# Neuropathic itch caused by nerve root compression: brachioradial pruritus and notalgia paresthetica

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# VERSITA

### Abstract

Neuropathic itch (itching or pruritus) arises from a pathology located at any point along the afferent pathway of the nervous system. It may be related to damage to the peripheral nervous system, such as in postherpetic neuropathy, brachioradial pruritus or notalgia paresthetica. It has many clinical features similar to neuropathic pain. Patients complain of itching, which is associated with burning sensation, aching, and stinging. Brachioradial pruritis (BP) is an intense itching sensation of the arm, usually between the shoulder and elbow of one or both arms. It is an enigmatic condition with a controversial etiology; some authors consider BP to be a photodermatosis, whereas other authors attribute BP to compression of cervical nerve roots. Notalgia paresthetica is an isolated mononeuropathy involving the skin over or near the scapula. Patients have a pruritus on the mid-upper back. The treatment is usually difficult, but capsaicin and local analgesic agents are the options of choice. Brachioradial pruritus and notalgia paresthetica are often unrecognized neurocutaneous conditions and therefore, a thorough history and physical examination are of utmost importance to distinguish symptoms and apply accurate therapeutic options.

Itch (itching or pruritus) is defined as a cutaneous sensation that provokes the desire to scratch. It has a protective function: to remove pruritogenic stimuli. Pruritus is a common manifestation of dermatologic conditions including xerotic skin, atopic dermatitis, and contact dermatitis, but may also result from systemic diseases. Up to 50% of patients with pruritus and without any obvious dermatological condition have an underlying systemic disease, such as chronic renal failure, cholestasis, hematological or neurological disorders (1).

#### **Classification of pruritus**

A neuropathophysiologically-based classification of itch was proposed in 2003 (2). Twycross et al. (2) classified itch according to its origin: cutaneous (pruritoreceptive-cutaneous nerves are activated by pruritogens at their sensory endings), neuropathic (damaged or lesioned pruritic neurons generate itch), neurogenic (itch is induced by mediators acting centrally in the absence of neural damage), psychogenic and mixed (e.g. uremia) (2,3). In 2007, Ständer et al. (3) proposed a clinical classification created by the members of the International Forum for the Study of Itch, which focuses on clinical signs and distinguishes between diseases with and without primary or secondary skin lesions. Three groups of conditions were proposed: pruritus on affected (inflamed) skin (group I), pruritus on non-affected (non-inflamed) skin (group II), and pruritus presenting with severe chronic secondary scratch lesions, such as prurigo nodularis (group III). The next part classifies the underlying diseases according to different categories:

I Dermatological diseases such as: inflammatory, infectious, autoimmune dermatoses, genodermatoses, dermatoses of pregnancy and neoplasms;

II Systemic diseases, including diseases of pregnancy and drug-induced pruritus, endocrine and metabolic diseases, infectious diseases, hematological and lymphoproliferative diseases;

III Neurological diseases: neurogenic origin - without neuronal damage and neuropathic diseases such as brachioradial pruritus and notalgia paresthetica, post-herpetic neuralgia etc.; IV Somatoform pruritus: psychiatric/psychosomatic diseases;

V Mixed category - overlapping and coexistence of several categories;

VI Pruritus of unknown origin (3).

While many pruritic skin diseases can be diagnosed readily, this is more difficult with pruritus that occurs in apparently normal skin or accompanying secondary scratch-evoked lesion as a consequence of systemic disease (4).

## Neuropathic itch:

#### definition and clinical features

Neuropathic itch is defined as an itch initiated or caused by a primary lesion or dysfunction at any point along the afferent pathway of the nervous system. It can be acute, but in most cases it is chronic and persistent. In many cases neuropathic itch is accompanied by sensory impairment experienced as paresthesia, hyperesthesia, or hypoesthesia. It may also occur during recovery from isolated nerve injury such as after burns. Patients may feel both pain and itching at the same site. In many cases it involves peripheral and central sensitization of nerve fibers. This sensitization induces alloknesis, which is an itchy phenomenon that results from an innocuous stimulus that normally does not provoke itching. The characteristic features of neuropathic itch that differentiate it from other forms of pruritus are as follows: it is associated with other sensory symptoms in a dermatomal distribution and frequently with other neurological sensory signs or neural damage including motoric, or autonomic damage (4).

