Pulmonary Alveolar Proteinosis

Lung Transplant or Bone Marrow Transplant?

To the Editor:

We read with interest the report by Parker and Novotny (May 1997) regarding the recurrence of pulmonary alveolar proteinosis (PAP) after double lung transplantation. Although the authors acknowledge that the disorder in this case might result from diminished alveolar macrophage function and hypothesize that this might be caused by a primary defect in circulating monocytes, they state that the fundamental cellular alteration has yet to be determined. The molecular defect in a murine model of PAP has been established. It supports the authors’ hypothesis and has a direct bearing on the treatment and outcome of this case.

Mice bearing a homozygous targeted disruption of the granulocyte-macrophage colony-stimulating factor (GM-CSF) gene develop PAP at approximately 1 year of age. An identical phenotype has been observed in mice with a targeted disruption of the common beta chain of the GM-CSF receptor (GMR ‘c’). More recently, defective expression of the GMR ‘c’ gene has been shown in several human patients with PAP, perhaps as a result of germline mutation of the GMR ‘c’ gene. These data suggest that a subgroup of individuals with idiopathic PAP (perhaps including the patient reported by Parker and Novotny) have a deficiency of GM-CSF or its receptor. Bone marrow transplantation can reverse the lung disease in GMR ‘c’ mice, thus indicating that this form of PAP is clearly a disorder of bone marrow-derived monocytes. Therefore, it is not surprising that PAP might recur after lung transplantation in these cases. This case illustrates the need to consider a congenital defect in GM-CSF signaling as a cause of PAP before lung transplantation.

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REFERENCES