are indicators of the severity of the disease and there is usually a reduction in the vital capacity, SaO_2 and PaO_2.

A case study of a patient with this diagnosis treated at Tygerberg Hospital is reported. He was admitted complaining of the above mentioned symptoms, his lung functions and blood gases were extremely poor and the chest X-rays showed bilateral diffuse opacifications. He had to be ventilated with high percentages of oxygen and a high PEEP to maintain an adequate SaO_2 and PaO_2. The infection was treated with antibiotics and corticosteroids. Because of the presence of a tremendous amount of bronchial secretions, chest physiotherapy was very important. General techniques used were bagging, percussion and shaking in alternative side-lying and were combined with Mistabron:Saline inhalations to help dissolve the proteinaceous material in the alveoli. Over a period of 8 weeks he recovered remarkably, but two months after admission his condition unexpectedly deteriorated and he died three days later.

OPSOMMING

Alveolêre proteïenose is 'n baie rare siekte van onbekende oorsaak waarin die alveoli gevul is met lipied-proteïenagtige materiaal. Die diagnose word gewoonlik met behulp van 'n oop longbiopsie gemaak. Die mees algemene simptome is borskaspyn, moegheid, sweet en 'n produktiewe hoes met purulente, bloedbevlekte sputum. Inspanningsdispnee word as die belangrikste simptoom beskou. Die borskas X-strale stem ooreen met die van ernstige pulmonale edeem. Die longfunksies en die bloedgasse dui die erns van die siekte aan en daar is gewoonlik 'n vermindering van die longvervormbaarheid, SaO_2 en PaO_2.

'n Gevalstudie van 'n pasiënt met dié diagnose wat in Tygerberg Hospitaal behandel is, word hier beskryf. Sy simptome by opname het met die tipiese beeld ooreengestem, die longfunksies en bloedgasse was baie swak en die borskas X-strale het bilaterale diffuse versluierings getoon. Hy het ventilasie met hoë PEEP benodig om 'n aanvaarbare SaO_2 en PaO_2 te handhaaf. Die infeksie is met antibiotika en kortikosteroïede behandel. As gevolg van die groot hoeveelheid brongiale sekresies was borskas fisioterapie baie belangrik. Algemene tegnieke gebruik was manuele hiperinflasie, beklopping en skud in alternatiewe sylê en dit is gekombineer met Mistabron:Saline inhalasies om te help met die oplossing van die proteïenagtige materiaal in die alveoli. Oor 'n tydperk van 8 weke het die pasiënt merkwaardig herstel, maar twee maande na opname het sy toestand egter onverwags verswak en hy is drie dae later oorlede.

INTRODUCTION

Alveolar proteinosis is a very rare disease of unknown etiology in which the alveoli are filled with lipid-proteinaceous material.[1] The disease was first described by Rosen et al in 1958 and the material from the first patient was obtained at lung biopsy in July 1953 at Massachusetts General Hospital.[2] During the 12 year period (1953-1965) only 85 cases (the original histological criteria of Rosen et al have been adhered to in all the recorded cases) have been reported in the literature,[3] giving some indication of the rarity of this disease. To date, no South African cases have been reported in the literature. Tygerberg Hospital (a large academic hospital in Cape Province, South Africa) has treated only 5 cases during the period 1975–1989.[4]

HISTORY

There is usually a history of exposure to dust – especially silica dust.[2] According to Larson and Gordiner (1965) a more universal inhalant is tobacco smoke.[3] This condition is three times more common in men than in women and can affect persons of any age but is uncommon in neonates and infants.[5] In most cases it is difficult (or impossible) to establish the exact time of onset of the pulmonary disease. Almost half of the patients in Rosen's study had premonitory febrile illnesses that were considered to be pneumonia.[2]

DIAGNOSIS

The diagnosis can only be made on a microscopic examination of the sputum, an open lung biopsy or bronchial lavage.[5]

PATHOLOGY

The disease results from an initial type 2 granular pneumocyte hyperplasia which causes excessive production of a phospholipid material combined with protein, similar to surfactant but lacking its surface-tension-reducing properties. This overwhelms the phagocytic potential of the alveolar phagocytes. The result is an accumulation within the alveolar lumen as well as within intra-alveolar macrophages of the phospholipid material which both fills it and destroys it as an effective aerating unit. According to Heppleston et al (1972)[6] there is no evidence to support the view that the alveolar macrophages lack their normal mobility, but Corrin et al (1970)[7] said that once the macrophages become distended with lamellar lipids they round up and their mobility is seriously impaired. Alveolar lipoproteinosis does not result from disordered bronchiolar and bronchial clearance mechanisms. There is also no evidence that it is due to Pneumocystis carinii infections.[6]

Microscopically the respiratory bronchioles and alveolar walls are usually of normal thickness but may be slightly thickened due to a mainly lymphocytic infiltration. The alveoli are lined by flattened epithelial cells which, in more chronic cases, may partially or completely disappear. The lining cells secrete the proteinaceous material which fills the alveoli and some of the respiratory bronchioles. This is the most striking feature of the disorder.[5,7]