Mechanisms of neuropathic itch are incompletely understood. Some of the proposed mechanisms include itching associated with local nerve damage, central neuronal deprivation of afferent input and central hypersensitivity of nerve fibers. The first mechanism suggests that itching fibers, which have large innervation territories extending beyond dermatomes, arise from local damage to C nerve fibers that transmit both pain and itch. The second hypothetical mechanism suggests that central itch neurons fire excessively when they are deprived of their afferent input. Another possible mechanism is lack of inhibitory neurons for itch in the spinal tract (5). Neuropathic itch can originate at any point along the afferent pathway as a result of damage to the nervous system. Localized pruritus has been reported with peripheral nerve lesion in postherpetic neuralgia, notalgia paresthetica and HIV infection. Paroxysmal pruritus has been reported in multiple sclerosis. Unilateral pruritus is occasionally found with cerebral tumors, abscesses or thrombosis (2).

Neuropathic itch may coincide with pain, for example in postherpetic neuralgia. Patients with neuropathic itch may present with varying symptoms. Therefore, a thorough history and physical examination are essential in the evaluation of pruritus (1, 4). History-taking should include a detailed drug history, constitutional symptoms (fever, night sweats, weight loss). An accurate timing (e.g., predominantly nocturnal or diurnal) of itching helps fine-tune the antipruritic treatment (6). Close attention to features such as paresthesia, hypoesthesia, and hyperalgesia can help the clinician to diagnose neuropathic itch. A thorough neurologic examination, performed by a neurologist, may help finding associated sensory abnormalities, e.g., light touch, pinprick, thermal stimulation, perception, and vibratory sense. Electromyography and nerve conduction studies in cases suspected of nerve roots impingement may be considered. Magnetic resonance imaging of the spine is recommended to locate the suspected nerve impingement such as in brachioradial pruritus and notalgia paresthetica (4). Chest X-ray imaging may also be useful in localized neuropathic itch, e.g., due to spinal cord tumors, and nerve entrapment, due to degenerative spinal diseases (6). Neuropathic itch may occur with secondary skin findings, such as prurigo, lichenification, as well as excoriations; however, itching may also be without any skin signs (4).

#### **Brachioradial pruritus**

Brachioradial pruritus (BP) is a localized neuropathic pruritus affecting the dorsolateral aspect of the upper arm. It may also involve shoulders and the neck (7-9). There is a continuous controversy regarding the cause of brachioradial pruritus: is it caused by nerve compression in the cervical spine, or a prolonged exposure to sunlight. Brachioradial pruritus was first reported by Waisman (10) in 1968, who termed it "solar pruritus" of the elbows, describing its occurrence in patients in Florida who suffered from a localized itch of the skin on the dorsolateral aspect of the arm. A group of 110 Hawaiian patients with chronic intermittent pruritus have been described in two reports (11, 12). In one of these, Walcyk and Elpern (11) suggested that brachioradial pruritus is a photoneurological disorder caused by sun-induced damage to nerve endings that results in pruritus and altered sensation in susceptible individuals. On the other hand, Heyl (13), in South Africa, suggested that brachioradial pruritus may be caused by nerve injury to the cervical spine, or by nerve compression at other locations, because five of his 14 patients had a history of neck trauma or arthritis.

In recent years, Wallengren at al. (14) showed that BP is associated with a reduction in epidermal and dermal nerve fibers. These findings strikingly resemble the ones they observed in the skin after serial phototherapy (14). The cutaneous innervation of pruritic skin normalizes during the symptom-free period. The results indicate that BP can be elicited by exposure to sunlight or by heat. The occurrence of brachioradial pruritus in black patients suggests that melanin offers no protection. The localization of BP to dermatome C5-7, frequent neck pain and spinal pathology, as shown radiologically, indicate the cervical spine disease to be a predisposing factor. Hypothetically, photodamaged nociceptors can start firing spontaneously, and nerve impulses generated in this way can be amplified by neurogenic mechanisms elicited by nerve compression, which is secondary to the cervical spine disease (8). Rarely, BP can also be associated with spinal tumors, especially in those patients who present with multiple sensory and motor deficits (4).

Brachioradial pruritus is often refractory to treatment. However, successful treatments were achieved with topical capsaicin, oral gabapentin and pregablin, carbamazepine, lamotrigine, and surgical procedures for tumors, or when there are significant sensory and motor deficits. Capsaicin, isolated from pepper plants of the genus *Capsicum*, depletes substance P release from C- fibers when applied repeatedly and reduces both pain and itch (2). Topical capsaicin exerts its effects by rendering the skin insensitive to pain. At higher concentrations than 0.075% and 0.1% topical capsaicin seems to be significantly more effective than the lower one of 0.025%. Addition of topical anesthetic EMLA<sup>\*</sup> cream, prior to initiation of topical capsaicin has been instituted to further counteract the sensation and irritation, and can also increase the antipruritic effect, as both medications target different receptors (7, 15). Sometimes, the only treatment that can provide relief is application of an ice pack, chilling the skin to numbness, therefore a common clinical symptom in patients with BP is the "ice pack sign" (4).

