

Mechanisms of chronic urologic pain

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Cite as: *Can Urol Assoc J* 2018;12(6Suppl3):S147-8. <http://dx.doi.org/10.5489/auaj.5320>

Introduction

Chronic urologic pain can refer to a host of conditions ranging from chronic pelvic pain syndromes (chronic prostatitis/chronic pelvic pain syndrome [CP/CPPS] or interstitial cystitis/bladder pain syndrome [IC/BPS]) to chronic scrotal pain. These syndromes are largely characterized by persistent pain affecting different urological systems for at least six weeks to three months in duration, significantly affecting the daily activities of the patient and prompting them to seek medical attention. These conditions present commonly to urologists and can be quite challenging and frustrating to manage. Although these pain conditions can be caused by varying etiologies, oftentimes their natural history remains unknown. The purpose of this article is to serve as a general overview of the different types of urologic pain, potential causes, and putative mechanisms that contribute to chronicity in order to better inform these patients and help guide management. The prevalence, evaluation, and management of these conditions will be discussed in the other articles in this series.

Practice tips

Tip 1: Is the pain neuropathic, nociceptive, or both?

Genitourinary pain in general can be neuropathic, nociceptive, or have elements of both. Neuropathic pain refers to some injury to peripheral nerves either by trauma, infection, or surgery. The resulting pain occurs in the peripheral distribution of that nerve. In some instances, though the original stimulus may be gone, residual injury to the nerve may cause autonomous generation of a pain signal to non-painful stimuli (allodynia) or exaggerated response to pain (hyperalgesia). Nociceptive pain refers to direct activation of nociceptors (pain receptors) in nerve endings within tissues from noxious stimuli, such as tissue damage or inflammation.

Tip 2: How to differentiate neuropathic from nociceptive pain

In neuropathic pain, sensory changes are confined to the distribution of a specific peripheral nerve, with a temporal link between lesion or disease causing the pain. There may be associated sensory changes on clinical examination, such as loss of sensitivity to pinprick or cutaneous hyperalgesia or allodynia. Neuropathic pain has been described as tingling, burning, or shooting pain with hypersensitivity. Patients may endorse not being able to wear tight clothing, or have limited activity levels due to this pain.

With nociceptive pain, there generally is a specified distribution of pain localizing to an area of tissue damage/inflammation, which resolves as the inciting factor is removed. Chemicals released from damaged tissues may include prostaglandins and bradykinins. Nociceptive pain is usually described as sharp, throbbing, or aching pain. Nociceptive and neuropathic pain can coexist.

Tip 3: The causes of chronic urologic pain

Various theories exist on the potential causes of chronic urologic pain. These include infection, anatomic abnormalities, voiding dysfunction, immunologic alterations, endocrine, neurological, musculoskeletal, and psychological associations. What is clear is that no single postulated mechanism is responsible for all presentations of urologic pain. In fact, many patients may have a combination of etiologies that contribute to their symptoms. Any pain persisting after three months is usually classified as chronic.

Tip 4: Establishment of chronicity

What causes the development of chronicity from an acute pain process? This is still unclear. However, some studies have shown that factors such as genetic susceptibility (certain genetic polymorphisms may have altered sensitivity to pain), preceding pain conditions (i.e., fibromyalgia), psychosocial factors (expectation of pain, social environment, work, levels of physical activity), and patient age may play contributing roles.

Tip 5: There are numerous pathways involved that may perpetuate the pain

It is postulated that numerous pathways may lead to chronic pain, including inflammatory, musculoskeletal, neurological, and endocrine pathways. Long duration of pain stimuli may ultimately modulate the peripheral nervous system, leading to sensitization of pain receptors. Nerves that regenerate following injury may have anomalous connections, leading to inappropriate propagation of pain signals proximally, further leading to cross-talk and the perception of non-painful stimuli as painful.

Tip 6: The central nervous system plays a role in the modulation of the pain process

Once the pain signal reaches the central nervous system, psychosocial factors have a significant effect on the perception of pain. Studies have shown that factors such as social supports, personal expectations of pain, economic factors, work, activity level, and anxiety level can modulate the propagation of pain. Patients may catastrophize, undergoing negative pain-related thoughts. Patients who catastrophize have poorer relationships with social supports and tend to feel helpless. This can negatively impact the therapeutic relationship with the treating physician.

Tip 7: Central sensitization or cross-talk may occur

As chronicity develops, it is important to know that the pattern of pain can evolve. There may be central nervous system-mediated cross-talk, in which pain can also be referred to other areas. For example, scrotal pain may switch laterality or become bilateral. CP/CPSP patients may develop concomitant scrotal pain. There may also be visceral cross-sensitization, where transmission of a noxious stimulus may be transferred from one organ system to a nearby structure, causing functional changes in this other system. Though the

exact mechanisms are not well-known, some theories suggest this may be through the cross-sensitization of the dorsal root ganglion neuron. Phenotypic progression has been reported, in which women with IC/BPS develop irritable bowel syndrome.

Tip 8: Patients' pain phenotypes are expressed differently

One helpful way to classify patients with urologic pain conditions is through the UPOINT system. This classification was initially developed for patients with CPPS (NIH category III prostatitis), although it may also be applicable to urologic pain in general. Through the lens of this classification system, urologic pain is classified into six expressed phenotypes or domains: urinary, psychosocial, organ-specific, infection, neurologic/systemic, and tenderness of skeletal muscles. Targeted multimodal treatment approaches can be suggested based on the type of pain and associated symptoms that the patient endorses.

Competing interests: Dr. Jarvi has participated in clinical trials supported by Allergan. Dr. Wu reports no competing personal or financial conflicts related to this work.

This paper has been peer reviewed.

Recommended reading

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