Surgical Injury Modifies the Tumor Immune Response to Photodynamic Therapy

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The killing of tumor cells by photodynamic therapy (PDT) in cancer treatment relies upon two factors: the direct killing of cells by oxidative damage and the indirect killing by damaged tumor vasculature and/or the induction of an anti-tumoral immune response. The cellular and vascular damage induces acute inflammation within the tumor site immediately after PDT. This is characterized by an influx of neutrophils and other immune cells responding to danger signals released by damaged tumor cells. Neutrophils are a vital aspect of the PDT response, as they facilitate the transition from innate immunity to adaptive responses. In treating mesothelioma, however, surgery is often done prior to photodynamic therapy, resulting in residual injured tumor tissue before light treatment. Our research suggests that this injured tumor tissue initiates early acute inflammation throughout the tumor site, which is either sustained or enhanced after the completion of PDT. Although inflammation is necessary for anti-tumoral immunity, chronic inflammation can be counteractive. In some of our recent studies, mice with tumors surgically insulted prior to PDT had a worse prognosis than those mice with tumors treated with photodynamic therapy alone. This study focused upon the immunomodulatory effects of surgical insult and photodynamic therapy. We completed these studies through non-invasive, chemiluminescent imaging for neutrophil activity with luminol within the treatment site. In addition, we determined treatment-dependent differences in the percentage of Gr1+ myeloid-derived cells within the tumor and tumor-draining lymph node tissue via immunohistochemistry of frozen sections. Together, our research demonstrates that insults sustained during surgery and PDT generate a potent inflammatory response that influences long-term treatment outcome.