(45 mg/day) and therapeutic BAL. BAL was performed weekly with 100 to 150 mL of saline instilled through a fiberoptic bronchoscope into a segmental bronchus under local anesthesia. The recovered lavage fluid was initially milky, and the lavage was repeated until the fluid became clear. After 3 series of therapeutic lavages, his radiographic infiltrates have cleared significantly (Fig. 1b). He is now living and well 2 years following our treatment with no evidence of recurrence of the disease.

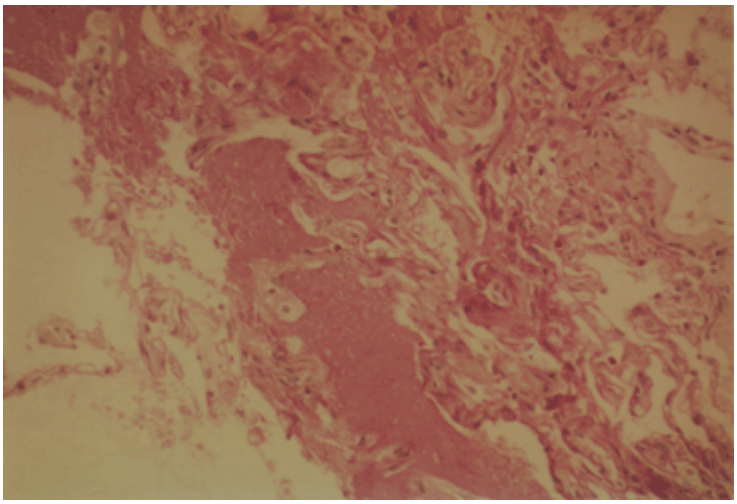

Fig. 2a. Photomicrograph of lung biopsy. Alveolar spaces are filled with dense, periodic acid Schiff (PAS)-positive and proteinaceous material. Alveolar septa are thin throughout the section. PAS stain, × 400.

Discussion

PAP is characterized by the deposition of proteinaceous material in air spaces, originally described in 1958 (Roen et al., 1958). Associated conditions include immunocompromised states, which suggests that malfunction of alveolar macrophages allow for the accumulation of abnormal intra-alveolar material. This material consists of lipid bilayer membranes separated by amorphous proteinaceous material containing phospholipids and proteins similar to surfactant or one of its components. The lung surfactant system is a mixture of phospholipids and protein synthesized and secreted in the alveolar spaces primarily by type II pneumocytes. Its main function is the reduction of surface tension to insure stability of alveolar units. Surfactant is also thought to be involved in mucus transport and to interact with the pulmonary defense system (Luisetti et al., 1987). SP-A is a major hydrophilic (28 to 36 kDa) glycoprotein of pulmonary surfactant and is specific for pulmonary surfactant, synthesized by type II cells and secreted into the alveolar space. An immunohistochemical study using a polyclonal antibody to surfactant-specific apoprotein has demonstrated that SP-A is a useful immunohistochemical marker for the diagnosis of PAP (Honda et al., 1993). In our case, the concentration of SP-A in

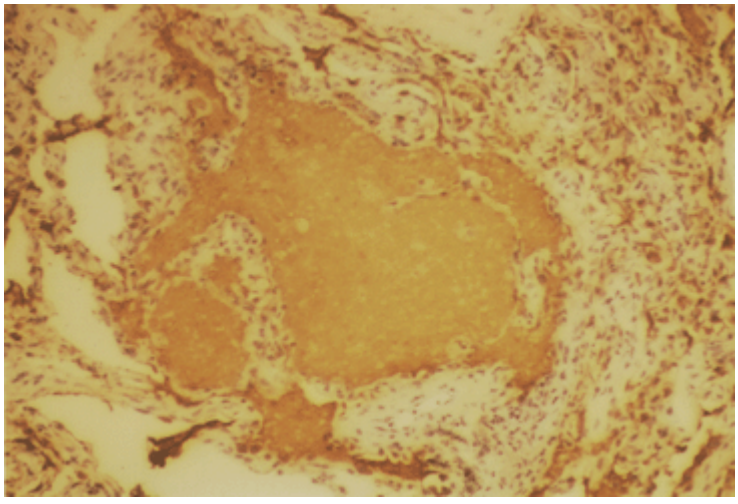

Fig. 2b. Immunostaining for surfactant protein A (SP-A) of lung biopsy specimens shows positivity, × 100.

BAL fluid was significantly higher, confirming the diagnosis of PAP.

The established treatment of choice for PAP is therapeutic whole lung lavage (WLL), performed under general anesthesia, although this method may be associated with severe hypoxia. After such WLL, migration of alveolar macrophages increases to supernormal levels, and subsequent clinical relapse is associated with a decreased level of migration. These results support the conclusion of a previous study that the abnormal alveolar macrophage function in PAP is an acquired defect (Robert et al., 1989).

Problems with WLL include hypoxia, flooding of the contralateral lung, ipsilateral hydrothorax, airway trauma, hypothermia and electrolyte disequilibrium, and thus WLL requires a trained and experienced staff of physicians and nurses (Rodi et al., 1995). So this technique must be reserved for clinically progressive forms of the disease and for experienced hands (Diaz et al., 1984). In our patient, after treatment with oral ambroxol hydrochloride and therapeutic BAL the radiographic infiltrates have cleared.

The main pharmacodynamic effects of ambroxol hydrochloride are surfactant stimulation, mucokinetic activity and some secretagogue activity (Karl, 1987). The lung surfactant system is a mixture of phospholipids and protein synthesized and secreted in the alveolar spaces primarily by type II pneumocytes. So type II pneumocyte stimulation with ambroxol hydrochloride can lead to chemico-physical and functional changes in alveolar macrophages, probably through an increase in surfactant secretion and uptake (Luisetti et al., 1987).

Thus, we propose that oral ambroxol hydrochloride and therapeutic BAL should be the first choice in treating PAP.

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