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Review article

Prostate inflammation: A brief review☆

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ABSTRACT

Prostate inflammation, also known as prostatitis, is defined as a pathological inflammatory change in prostate tissue. Based on clinical and laboratory findings, it can be categorized into different groups. Recent prostate inflammation researches are focusing on the immunological events within prostate. Despite the etiology of inflammation, prostate may go through similar serous and cellular reactions to defend itself from all types of danger signals. These reactions may have further interaction with different prostate pathologies, such as benign prostate hyperplasia or prostate cancer. Potential treatment options may be derived from understanding of inflammatory mechanism.

Prostate is vulnerable to inflammation in urinary tract, because there are waste stimuli in urine, possible microbes colonization, and potential urinary tract stones with related mechanical obstruction. These all contribute to the potential inflammation of prostate. Inflammation is an immune response to stimuli. It begins with activation of the innate immune system by infectious or noninfectious (sterile) stimuli, and inflammasomes act as sensors and effectors of these stimuli. We will discuss recent findings on the cause of inflammation, immune system responses, and possible results when prostate is inflamed.

1. What is inflammation

Inflammation refers to the immune response against certain events, while infection often refers to pathogen invasion. Inflammation occurs when the body attempts to protect itself. It is a process involved in removing harmful stimuli, including pathogens, irritants, or damaged cells, and beginning the healing process.

Inflammation does not equal infection, because infection is only one of the events that causes of inflammation. Infection can be caused by bacteria, virus or fungus, but also other stimuli. Inflammation is the human body's response to it.

When something harmful or irritating affects a part of our body, there is a biological response to try to remove it. The signs and symptoms of inflammation, specifically acute inflammation, show that the body is trying to heal itself. While chronic inflammation may demonstrate some failed attempts to dispel harmful stimuli, immune system is generally designed for protection.

1.1. Classification

The classification still widely used today for prostatitis is the National Institutes of Health (NIH) consensus. It has categorized prostatitis into four distinct types: I. acute bacterial, II. Chronic bacterial, III. Inflammatory/noninflammatory chronic, and IV. asymptomatic inflammatory.[35]

Although bacterial prostatitis is a common diagnosis, well documented infections of the prostate are uncommon. One study showed that only 8% patients with chronic prostatitis had positive specific PCR assays. Many patients with chronic prostatitis have a wide variety of bacterial DNA-encoding sequences despite extensive negative microbiological investigations.[36]

Acute and chronic inflammatory infiltrates can both be found in the prostate.[44] They may occur silently or come with prominent symptoms. Previous studies showed that in prostate biopsies done

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for suspected prostate cancer, between 35% and 100% of them had some histological evidence of inflammation.[18,52,62,63] This inflammation not only is present in prostate biopsies, it is also found in radical prostatectomy specimens and tissue resected for benign prostatic hyperplasia treatment. Most factors associated with inflammatory changes in the prostate undergoing biopsy remain undetermined. And the clinical significance of asymptomatic prostatic inflammation in negative biopsies for prostate cancer is still not completely known.[43]

1.2. Cause of prostate inflammation: infectious stimuli

Bacterial prostatitis is most often caused by uropathogens, mainly Gram-negative bacilli. But Gram-positive and atypical microorganisms have also been identified as causative organisms of chronic prostatitis. *Chlamydia trachomatis* and *Trichomonas vaginalis* are among common pathogens, making chronic prostatitis a sexually transmitted disease.[72]

1.3. Cause of prostate inflammation: noninfectious stimuli

Prostatic inflammation is of multiple etiologies.[6] Urine refluxed freely into the prostatic ducts[32] can provide a route for bacterial colonization.[36,75] Other potential factors include dietary components, changes in serum testosterone and estrogen levels, autoimmunity, and reflux of noxious chemicals in the urine.[15] Besides, prostate inflammation can be triggered by metabolic alterations including metabolic syndrome and dyslipidemia.[10,14,73]

Recent studies showed that smoking and high-fat diet may be related with prostate inflammation. In univariable analysis in Reduction by Dutasteride of Prostate Cancer Events study, smoking is associated with prostate chronic inflammation. Current smokers were more likely to have acute inflammation and chronic inflammation in the baseline biopsy.[44] On the other hand, high-fat diet may induce oxidative stress and inflammation in the prostate gland by driving the NADPH (Nicotinamide adenine dinucleotide phosphate) oxidase system and generating reactive oxygen species.[65] High-fat diet also causes a significant increase in pro-inflammatory cytokines through activation of Signal Transducer and Activator of Transcription (STAT)-3 and Nuclear Factor-kappa B (NF-kappaB) pathway. Both these pathways involved in proliferation, survival, angiogenesis, invasion and inflammation in prostate.

