Pulmonary Oxidative Stress, Inflammation, and Fibrosis Induced by Single Wall Carbon Nanotubes

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Society is currently amidst a revolutionary development of remarkable new technologies based on novel applications of nanomaterials. From drug delivery tools and micro-circuitry elements to microcomputer networks and super-durable composite materials – this is just an illustration of the unprecendentedly broad range of applications and approaches using nanomaterials. One of the most interesting examples of nanomaterials is carbon nanotubes (SWCNT), new members of carbon allotropes similar to fullerenes and graphite. Previously, we reported that exposure of human bronchial epithelial cells to SWCNT induced oxidative stress, depletion of antioxidants, morphological changes, cytotoxicity, and apoptosis. In the current study, we investigated pulmonary toxicity of SWCNT after pharyngeal aspiration by C57BL/6 mice. Administration of SWCNT to C57BL/6 mice resulted in a dose-dependent augmentation of bio-markers of inflammation and oxidative stress indices quantified by cell counts, total protein, lactate dehydrogenase (LDH) and □-glutamyltranspeptidase (GGT) activities, reduced level of GSH, and accumulation of lipid peroxidation products in bronchoalveolar lavage (BAL) fluids and lungs. Markers of pulmonary cytotoxicity were associated with the development of inflammation, collagen accumulation, and pulmonary fibrosis. Dense aggregated forms of SWCNT were associated with the formation of granulomatous pneumonias that involve typical neutrophil/macrophage sequential shift. Dispersed SWCNT structures were likely inducers of (epithelial) cell damage and death, and robust release of fibrogenic factors via pathways that are not associated with their effective phagocytosis. TGF-□ was maximally increased in BAL fluid of mice 7 days after CNT exposure and correlated with morphometric evidence of collagen formation as well as pulmonary function changes. Mice exposed to an equal mass of ultrafine carbon black or fine crystalline silica exhibited less PMN recruitment and cytotoxicity than mice receiving SWCNT. In conclusion, our data suggest that pharyngeal aspiration of SWCNT elicited unusual pulmonary effects in C57BL/6 mice that combined a robust acute inflammatory reaction with a very early onset of a fibrogenic response and the formation of granulomas. The latter were mainly associated with epitheliod macrophages surrounding dense micrometer scale SWCNT aggregates while the former were apparently associated with more dispersed SWCNT structures. The SWCNT pulmonary response also included functional respiratory deficiencies and decreased bacterial clearance.

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