



*"When you can't breathe...
nothing else matters"*TM

Pulmonary Alveolar Proteinosis

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Introduction: This rare diffuse lung disease is characterised by the excess accumulation of surfactant –like material in alveolar spaces or air sacs. Surfactant is normally present in small amounts to reduce surface tension but excess causes disease. Shortness of breath is the main symptom and is usually worsens slowly. There are several distinct clinical presentations which involve both children and adults. Diagnosis is confirmed by the finding excess surfactant in the alveoli on lung biopsy or washing the lung spaces at bronchoscopy. Treatment involves lung washout to remove the excess surfactant material.

Disease: Pulmonary alveolar proteinosis (PAP) is rare affecting approximately 3.7 per million population worldwide with no recognised geographical or racial clustering. The accumulation of the surfactant material in alveolar spaces is believed to be due to either overproduction or, more likely, defective clearance, of surfactant. However, the cause remains unknown. Symptoms include slowly progressive shortness of breath and a dry cough. The clinical course is variable and ranges from spontaneous resolution (in 10-30% of cases) to respiratory failure and death. There are 3 distinct types of PAP.

Congenital/Hereditary PAP: This is a very rare but rapidly progressive form that is usually fatal within the first year of life. It appears to be inherited with one abnormal gene from each parent (autosomal recessive) and manifested in those with two abnormal genes i.e. the parents are not affected. Several genetic mutations have been described.

Secondary PAP: Secondary PAP can occur in association with respiratory infections, exposure to environmental agents or with some immune disorders and blood malignancies.

Acquired PAP: Most adult cases of PAP fall into this category. Although the aetiology is unknown, self made or autoantibodies against a substance called granulocyte-macrophage colony stimulating factor (GM-CSF) have been identified in these patients and this impairs the ability of specific cells in the lungs (alveolar macrophages) to remove surfactant leading to its accumulation in the lungs.

Clinical Presentation: Acquired PAP presents in young adults with slowly progressive shortness of breath and dry cough. It is more common in men (male to female ratio approximately 3:1) and most patients are smokers. The disease remains quiescent or remits spontaneously in some patients but others have progressive disease and require treatment. Most patients respond well to treatment but a small proportion develops respiratory failure ultimately leading to death.

Investigations: Chest x-ray and computerised tomography (CT) scan demonstrate widespread abnormality in the lung (called ground glass opacities) and the CT scan often shows a characteristic appearance with “crazy paving”.

The diagnosis is usually confirmed with fiberoptic bronchoscopy and biopsies or washing of the lungs (lavage) which show characteristic changes.

Treatment: The main treatment is whole lung washing or lavage, a procedure performed under general anaesthesia and which involves washing each lung with large volumes of saline or salt solution to mechanically remove the accumulated surfactant. It is effective but the material often reaccumulates and repeated procedures are then required.

More recently, the finding of autoantibodies against GM-CSF has led to trials of treatment using recombinant GM-CSF made in the laboratory to replace the deficiency of this substance. It is given either subcutaneously or inhaled. Preliminary results indicate a response rate of 50-75%.

References:

Pulmonary Alveolar Proteinosis: State of the Art. Am J Respir Crit Care Med 166: 215-235. 2002.

Inhaled Granulocyte/Macrophage-Colony Stimulating Factor as Therapy for Pulmonary Alveolar Proteinosis. Am J Respir Crit Care Med 181:1345-1354. 2010.

The Molecular Basis of Pulmonary Alveolar Proteinosis. Clin Immunol 135(2): 223-235. 2010

Weblinks:

PAP Foundation (USA): www.papfoundation.org

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Please consult your family doctor or specialist respiratory physician if you have further questions relating to the information contained in this leaflet. For details of patient support groups in Australia please call 1800 654 301.



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