#### Notalgia paresthetica

Notalgia paresthetica (NP) was first described and named in 1934 (16). It is a sensory nerve entrapment syndrome involving the posterior rami of T2-T6 nerve roots associated mainly with degenerative vertebral changes (17). The etiology of this condition has not been completely elucidated. Some hereditary cases have been noted, mainly in young patients, associated with multiple endocrine neoplasia type 2A. However, NP mainly occurs in older patients, and most of observed disturbances are sporadic pathologies associated with musculoskeletal spinal nerves compression (18). In their studies, Springall at al. (19) have shown that there is an increase in the sensory epidermal innervation in the affected skin areas in notalgia paresthetica, which may contribute to the symptoms, and that neural immunohistochemistry of skin biopsies can be helpful in diagnosing the disease. Patients typically present with unilateral, well-demarcated itching of the mid and upper back in the distribution of T2-T6 dermatomes, sometimes accompanied by sensory neuropathies and/or electrical conductivity disorders, or burning pain. A well-circumscribed hyperpigmented patch in the symptomatic area, similar clinically to macular amyloidosis, is frequently observed due to long-term scratching (4, 19, 20). It is very characteristic that patients may easily draw the itchy area under the skin.

Notalgia paresthetica can be successfully treated with capsaicin, gabapentin, EMLA <sup>•</sup> cream, and paravertebral local anesthetic blocks, cervical epidural steroid injections, and phenytoin. Other therapies include physiotherapy, neck traction, and cervical manipulation (4).

Recently, a pilot study described the successful use of botulinum toxin A in the treatment of NP in two patients. The toxin was injected to several points along the involved dermatome at doses ranging between 16 and 25 units. The rationale for using botulinum toxin is that it blocks acetylcholine, which is a mediator involved in itch transmission (21, 22).

#### Conclusions

Pruritus is a major symptom of various skin diseases and many systemic diseases. Despite this, a clinically based classification of pruritic diseases did not exist, to assist diagnosing, and managing these patients. In 2007, Ständer et al. (3) created the first version of clinical classification of itch, formulated by the members of IFSI (International Forum for the Study of Itch). It considered the origin and clinical manifestations of pruritus occurring in the affected and normal skin. This classification provides practical and useful clinical approach to patients with chronic pruritus. Increased knowledge and understanding of itch mechanisms, including neuropathic diseases such as notalgia paresthetica and brachioradial pruritus, should encourage us to develop new therapeutic regimens to treat severe and distressing symptoms of pruritus (23).

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# Neuropatski pruritus (svrab) prouzrokovan kompresijom nervnih korenova - brahioradijalni pruritus i nostalgija parestetika

## Sažetak

Savremeni koncept: Neuropatski pruritus (svrab) povezan je s patološkim procesom koji može da se pojavi na bilo kojoj tački duž aferentnog toka nervnog sistema, a mogu da ga prouzrokuju povrede perifernog nervnog sistema.

Etiopatogeneza: Mogu da ga prouzrokuju povrede perifernog nervnog sistema, kao što je slučaj kod postherpetične neuropatije, brahioradijalni pruritus i notalgija parestetika.

Kliničke osobenosti: Mnoge kliničke osobine neuropatskog svraba slične su osobinama neuropatskog bola. Bolesnici se žale na svrab udružen sa žarenjem, probadanjem i jakim bolom.

Brahioradijalni pruritus: Predstavlja intenzivan svrab koji se najčečće javlja između ramena i lakta jedne ili obe ruke. To je zagonetno stanje sa kontroverznim uzrocima; neki autori smatraju da je brahioradijalni pruritus fotodermatoza, dok ga drugi smatraju posledicom kompresije cervikalnih nervnih korenova. Notalgija parestetika: Ovo je posebna mononeuropatija koja zahvata kožu iznad ili u blizini skapule. Oboleli se žale na svrab gornjeg i središnjeg dela leđa.

Lečenje: Obično je teško, dok *Capsaicin* i lokalni analgetici predstavljaju terapiju izbora. Zaključak: Brahioradijalni pruritus i notalgija parestetika su patološka stanja koja često nisu prepoznata i zbog toga je veoma važno uzeti detaljnu istoriju bolesti i izvršiti detaljan klinički pregled radi prepoznavanja simptoma i primene odgovarajućih terapijskih opcija.