Alleviating Sulfur Mustard-Induced Oxidative Stress by Anti-TNFα Antibody Treatment in Rat Lung

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Exposure to Sulfur Mustard (SM), a blistering chemical warfare agent, is associated with acute oxidative stress in the lung. Tumor necrosis factor (TNF)α, a pro-inflammatory cytokine, plays an important role in the pathogenic response to SM inhalation. In this study, we examined the effect of anti-TNFα antibody treatment on SM-induced oxidative stress in rat lung. Spontaneously breathing male Wistar rats were anesthetized, intratracheally intubated and exposed to 0.4 mg/kg SM by vapor inhalation. After 15 minutes of SM exposure, a subset of these rats was treated with anti-TNFα antibody (15 mg/kg, i.v., 1x). Animals were euthanized 3 days after exposure and lung tissue was fixed and excised. Expression of oxidative stress markers including heme oxygenase (HO)-1 and Ym-1 was analyzed using immunohistochemistry and the numbers of positively stained macrophages quantified. SM exposure resulted in significant increases in the numbers of HO-1+macrophages, as compared to air exposed controls. Similarly, the numbers of YM-1+ macrophages also increased following SM exposure. Treatment of rats with anti-TNFα antibody reduced the numbers of HO-1+ and Ym-1+ alveolar macrophages. These findings suggest that blocking TNFα is an effective approach to control vesicant-induced lung injury. Supported by NIH Grants U54AR055073, R01ES004738, P30ES005022 and R25ES020721 and ORED.