Pulmonary emphysema in SP-D gene-targeted mice.

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Surfactant protein D (SP-D) is a 43-kDa member of the collectin family of collagenous, lectin-domain-containing proteins. SP-D is expressed primarily in the respiratory epithelium. Targeted deletion of the SP-D gene in mice resulted in pulmonary lipidosis and enlarged airspaces with multiple focal accumulations of lipid-laden macrophages by 6 mon of age. Hypertrophic Type II cells that stained intensely for proSP-C were observed. Surfactant lipids, but not surfactant proteins, were increased in the lungs of SP-D -/- mice. There was no evidence of viral or bacterial infection. In order to further characterize the role of SP-D deficiency in the formation of enlarged airspaces, histologic analysis of the lungs of SP-D -/- mice was performed at approximately 6 wk and 6 mon of age. Computer-assisted morphometry was utilized to further clarify changes in lung structure at 6 wk of age. Three wild type and three SP-D -/- mice at each age were sacrificed by lethal injection of sodium pentobarbital. The lungs were inflation-fixed with 4% paraformaldehyde and immersion-fixed in 4% paraformaldehyde in the cold for an additional 16 hr. Each lobe was weighed and measured along its longest axis then processed into paraffin blocks. Five-?m paraffin sections were cut in series throughout the length of each lobe and stained with hematoxylin and eosin. Immunostaining for SP-B, a Type II cell marker, was performed to determine the number of alveolar Type II cells per unit volume of lung tissue. Cell counts and area measurements of tissue mass and airspace were performed on sections taken at intervals throughout the length of each lobe using computer-assisted image analysis. Standard morphometric measurements were done to determine the overall fractional volume of each compartment as a percentage of total lung volume. Focal accumulation of alveolar macrophages and increased size of airspaces in airspace size were readily apparent at 6 wk and 6 mon of age. These results suggest that SP-D deficiency causes progressive changes in alveolar structure in association with an apparently spontaneous inflammatory lesion consisting of alveolar macrophage infiltrates.