We present a case report of unusual association of silicosis, pulmonary alveolar proteinosis and tuberculosis occurring in a 30 year old stone quarry worker exposed to sand dust since 15 years. Pulmonary alveolar proteinosis (PAP) is an uncommon disease in which there is progressive and inappropriate occupation of the lung alveoli by an excessive amount of unprocessed surfactant. Untill recently the gold standard for diagnosis of PAP was considered to be open lung biopsy followed by histopathological and ultrastructural examination. With the introduction of improved bronchoscopic techniques, bronchoalveolar lavage (BAL) is now employed as a useful diagnostic and therapeutic modality in the management of PAP. The cytological features of BAL fluid in PAP are unique and with supporting clinical and radiological evidences a confident diagnosis of PAP can be given so that the patient can be spared of a more invasive diagnostic procedure. The authors present a case report where a cytological diagnosis of PAP was made possible by routine Papanicolaou stained smears and PAS-D stains. The utility of BAL cytology in the diagnosis of PAP is discussed. The conclusion is that study of the bronchoscopic lavage fluid is a useful diagnostic modality in PAP.

KEYWORDS:
- Pulmonary alveolar proteinosis
- Silicosis
- Tuberculosis
- Bronchoalveolar lavage (BAL)
- Cytological diagnosis
- Open lung biopsy
- CT imaging
- Ground glass attenuation
- Alveolar macrophages

Figure legends
Fig 1
a) PAP stain x 100 showing amorphous granular orange coloured material.
b) & c) PAP stain x 400 showing orange coloured globular masses
d) PAS-D stain x400 showing masses of reddish pink diastase resistant material.

Discussion:
Clinical presentation of progressive dyspnoea and fever along with radiological detection of fluid material in the lung alveoli can occur in different conditions and the fluid content could be pus, blood, necrotic...
tumor, gastric contents or a lipoproteinaceous material as occurs with PAP. Hence it is important to assess the nature of the material collected by laboratory methods so as to ensure the diagnosis and thereby to decide on the management strategy.

The golden yardstick for diagnosis of PAP was previously considered to be open lung biopsy or transbronchial lung biopsy where the lung tissue shows preservation of the alveolar architecture with the alveolar spaces filled by a granular eosinophilic PAS positive material. But with the advent of improved bronchoscopic techniques, bronchoalveolar lavage is shown to have both diagnostic and therapeutic advantages over open lung biopsy. With typical cytopathological findings, supported by radiological and clinical features, BAL specimen cytological examination is sufficient for a confident diagnosis of PAP.

In our case, the grossly milky appearance of the BAL specimen, typical cytopathological features of an amorphous granular material with orange coloured globules with Papanicolaou stain, PAS positivity and diastase resistance, very well supported by the CT findings of bilateral significant central interstitial disease with a crazy paving appearance in a patient with a known history of occupational exposure to dust and a compatible clinical presentation were sufficient to give a conclusive diagnosis of PAP. Our patient although a probable candidate for dustborn lung disease complicated by PAP, the radiological diagnosis was not conclusive of PAP. The "crazy-paving pattern" (resembling the structure of irregularly shaped paving stones) on CT was initially described as pathognomonic sign of alveolar proteinosis. But later, with high-resolution CT imaging, this pattern was described in a number of acute and chronic lung diseases thereby requiring cytopathological or histopathological correlation. In our case the BAL fluid study was very typical of PAP both grossly and microscopically. Hence the alternate differential diagnoses were easily excluded.

PAP is an uncommon disease with a variable clinical course. It may undergo spontaneous resolution, may resolve with repeated whole lung lavages and may remain stable with persistent symptoms or may even progress to respiratory failure despite treatment depending on various host factors. The intra alveolar material getting accumulated in PAP is considered to be surfactant proteins and the key mechanism in the pathogenesis of PAP is the excessive surfactant. Alveolar macrophages in the lungs are considered to play an important role in surfactant homeostasis. The granulocyte macrophage colony stimulating factor (GM-CSF) appears to be the critical regulator of this homeostasis. Auto immune PAP comprises 90% of cases of PAP. Patients affected by autoimmune PAP have circulating neutralizing anti-GM-CSF antibodies. Diagnosis in such cases is increasingly made by bronchial lavage from which estimation of residual GM-CSF activity is feasible. These antibodies cause a reduced localised GM-CSF activity in the lung thereby decreasing the alveolar macrophage surfactant degradation resulting in surfactant accumulation. GM-CSF is a cytokine stimulating the production of alveolar macrophages.

The other important clinical form of the disease is secondary PAP (non-idiopathic) which occurs in association with various conditions like toxic/dust exposure, infections like tuberculosis, pneumocystis carinii pneumonia, nocardiasis, malignancies like leukemia or lymphoma and in immunodeficiency states. In all forms of the disease there is a quantitative and/or qualitative dysfunction of the alveolar macrophages.

Another very important thing to be considered is occupation of the patient. This patient was initially diagnosed as a case of interstitial lung disease from the clinical history and image findings. It is a well known fact that silicosis is the most prevalent of the pneumoconiosis and the incidence of tuberculosis among patients with silicosis is up to 40 times or more higher than in those without silicosis. The co-existence of silicosis and tuberculosis, the so-called Silicoproteinotuberculosis, is a well known clinical entity. In any case of PAP coexisting tuberculosis has to be ruled out. Diagnostic delay on morbidity and mortality of the patient. If the patient had tuberculosis as a superinfection on PAP, the relationship could be termed as temporality. The diagnosis of PAP is based on four main criteria: Clinical presentation, cytopathological features of an amorphous granular material with orange and pinkish granules in the BAL fluid, absence of malignancy and no other cause for the alveolar macrophage dysfunction. 

Conflicts of interest: none declared.

REFERENCES