Radiation damage to the lung: is fibrosis an independent process or consequently to early pneumonitis?

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A review of the literature shows that late lung fibrosis is always associated with an initial pneumonitis reaction. This reaction may appear to resolve prior to the onset of late fibrosis and/or represent a continuum, leading to the suggestion that late fibrosis is a consequence of the initial inflammatory reaction. In a novel series of experiments, the lungs of rats were locally irradiated with single doses of radiation of differing quality; x-rays versus thermal neutrons (mixed beam irradiation, predominantly from the products of neutron capture by hydrogen and nitrogen), and different dose distributions produced by administering a boron-10 capture agent,p-boronophenylalanine (BPA), to the thermal neutron exposure; approximately 50% of the total physical dose coming from the short range products, alpha-particles and lithium-ions, of the ^{10}B capture reaction. Damage was assessed by lethality, serial measurements of breathing rate and terminal histology after 180 days. Animal deaths, related to lung damage, were only seen in the higher doses selected for use, $\geq$11.8 Gy, 9.7 Gy and $\geq$9.5 Gy for x-rays, thermal neutrons and neutrons plus BPA, respectively. Nearly all deaths occurred in the first 100 days after irradiation, the period of the pneumonitic reaction. The pneuonitic reaction (approximately 20 -100 days) was reflected in a significant increase in the breathing rate (defined as a 20% increase, relative to controls). This increase was most marked after x- and thermal neutron irradiation; the incidence in responders in these groups tended to decline around day 100, only to increase again at later times. In animals receiving thermal neutron irradiation in the presence of BPA (doses of $\leq$8.8 Gy), a higher incidence of late compared with early responders was seen. This was reflected in the dose-effect relationships for the early ($<$ 100 days) versus late ($>$ 100 days) responders for a significant increase in breathing rate. In the $<$ 100 day period the ED_{50} ($\pm$SE) for the thermal neutron/thermal neutron plus BPA were comparable at 9.2 $\pm$ 0.6 Gy and 8.8 $\mp$ 0.6 Gy, respectively. For the $>$ 100 day period the ED_{50} ($\pm$SE) for the neutron plus BPA group of 6.7 $\pm$ 0.4 Gy was significantly lower than for thermal neutrons alone; 9.6 $\pm$ 0.6 Gy. The animals receiving BNCT type irradiation also showed more marked changes on terminal histology, reflected in a lower ED50 for a histological score. Thus, given appropriate exposure conditions, late radiation changes in lung can develop independently of early pneumonitis.

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