(248) ANALYSIS OF BIOMARKERS (MMP-9, TIMP-1, KI-67 AND TYPE IV COLLAGEN) IN THE DIAGNOSIS OF PROSTATE DISEASES
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Introduction: The combination of inflammatory, benign and malignant processes in the prostate reduces the sensitivity, specificity and diagnostic accuracy of modern examination methods. The development of immunohistochemical methods (IHC) promotes the search for molecular markers that are diagnostically significant in various processes in the prostate. This will improve the detection of malignant neoplasms and reduce the number of "unnecessary" prostate biopsies.

Objective: to study in biopsies of patients with various prostate diseases the relationship of type 9 metalloproteinase (MMP-9) and its inhibitor (TIMP-1), the role of the Ki-67 protein proliferation level and the diagnostic value of the type IV collagen distribution indicator.

Methods: The study included 263 patients. They were divided into 4 groups: chronic prostatitis - 21 patients (mean age 65.2 ± 0.7 years), benign prostatic hyperplasia (BPH) - 65 patients (69.3 ± 1.1 years), BPH + prostatic intraepithelial neoplasia (PIN) - 59 patients (68.9 ± 0.9 years), prostate adenocarcinoma (PC) - 118 patients (68.2 ± 0.9 years). IHC was used to analyze type 9 metalloproteinase (MMP-9) and its inhibitor (TIMP-1), the role of the Ki-67 protein proliferation level and the diagnostic value of the type IV collagen distribution indicator.

Results: BPH is characterized by high production of MMP-9 (intensity 3 points), lack of proliferative activity of the secretory cell layer (Ki-67 less than 3.2 ± 0.61%) and degradation of collagen IV of the basement membranes, which associated with a compensatory increase in the activity of the inhibitor of matrix metalloproteinases TIMP-1 (intensity 3 points). In prostate cancer, as neoplastic changes increase, the production of the Ki-67 protein significantly increases, reflecting the proliferative activity of the secretory cell layer (from 5.3 ± 1.1% to 17.2 ± 9.4%). With an increase in the Gleason number over the 3rd grade, collagen fibers around the tumor cells completely disappear. The production of MMP-9 type in adenocarcinomas is significantly reduced and the destruction of collagen IV of the basement membrane of glandular structures and stroma occurs due to a progressive (up to an intensity of 0.8 ± 0.4 points as anaplastic changes increase) decrease in the production of the inhibitor of matrix metalloproteinases TIMP-1 (p≤0.05). High production of MMP-9 in BPH is blocked by a high content of the TIMP-1 inhibitor. In adenocarcinomas, the production of MMP-9 is significantly reduced, but this protease destroys collagen IV of the basement membrane of glandular structures due to the absence or weak production of TIMP-1, which blocks the proteolytic effect of this enzyme on connective tissue collagen. The low production of the TIMP-1 inhibitor in adenocarcinomas can also explain the invasive properties of these tumors.

Conclusions: Comprehensive analysis of biomarkers in IHC can improve the diagnosis of prostate cancer and reduce the number of "unnecessary" biopsies.

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