SMALL FIBRE NEUROPATHY IN GENERAL CLINICAL PRACTICE: WHEN IS SKIN BIOPSY NEEDED?

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Small fibre sensory neuropathy (SFSN) is a concept that has become deeply rooted in neurological clinical practice. It implies the impairment of small myelinated A and unmyelinated C nerve fibres that convey pain and temperature sensations and autonomic functions. Symptoms of somatic nerve fibre dysfunction, such as burning, pain, and hyperaesthesia are prevailing, thus the term 'painful neuropathy' is often used as a synonym of SFSN. The reason for that particular vulnerability of this type of nerve fibres to such a large list of etiologic agents as shown in table 1 is currently subjected to numerous researches. Impairment small sensory nerve can be selective (pure SFSN) but sometimes it represents the initial stage of a more generalized affection with progression to large sensory fibre involvement (mixed sensory neuropathy), or even to a multisystem or multiorgan disorder.

Clinical Picture: Suspicion of SFSN arises before a picture of pain, burning, tingling, or numbness that typically affects the limbs in a distal-to proximal gradient. In rare cases the distribution follows a non-length-dependent pattern in which symptoms may be manifested predominantly in the arms, face, or trunk. Severe autonomic disturbances are quite rare, though patients may complain of abnormal sweating, flushing, skin discoloration, dry eyes, dry mouth, impotence, and, less commonly, of constipation or diarrhea, and orthostatic hypotension. Examination often reveals allodynia hyperalgesia or reduced pinprick and thermal sensation in the affected area. Vibratory sensation can be mildly reduced at the toes. Motor strength, tendon reflexes, and proprioception, however, are preserved because they are functions of large nerve fibers.

Diagnostic : There is no consensus for the diagnosis of SFSN, although an accepted criteria definition is a suspected SFSN sensory neuropathy with objective abnormalities at least one of the following: neurological examination, quantitative sensory testing (QST), quantitative sudomotor axonal reflex test (QSART), specialized neurophysiological testing, or skin biopsy. These restrictive criteria are necessarily required in a research setting. However in general clinical practice (GCP) there is initial important goals to deal with. They include discarding other causes mimicking SFSN, the search for etiologic conditions, particularly those that are treatable or requiring an early intervention, and symptomatic treatment of pain.

Initial evaluation: In addition to features regarding neuropathy symptoms, details history should be taken to ascertain whether the patient has any associated conditions as mentioned in the table. At the same time a battery of basic laboratory tests, oral glucose tolerance test, lipid panel, thyroid screening, serology for connective disorders, angiotensin-converting enzyme level, serum and urine immunofixation tests and Vitamin B12 level. Nerve conduction function of large nerve fibers only and are thus normal in small fiber neuropathy, unless a mixed sensory neuropathy is present. These tests should still be ordered not only for confirmatory interest but for excluding nerve atrapment causing foot and hand pain. Neuroimage may also be required to exclude radiculopathy spinal stenosis, mylopathy or CNS lesions causing pain and disestesia

Special laboratory tests: If there is history or a suspected background should be ordered gluten serology and bowel biopsy for celiac disease, serological tests for HIV or hepatitis C, or Lip biopsy for Sjögren disease or amyloidosis. Sural nerve biopsy is not indicated for diagnosis of SFSN but can yield useful information is suspected vasculitis or amyloidosis. Finally, genetic testing should be required if there is family history or isolated patients with high suspicion of Fabry disease or amyloidosis

Referral to specialized centre: Confirmatory assessment of suspected SFSN by skin biopsy or other psychophysical, autonomic or neurophysiological evaluation is required if clinical examination is normal, atypical features are present and no etiological justification is found. However, those procedures are usually not available and require referral .

Table 1. Causes of small fibre neuropathy

Metabolic

- Diabetes
- Impaired glucose tolerance
- Hyperlipidemia

Immune-mediated

- Sjögren's syndrome
- Lupus erythematodes
- Vasculitis
- Coeliac disease
- Sarcoidosis
- Inflammatory bowel diseases
- Monoclonal gammopathy of undetermined origin
- Anti-sulfadite antibodies
- Paraneoplastic neuropathies

Drugs and toxics

- Alcohol abuse
- Antineoplastic agents
- Antiretroviral agents
- Metronidazole and linizolid
- Industrial and environmental toxics

Infections

- HIV
- Leprosy
- Epstein-Barr virus

Idiopathic

- Idiopathic small fibre neuropathy
- Erythromelalgia
- Burning mouth syndrome
- Faecal urgency and rectal hypersensitivity

Hereditary

- Fabry's disease
- Familial amyloidosis
- Hereditary sensory autonomic neuropathies
- Charcot-Marie-Tooth type 2B
- Tangier's disease
- Ross' syndrome
- Familial burning feet syndrome

Miscelaneous

- Systemic amyloidosis
- Vitamin B12 defiency and Copper deficiency

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