Diagnosis and Management of Neuropathic Itch

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KEYWORDS

• Itch • Pruritus • Neuropathic • Diagnosis • Treatment • Peripheral nerves

KEY POINTS

- Neuropathic pruritus is any injury or dysfunction along the afferent itch pathway that results in a sensation to scratch.
- Numerous neuropathic itch syndromes, affecting the peripheral and central nervous systems, exist and should be recognized by clinicians.
- Keys to diagnosis include obtaining a full clinical history and skin examination, imaging, and neurophysiologic studies.
- Treatment is challenging and requires tailoring therapies. The most common treatments are GABAnergic anticonvulsant medications and topical anesthetics.

INTRODUCTION

Neuropathic pruritus, also known as neuropathic itch, is a form of nondermatologic chronic itch. When defined broadly, neuropathic pruritus refers to any injury or dysfunction along the afferent itch pathway that results in a sensation to scratch.[1] Neuropathic itch accounts for 8% to 19% of patients affected by chronic pruritus.[2,3] Furthermore, patients with chronic itch owing to neuropathic pruritus tend to have severe pruritus. A retrospective analysis of 597 patients with chronic pruritus investigated the intensity of itch of different origins and found neuropathic itch to be of severe intensity with a mean of 7.8 $\pm$ 1.8 on a numerical scale of 0 to 10.[3] Injury most commonly occurs within the peripheral nervous system, or, less commonly, within the central nervous system. Neuropathic itch can be distinguished from systemic forms of pruritus that occur in the absence of direct damage to the nervous system. Patients with chronic itch frequently suffer from depressed mood, interrupted slumber, strained interpersonal relationships, and an impaired quality of life.[4] Neuropathic itch can be challenging for clinicians to diagnose and manage because of the variety of clinical presentations and limited treatment options. Recent developments offer improved insight into the underlying pathophysiology, relevant clinical associations, and novel treatment options.

PATHOPHYSIOLOGY

Neuropathic itch may develop from a variety of etiologies, but the underlying pathophysiology has not been completely ascertained. It is understood

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that damage to itch neurons or other cells involved in the itch circuitry causes neuropathic itch. Given their vulnerability, damage to the peripheral nerves is more likely to cause neuropathic itch than central nervous system injury. In neuropathic itch, compression, trauma, and other modes of direct damage to peripheral nerve fibers characteristically results in a dermatomal distribution of pruritus. However, extensive damage or central lesions may cause pruritus that expands beyond or involves multiple dermatomes. Moreover, pruritus owing to compression is typically localized to the corresponding dermatome, whereas nerve fiber degeneration can present as either localized or generalized pruritus. The location of the insult and the involvement of other neural pathways determine whether other symptoms, such as pain or autonomic changes, are also present. Allokinesis (itch evoked by light touch) and other forms of hypersensitivity result from peripheral and central sensitization of neurons, and are frequently associated with neuropathic itch. Although the changes in the underlying neural pathway that result in neuropathic pruritus are not known, the following mechanisms have been proposed: (1) disinhibition of inhibitory spinal interneurons, (2) overactivation of adjacent undamaged sensory nerves, (3) hyperexcitation of central itch neurons in the absence of ascending signaling, or (4) dysfunction of cortical somatosensory pathways. Recent findings have also implicated (5) alterations in neuronal ion channels as a possible mechanism.

Table 1
Causes of neuropathic itch

Peripheral Nervous System	Central Nervous System
Postherpetic neuralgia	Spinal cord disorders
Small fiber neuropathy	Syringomyelia
Diabetic neuropathic itch	Tumors
NaV1.7 mutations	Abscesses
Notalgia paresthetica	Transverse myelitis
Brachioradial pruritus	Neuromyelitis optica
Neuropathic anogenital pruritus	Brain disorders
Cheiralgia paresthetica	Stroke
Meralgia paresthetica	Multiple sclerosis
Suprascapular entrapment syndrome	Traumatic brain injury
Pudendal neuralgia	Abscesses
Scalp dysesthesia	Scrapie
Multilevel symmetric neuropathic pruritus	Creutzfeldt-Jakob disease
Prurigo nodularis	Trigeminal trophic syndrome
Dry eye itch	Uremic pruritus
Postburn itch	
Scar and keloid Itch	

PRINCIPLE DISEASE ENTITIES

There are multiple ways to group the various etiologies of neuropathic itch. In this article, neuropathic itch is categorized based on the location of the primary insult in the peripheral or central nervous system (**Table 1**).

Peripheral Nervous System

Postherpetic neuralgia

Shingles is a neurocutaneous condition caused by the reactivation of latent varicella zoster virus in somatic sensory ganglia. Nonspecific symptoms (ie, fever, malaise) may present before skin manifestations, and the skin manifestations are often followed by the onset of postherpetic neuralgia (PHN). PHN is classically characterized by allodynia, pain, and parasthesias. Studies in the last 2 decades have provided evidence to support the association of neuropathic itch with acute shingles and PHN. An epidemiologic study of 586 adults with shingles demonstrated that itch, usually mild or moderate, affected up to 58% of patients with acute shingles or PHN.[5] Postherpetic itch is more likely to occur after facial shingles than after truncal shingles.[5] The skin changes and sensory symptoms of PHN classically present in a single dermatome, but multiple adjacent dermatomes may also be involved. Risk factors for PHN include advanced age, immunosuppression, polyneuropathy, and herpes zoster ophthalmicus or oticus.[2] Treatment options include anticonvulsants such as carbamazepine and gabapentin; antidepressants such as amitriptyline, desipramine, fluoxetine, or paroxetine; and topical agents such as capsaicin or anesthetics.

Small fiber neuropathies and diabetic itch

Small fiber neuropathies (SFN) are diseases of thinly myelinated A-δ and unmyelinated C fibers. SFN are characterized by autonomic and sensory symptoms, such as burning, allodynia, hyperalgesia, itch, and excessive sweating. The major diagnostic criterion of SFN is the diminution of intraepidermal nerve fiber density (IENF).