

Evidence for oxidative stress in bronchiolitis obliterans syndrome after lung and heart-lung transplantation. The Munich Lung Transplant Group.

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Bronchiolitis obliterans syndrome (BOS) is the most serious long-term sequel of lung or heart-lung transplantation (H/LTX). Neutrophilia in the lower respiratory tract is a prominent feature of BOS. Because polymorphonuclear leukocytes (PMN) are capable of releasing large quantities of reactive oxygen species, we measured indicators of oxidative stress and glutathione levels representing antioxidant defense in H/LTX patients (HLTX, n=6; double-LTX, n=7; single-LTX, n=9). We analyzed 19 bronchoalveolar lavage (BAL) samples from 13 non-BOS patients (nine female, four male: age 39+/-4 years) and 17 BAL samples from nine BOS patients (five female, four male: age 33+/-2 years). PMN were the predominant BAL cell population in BOS (61.7+/-7.8% vs. 12.3+/-3.4%, P<0.001). Myeloperoxidase activity in the epithelial lining fluid and oxidized methionine residues in BAL-derived proteins were elevated in BOS (8.6+/-1.6 U/ml vs. 2.2+/-0.6 U/ml, P<0.01; and 12.6+/-1.1% vs. 7.7+/-0.8%, P<0.001, respectively). In addition, the concentration of reduced glutathione in epithelial lining fluid was decreased in BOS (162.6+/-20.1 microM vs. 345.8+/-57.1 microM, P<0.01), whereas the proportion of oxidized glutathione was increased (13.9+/-2.00% vs. 6.7+/-1.2%, P<0.001). PMN, myeloperoxidase, and oxidized methionine residues were inversely correlated, whereas reduced glutathione was positively correlated with forced expiratory volume in 1 sec (P<0.05 to P<0.001). We conclude that excessive oxidative stress and a lack of glutathione are associated with BOS after H/LTX and may play relevant roles in the development of this disorder.

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