SYMPTOMS

The disease may be asymptomatic and only suspected after routine chest X-rays. Other symptoms include complaints of chest

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pain, tiredness, persistent pyrexia and a productive cough with purulent, bloodstained sputum. The most common symptom is one of exertion dyspnoea.[2,5]

CHEST X-RAYS

Chest X-rays show a fine, diffuse, perihilar, radiating, vaguely nodular "butterfly" distribution as also seen in severe pulmonary oedema.[2,5,8,9] The clue to the diagnosis is the inappropriateness of the symptomatology in view of this appearance, When resolution occurs, the lesions seem to disappear, beginning peripherally and progressing towards the hilus. In some cases, however, they become increasingly radiopaque focally, suggesting deposition of fibrous connective tissue. Absence of significant enlargement of the hilar nodes as in the case of sarcoidosis is characteristic of alveolar proteinosis.[2]

LUNG FUNCTIONS

Lung functions and blood gases are the indicators of the severity of the disease. There is a reduction in the vital capacity and compliance and also of the oxygen uptake, which leads to a reduction of the SaO_2 at rest. There is also a reduction of the PaO_2 because of the increased right-to-left shunt.[1,2,3,5] Interpretation of these findings has been generally that of a restrictive type of ventilatory defect with impairment of diffusion and a venous-arterial admixture.[8]

LABORATORY DATA

While there is no evidence of anaemia, there may be a tendency to polycythaemia (high red cell count, raised hemoglobin). Leucocytosis is the result of an infection superimposed on the underlying pathology but varies from normal to as high as
20 000/mm^2.[5,9]

COURSE

In the absence of an infection the prognosis varies and in about 50% of the cases there is a partial or complete spontaneous remission. Interstitial fibrosis may supervene in longstanding cases and cholesterol crystal aggregations are found. The course of the disease is uninfluenced by steroid or antibiotic therapy.

CASE REPORT

A 24 year old man from the Defence Force presented with a 5 month history of dyspnoea, chest pain, sleeplessness, loss of appetite, weight loss and a productive cough with purulent, bloodstained sputum. There was no known exposure to any industrial toxins and no history of lung or cardiovascular disease. Two weeks before admission a country general practitioner diagnosed pneumonia.

On admission in the respiratory intensive care unit at Tygerberg Hospital he had tachypnoea (36/min), tachycardia (130/min), bilateral crackles and was in respiratory failure (PaO_2 = 6,1; $PaCo_2$ = 5,O). The chest X-rays showed bilateral diffuse opacifications. An initial differential diagnosis of interstitial lung disease was made.

COURSE AND MEDICAL TREATMENT

The patient was initially treated on a 40% oxygen CPAP-mask. His blood gases worsened and on the day after admission he was intubated and ventilated with a Servo ventilator (F_1O_2 = 0,6; V_T = 782 ml; T/IVV=15/15; PEEP = 10cm H_2O; with a peak pressure of 50 cm H_2O. He was very restless and had to be sedated and relaxed. An open lung biopsy was performed on the third day and a diagnosis of alveolar proteinosis made. On day 7 a left pneumothorax was diagnosed and an underwater drain inserted. A tracheostomy was performed the following day.

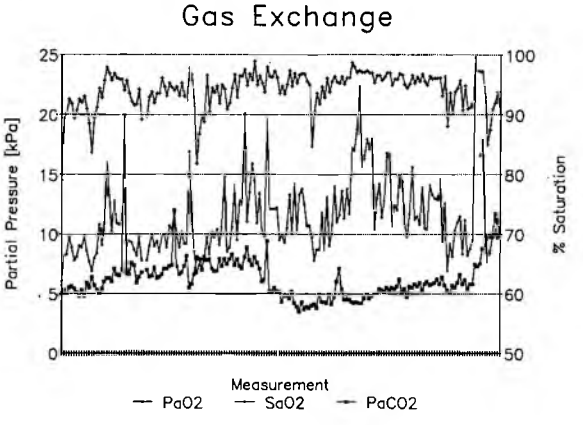
To help dissolve the proteinaceous material in the alveoli, 4% Lichnocaine (7,5 ml):70% Alcohol (7,5 ml) inhalations were begun on day 5 but were stopped 5 days later. Joubert[4] states that Lichnocaine:Alcohol inhalations would have had to be given for at least 3 weeks to be effective and therefore, in this application, cannot be regarded as therapeutic. One week after admission Mistabron (2 ml):Saline (2 ml) inhalation was started in conjunction with chest physiotherapy and the proteinaceous material was successfully dissolved.

Five weeks after admission fever spikes developed and for the first time lung abscesses were suspected. Five days later he developed a left-sided bronchopleural fistula. The bronchopleural fistula began to drain pus twenty days later and an abscess was again suspected. Bronchopneumonia was also now suspected.

The patient had to be ventilated on high percentages of oxygen and a high PEEP for a long time to maintain efficient ventilation and adequate blood gases. However, he improved so much that he could be put on a 30% oxygen Blue Blower two months after admission. A Negus tube could be put in two days later, but this led to increased sputum production. The tracheostomy tube had to be inserted again and the patient reconnected to the CPAP system. The nature of the secretions again suggested a lung abscess.

