
Pruritus: An underrecognized symptom of small-fiber neuropathies

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Background: Small-fiber neuropathies (SFN) are diseases of small nerve fibers that are characterized by autonomic and sensory symptoms.

Objective: We sought to evaluate sensory symptoms, especially pruritus, in patients with SFN.

Methods: A questionnaire was given to patients with SFN.

Results: In all, 41 patients responded to the questionnaire (71.9% response rate). The most frequent sensory symptoms were burning (77.5%), pain (72.5%), heat sensations (70.2%), and numbness (67.5%). Pruritus was present in 68.3% of patients. It appeared most often in the evening, and was localized to the limbs in a distal-to-proximal gradient, although the back was the most frequent location (64%). Exacerbating factors were fatigue, xerosis, sweating, hot temperature, and stress. Cold water was an alleviating factor.

Limitations: Recall bias associated with filling out the questionnaire, relatively small sample size, and the uncontrolled, retrospective nature of the study were limitations.

Conclusion: Pruritus occurs frequently in patients with SFN and could be recognized as a possible presenting symptom, especially if there are other sensory or autonomic symptoms. (J Am Acad Dermatol 2015;72:328-32.)

Key words: pruritus; questionnaire; sensory symptoms; small-fiber neuropathy.

Small-fiber neuropathies (SFN) are disorders of thinly myelinated A- δ and unmyelinated C fibers. SFN have recently been described.¹ In a recent study, the incidence of SFN was 11.7 cases/100,000 people/y, and the overall minimum prevalence was 52.95 cases/100,000.² Hence, they are not rare disorders. SFN are usually idiopathic but may be associated with various diseases, such as metabolic diseases (eg, diabetes and prediabetes), infectious diseases (eg, HIV, hepatitis C infection), inflammatory diseases (eg, Sjögren syndrome), autoimmune diseases, paraneoplastic syndromes, or genetic diseases (eg, Fabry disease).^{3,4} The pathogenesis is

poorly understood and probably depends on the cause. SFN lead to a significant reduction in the overall quality of life.⁵ The clinical manifestations include autonomic symptoms such as dry eyes, dry mouth, dizziness, constipation, bladder incontinence, sexual dysfunction, excessive sweating, and red or white skin discoloration. Patients also have sensory symptoms that are often their main symptom, including pain, pruritus (itch), burning, tingling, or numbness, and typically affect the limbs in a distal to proximal gradient.⁶ Because their symptoms are mainly located in the skin in the initial stages, dermatologists may frequently be confronted

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with this disease. The following diagnostic criteria are generally accepted⁷: normal sural nerve conduction, clinical symptoms and signs considered suggestive of SFN, and/or altered quantitative sensory testing. A diminution of intraepidermal nerve fiber (IENF) density has become the major diagnostic criterion. Treatment of SFN is based on etiology; symptomatic treatments (eg, gabapentin, pregabalin, tricyclic antidepressants) can be used as well. The aim of this study was to evaluate the frequency and severity of sensory symptoms in patients with SFN with a special focus on pruritus and its characteristics. A questionnaire adapted from previous questionnaires was sent to each patient with SFN.⁸⁻¹⁰

METHODS

Patients were recruited at the Department of Pathology, University Hospital, Brest, France, in which all biopsy specimens for the area are sent when the diagnosis of SFN is suspected. After a positive biopsy specimen, we checked in patients' reports if they filled eligibility and exclusion criteria. The questionnaire was sent to all patients with SFN who had been given a diagnosis in the last year.

Eligibility was based on the following criteria: (1) age 18 years and older; and (2) diagnosis of SFN according to criteria of Devigili et al⁷: (a) clinical signs of small-fiber impairment (pinprick and thermal sensory loss and/or allodynia and/or hyperalgesia), the distribution of which is consistent with peripheral neuropathy (length- or non-length-dependent neuropathy); (b) abnormal warm and/or cooling threshold in the foot, as assessed by quantitative sensory testing; and (c) reduced IENF density in the distal leg.

Eligible patients were ruled out based on the presence of the following: (1) any sign of large fiber impairment (light touch and/or vibratory and/or proprioceptive sensory loss and/or absent tendon reflexes); (2) any sign of motor fiber impairment (muscle waste and/or weakness); and (3) any abnormality on sensorimotor sural nerve conduction.

The exclusion criteria were as follows: (1) other putative causes of pruritus; or (2) inability to complete the questionnaire because of cognitive or physical impairment.

The study used an exploratory approach with a questionnaire in French adapted from previous questionnaires^{8,10} that had been used in a previous study to investigate pruritus characteristics in different dermatoses.⁹ The questionnaire first asks patients about the duration of their symptoms and then asks whether they have any sensory

symptoms. Patients evaluated the following symptoms from 0 (nonexistent) to 3 (severe): pain, stinging, tickling, crawling, stabbing, pinching, burning, biting, stroking, electric discharge, numbness, heat sensations, and cold sensations. Next, patients reported whether they had pruritus. If they answered "yes," the patient filled out the second part of the questionnaire about the characteristics of their pruritus that included questions

about the chronology, localization, intensity, disruption of daily activities, and characteristics of scratching. Written informed consent was obtained from all patients.

RESULTS

The questionnaire was sent to 57 patients, 41 of whom responded (71.9% response rate). The demographic and baseline clinical characteristics of the patients are summarized in [Table I](#).

Concerning the duration of their symptoms, 10.3% of patients declared that sensory symptoms had been present for just a few months; for most patients (89.7%), sensory symptoms had been present for 1 year or more.

Each sensory symptom was evaluated by the patient from 0 (nonexistent) to 3 (severe). The frequency of these symptoms is presented in [Fig 1](#). Of 41 patients with SFN, 28 (68.3%) had mild or severe pruritus. The characteristics of pruritus were studied in these patients.

Itch appeared daily for 13 patients (46.4%), almost daily for 10 (35.7%), on a weekly basis for 1 (3.6%), on a monthly basis for 2 (7.1%), and infrequently for 1 (3.6%).

The occurrence of pruritus at different times of the day is presented in [Fig 2](#). Pruritus tended to appear more frequently in the evening than in the morning, afternoon, or night.

The areas of the body most commonly afflicted were the back (63%); foot (59%); shin (56%); forearm

CAPSULE SUMMARY

- Little is known about sensory symptoms in small-fiber neuropathies.
- Pruritus was present in 68.3% of our patients. It was intense, appeared most often in the evening, and was localized to the limbs in a distal-to-proximal gradient.
- Pruritus should be recognized as a possible presenting symptom of small-fiber neuropathies.

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