Therapeutic efficacy of granulocyte-macrophage colony-stimulating factor in patients with idiopathic acquired alveolar proteinosis


Alveolar proteinosis (AP) is characterized by excessive surfactant accumulation, and most cases are of unknown etiology. Standard therapy for AP is whole-lung lavage, which may not correct the underlying defect. Because the hematopoietic cytokine granulocyte-macrophage colony-stimulating factor (GM-CSF) is required for normal surfactant homeostasis, we evaluated the therapeutic activity of GM-CSF in patients with idiopathic AP. Fourteen patients received 5 microg/kg/d GM-CSF for 6 to 12 wk with serial monitoring of the alveolar-arterial oxygen gradient ([A-a]DO2), diffusing capacity of carbon monoxide, computed tomographic scans, and exercise testing. Patients not responding to 5 microg/kg/d GM-CSF underwent stepwise dose escalation, and responding patients were retreated at disease recurrence. Stored pretreatment sera were assayed for GM-CSF-neutralizing autoantibodies. According to prospective criteria, five of 14 patients responded to 5 microg/kg/d GM-CSF, and one of four patients responded after dose escalation (20 microg/kg/d). The overall response rate was 43% (mean improvement in [A-a]DO2 = 23.2 mm Hg). Responses lasted a median of 39 wk, and were reproducible with retreatment. GM-CSF was well-tolerated, with no late toxicity seen. The only treatment-related factor predictive of response was GM-CSF-induced eosinophilia (p = 0.01). Each of 12 patients tested had GM-CSF-neutralizing autoantibodies present in pretreatment serum. We conclude that GM-CSF has therapeutic activity in idiopathic AP, providing a potential alternative to whole-lung lavage.