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TREATMENT OF EXPERIMENTAL AUTOIMMUNE PROSTATITIS BY BXL-628, A VITAMIN D RECEPTOR AGONIST

Hypothesis / aims of study

Chronic non-bacterial prostatitis or chronic pelvic pain syndrome (CPPS, NIH category III) is a highly prevalent syndrome of suspected autoimmune origin, characterized by chronic pelvic pain with varying degrees of urogenital symptoms. Based on the marked inhibitory activity of the vitamin D receptor (VDR) agonist BXL-628 on basal and growth factor-induced proliferation of human prostate cells, and on its potent anti-inflammatory properties in different models, we have tested its capacity to treat experimental autoimmune prostatitis (EAP).

Study design, materials and methods

EAP was induced in non obese diabetic (NOD) mice, a strain genetically prone to develop different autoimmune diseases, by injection of mouse prostate homogenate in complete Freund's adjuvant (CFA). BXL-628 was administered orally 5 d/week at 100 g/Kg from day 14 to 28 post immunization.

Results

Administration of BXL-628, at non hypercalcemic doses, for two weeks in already established EAP is able to inhibit significantly the intra-prostatic cell infiltrate, leading to a profound reduction in the number of infiltrating leukocytes, in particular $CD4^+$ and $CD8^+$ T cells, B cells, macrophages and dendritic cells. Immunohistological analysis demonstrates decreased cell proliferation, assessed by reduced expression of the proliferation marker Ki 67, and increased apoptosis, shown by increased staining revealed by the TUNEL assay, in prostates from BXL-628-treated mice. In addition, decreased production of the pro-inflammatory cytokines IFN- and IL-17 is observed in T cells stimulated by TCR ligation of prostate-draining lymph nodes from BXL-628-treated NOD mice.

Interpretation of results

The results indicate that BXL-628, at non hypercalcemic doses, is able to interfere with key pathogenic events in already established experimental autoimmune prostatitis.

Concluding message

These data support the autoimmune pathogenesis of chronic non-bacterial prostatitis, and indicate that treatment with the VDR agonist BXL-628 may prove clinically beneficial in this syndrome.