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Pathologic Changes After Photodynamic Therapy for Basal Cell Carcinoma and Bowen Disease

A Histologic and Immunohistochemical Investigation

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Objective To investigate the in vivo reactions and the mechanisms of cell death after photodynamic therapy (PDT) for cutaneous carcinomas. Photodynamic therapy is a new treatment modality for nonmelanoma skin cancers. Its effects on target tissue have been well investigated in vitro, where apoptosis appears to be the main effector mechanism, but its effects remain undefined in vivo.

Design Skin biopsy specimens were obtained sequentially after PDT for basal cell carcinoma and in situ squamous cell carcinoma (Bowen disease). Evidence from routine histologic evaluation was compared with a panel of apoptosis-related (TUNEL [terminal deoxynucleotidyl transferase-mediated biotin–deoxyuridine triphosphate nick-end labeling], caspase-3, and Bcl-2) and inflammatory (CD4, CD8, CD20, CD68, and CD56) markers. We used electron microscopy to evaluate cell damage at the ultrastructural level.

Main Outcome Measures Evidence of the mechanisms of tumor cell damage after PDT, detection of histologic and/or immunohistochemical signs of apoptosis, and time course of the tumor destruction and inflammatory reaction.

Results Early epidermal damage and an acute dermal inflammatory response were detected 15 minutes after PDT. In basal cell carcinoma, nodule damage progressed from scant apoptotic cells seen at the dermal-epithelial junction to massive destruction seen after 1 and 2 days. The periphery of the basaloid nodules consistently showed earlier and predominant damage, as demonstrated by the perfect coincidence of histologic and immunohistochemical evidence with apoptotic markers (TUNEL and caspase-3 staining). Fibrosis and lentigolike changes were seen in late biopsy specimens.

Conclusions This study defines the time course and characteristics of the skin tumor response to PDT. Taken together, our observations suggest that direct damage to cancer cells is the main effector mechanism leading to PDT response. The involvement of apoptosis is demonstrated by the simultaneous appearance of histologic, immunohistochemical, and ultrastructural markers that occur in the early phases of the cutaneous reaction to PDT. These observations could help to develop future refinements of the PDT technique.

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