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Relationship between chronic inflammation and neoplastic progression in prostate tissue: A closer link

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Chronic inflammation has frequently been identified in prostate biopsies, radical prostatectomy specimens and tissue resected for treatment of benign prostatic hyperplasia, although its relationship with prostate cancer has not been established. In the peripheral zone of the prostate, sometimes adjacent to foci of high-grade PIN and cancer, certain morphologic changes are often identified, which may represent active and terminal phases of chronic inflammation. These changes are designated, respectively, proliferative inflammatory atrophy (PIA) and post atrophic hyperplasia (PAH), and their morphology is well documented in pathologic literature. We hypothesize that changes in the stromal microenvironment, characterized by infiltration of immune cells, with generation of reactive oxygen and nitrogen species, can induce oxidative stress in the surrounding proliferating epithelium and cause permanent genomic alterations. In the present study, we focused on several key proteins involved in the inflammatory process, COX2 and iNOS, cell survival, Bcl2 and GSTPπ, and evaluated immunohistochemical expression of alpha-methylacyl coenzyme A racemase (AMACR) and basal cell-specific markers 34βE12 and/or p63 to evaluate possible neoplastic alterations in epithelial cells in an inflammatory environment. We evaluated 16 prostate core needle biopsy specimens that exhibited the presence of chronic inflammation as well as PIA and PAH lesions. Immunohistochemical staining for P63/34βE12/AMACR cocktail, iNOS, COX2, GSTπ, and Bcl2was performed in each set of biopsies. The integrity of the basal layer was maintained in the area of chronic inflammation with high expression of p63 in 72% of these cells. Approximately 68% of luminal cells expressed high to moderate levels of iNOS and COX-2, whereas 55% of these cells express modest levels of GSTP1 and Bcl2. Interestingly, prostatic glands near the areas of chronic inflammation in the PIA lesions exhibit high AMACR expression in luminal cells and weak to patchy p63 expression in basal cells, which was associated with increased expression of the inflammatory markers COX2 and iNOS, as well as loss in pro-survival signal GSTP1 and Bcl2 in the adjacent luminal cells. These neoplastic alterations were observed in 6/16 (38%) of the needle biopsy specimens. Our findings suggest that basal cells undergo alterations in a setting of chronic inflammation. This is important because basal cells are considered to be progenitor cells capable of differentiating into secretory luminal cells, but under the influence of chronic inflammation, they may instead transform into the neoplastic cells that characterize high grade prostatic intraepithelial neoplasia and prostatic adenocarcinoma.