The chest X-rays on day 67 showed a big abscess in the left lower lobe which probably drained through the lung. Late that evening he became acutely dyspnoeic and cyanotic. A right pneumothorax was diagnosed and underwater drain inserted. He was again ventilated. The next day bilateral bronchopleural fistulas were diagnosed and a large amount of secretions were produced. His condition worsened and the blood gases were poor.

The afternoon of the following he had a cardiopulmonary arrest and resuscitation was not successful.



Fi 1. Variations in gas exchange 28/9/89 to 3/11/89

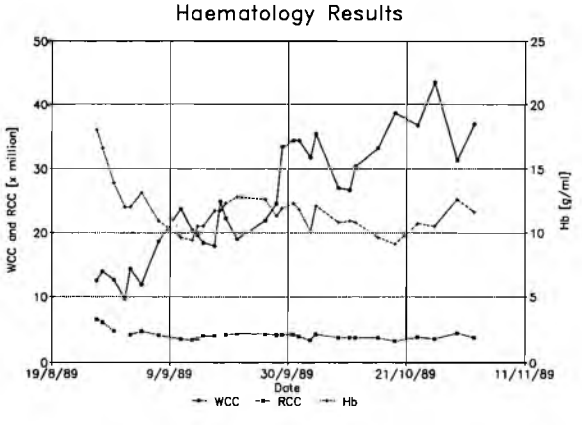


Fig 2. Haematology results

LUNG FUNCTIONS AND GAS EXCHANGE

There was a serious reduction of compliance and adequate

SaO_2 and PaO_2 could only be maintained with fairly high percentages of oxygen (Fig 1.)

MEDICATION

Throughout his hospitalisation the patient had leucocytosis (Fig 2) as a result of multiple opportunistic lung infections. Depending on the organisms cultured, the infection was treated with different antibiotics. Treatment with corticosteroids was begun six weeks post-admission and resulted in dramatic improvement, casting doubt on the diagnosis. It was only after the microscopic post mortem that the diagnosis could finally be confirmed.

PHYSIOTHERAPY

The first day auscultation revealed bilateral inspiratory and expiratory crackles (secretions). The chest physiotherapy consisted of localized breathing and percussion and shaking in alternate side lying. As he was sedated after the intubation, the chest physiotherapy then consisted of bagging, overpressure, and percussion and shaking in alternate side lying. On day 20 the chest X-rays showed bullae especially in the left upper lobe and the bagging was stopped. Following the introduction of Mistabron:Saline inhalations he produced a great amount of brown, purulent sputum. After two weeks auscultation revealed bronchial breathing in the anterior basal segment of the left lower lobe and treatment was concentrated there.

Passive movements of his limbs and stretching of all two-joint muscles were included in the treatment every day.

Sedation was stopped on day 38 and the patient's level of consciousness returned to normal. At that stage he was understandably very weak, but could start with strengthening exercises and 9 days later he was sitting in a chair for the first time. On day 66 his condition deteriorated suddenly and the exercises were stopped.

POST MORTEM

Macroscopic examination:

Lung – Emphysema (mucoid pus). Big abscesses especially in the right upper lobe and the left lower lobe which drained to the pleural cavities.

Heart – Mderate hypertrophy of the left and right ventricles.

Urogenital – Oedematous kidneys

Microscopic examination:

Lungs – Abscess, empyema, alveolar proteinosis, bronchopneumonia, aspiration

DISCUSSION

The main motivation for writing this article was the rareness and uniqueness of the disease.

While there are quite a number of similarities between the textbook description of the disease and the case history of this patient there are also some differences. It was difficult to establish the exact time of the onset of the pulmonary disease, and the first diagnosis was also one of pneumonia.

His initial symptoms of dyspnoea, chest pain, a productive cough and chest X-rays similar to severe pulmonary oedema, fitted the description of alveolar proteinosis. The open lung biopsy confirmed the diagnosis.

The gaseous exchange and lung funcions were poor and during ventilation high percentages of oxygen (60–100%) and high PEEP (as high as 22 cm H_2O) were needed to maintain adequate PaO_2 and SaO_2. A really effective tidal volume could never be reached due to the air-leak through the bronchopleural fistula.

In the case of this patient there was no evidence of polycythaemia, and the leucocytosis (see Fig 2) was the result of severe infection.

Although the corticosteroids brought temporary improvement, they impaired the immunologic response and lowered the body's resistance to infection, and that probably in the end caused his death.

The chest physiotherapy was very important because of the tremendous amount of bronchial secretions. Daily, at both treatments, he produced a copious amount of brown, purulent secretions.

When the sedation was stopped and the strengthening exercises began, he was very co-operative and each session was a rewarding experience.

Towards the end he improved so much that, three days before his death, we started planning a visit to the hospital garden.

The evening of day 65 his condition suddenly took a turn for the worse and he died two days later. Although from the start his prognosis was considered poor, he improved to such an extent that his sudden and unexpected death was a shock.

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