1.4. Serous component of prostate inflammation

Besides the cytokines directly produced by cellular counterparts of prostate inflammation, the innate immunity have special types of activation in prostate inflammation (Fig. 1). There are two types of patterns of the stimuli that will activate the innate immune system, one is PAMPs (pathogen-associated molecular patterns) and the

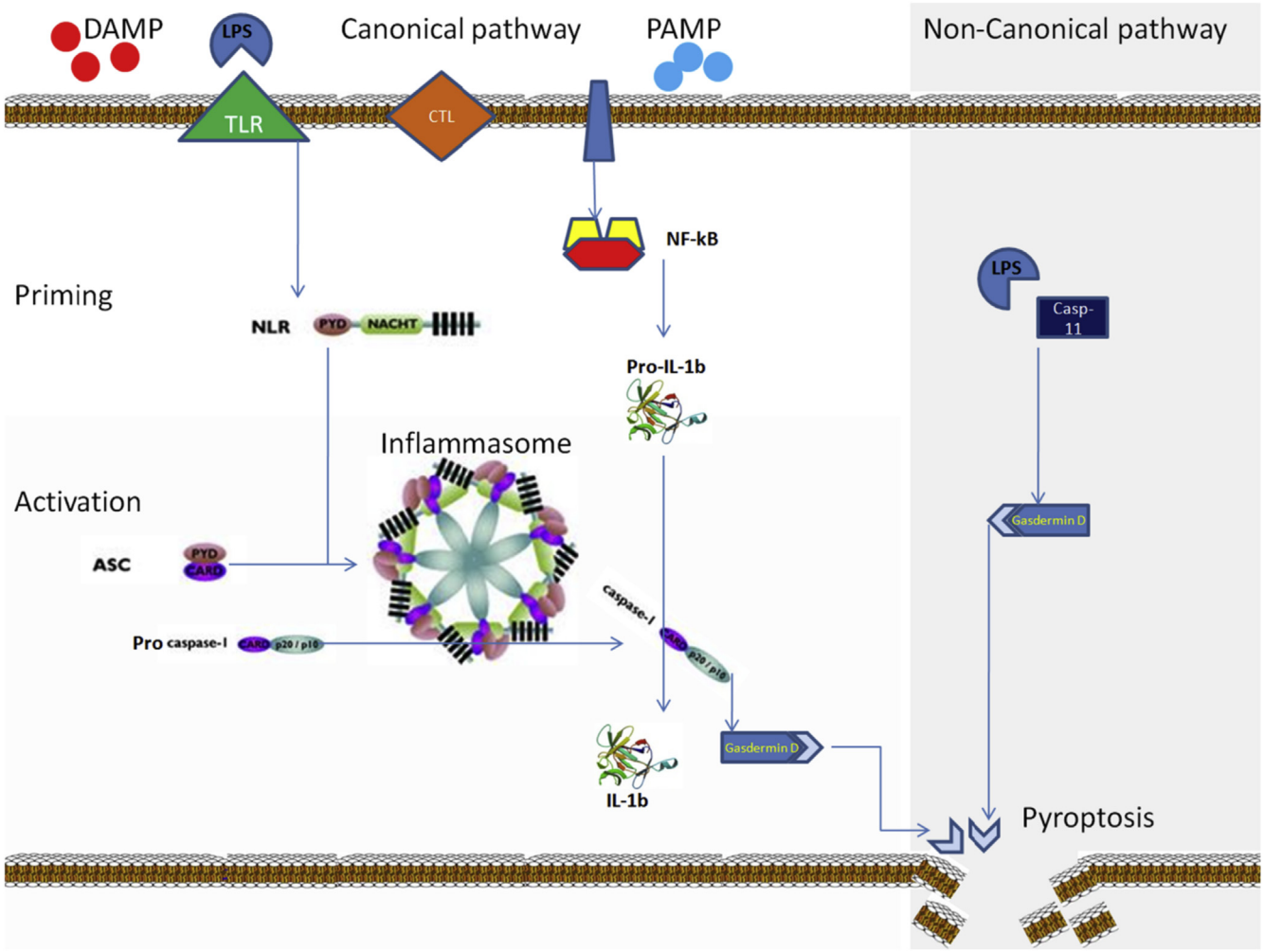

Fig. 1. Serous components of prostate inflammation.