GLOBAL YEAR AGAINST NEUROPATHIC PAIN

International Association for the Study of Pain

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Painful Polyneuropathies

Definitions

- Peripheral neuropathy is a disease or degenerative state of peripheral nerves in which motor, sensory, or autonomic nerve fibers may be affected.
- Polyneuropathy is a generalized, roughly symmetric hereditary or acquired disorder affecting peripheral nerves. It is the most common form of peripheral neuropathies.
- Small-fiber neuropathy is a subtype of sensory neuropathies, which exclusively or predominately affects small diameter fibers (Aδ) and unmyelinated (C) fibers.
- Neuropathic pain is defined as pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory system (see factsheet on "What is neuropathic pain").

Epidemiology

- Of the identifiable causes, diabetes is the most common cause of painful polyneuropathy.
- It has been estimated that diabetes affects 8.5 % of people in Europe and diabetic sensorimotor polyneuropathy occurs in 10-54 % of patients with either type 1 or type 2 diabetes. A third of patients with diabetic sensorimotor polyneuropathy suffer from neuropathic pain.
- For the majority of patients over 50 years of age, no specific cause for a painful polyneuropathy can be identified. Neuropathic pain has been estimated to be present in 65-80 % of idiopathic polyneuropathies.

Impact

- Painful diabetic neuropathy has negative impact on physical and mental quality of life compared with painless diabetic neuropathy.

Clinical features

- Typical clinical picture in painful neuropathies is a combination of negative (loss of sensation, hypoesthesia, hypoalgesia) and positive sensory symptoms (spontaneous pain, evoked pain, hyperalgesia).
- Pain follows usually a classical distal "glove and stocking" distribution.
- Distal sensorimotor polyneuropathy and small-fiber neuropathy are the most common subtypes of painful diabetic neuropathy. Other subtypes include diabetic lumbosacral radiculoplexus neuropathy, mononeuropathy and mononeuritis multiplex, which are all asymmetric. Treatment induced neuropathy is characterized by the acute onset of severe pain and autonomic dysfunction after starting insulin or oral hypoglycemic drugs.
- Patients with small-fiber neuropathy may present with a number of autonomic symptoms, including abnormally increased or decreased sweating, transient changes in distal extremity skin color and temperature, dryness of eyes and mouth, and impotence.
- Itching can be a manifestation of small-fiber neuropathy.
- In clinical examination, patients with painful large-fiber neuropathies usually have absent or reduced deep tendon reflexes. In small-fibre neuropathy, deep tendon reflexes are usually normal or slightly reduced, and in majority of the patients, reduced thermal and pinprick sensation is discovered.
- Non-length dependent form of small-fiber ganglionopathy has been described, in which there is early involvement of the face, trunk or proximal limbs and patients complain of burning, shooting or allodynic pain. This disorder may be related with metabolic or immunologic causes.

Causes of painful polyneuropathy

- Inherited diseases: hereditary sensory (and autonomic) neuropathy (particularly type 1), familial amyloid polyneuropathy (transthyretin-related, TTR-FAP), Fabry disease, Tangier disease, porphyria
- Metabolic and nutritional causes: diabetes, malnutrition and vitamin deficiency, uremia
- Immune-mediated disorders: Guillain-Barré syndrome, chronic inflammatory demyelinating neuropathy (CIDP), multifocal acquired demyelinating sensory and motor neuropathy (Lewis-Sumner syndrome), systemic vasculitides (for example, polyarteritis nodosa and granulomatosis with polyangiitis), isolated peripheral nervous system vasculitis, neuropathies in systemic connective tissue diseases (Sjögren's syndrome, systemic lupus erythematosus), sarcoidosis, coeliac disease, inflammatory bowel diseases

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- Infections: HIV, leprosy, herpes zoster, borreliosis (Lyme disease), hepatitis C
- Dysglobulinemias: primary systemic amyloidosis, cryoglobulinemia, macroglobulinemia, myeloma
- Neoplasia-related causes: direct infiltration of malignancy, sensory neuronopathy
- Toxic causes: alcohol, metals, drugs (for example platinum derivatives, bortezomib, vincristine, paclitaxel, thalidomide, linezolid, metronidazole, zalcitabine, stavudine)

Treatment

- A specific cause of painful polyneuropathy should always be attempted to identify. In some cases treatment of the underlying cause may also alleviate the pain.
- First-line pain medications include tricyclic antidepressants, gabapentin, pregabalin, and serotonin-norepinephrine reuptake inhibitors (duloxetine and venlafaxine). A topical lidocaine patch or capsaicin patch in nondiabetic adults may be a treatment of choice in localized neuropathic pain.
- Second-line drugs include tramadol and other opioids.
- Systematic evaluations of combination therapy are limited but individually tailored combination therapy may be considered in case of insufficient effect from one drug.
- It should be kept in mind that most RCTs published in painful polyneuropathy have been conducted in patients with diabetes and there is less scientific evidence on the efficacy of these drugs in other specific forms of painful polyneuropathy.
- Because only 20-35 % of the patients with painful polyneuropathy achieve $\geq$ 50 % pain reduction with available drugs, multidisciplinary approach to pain management is of utmost importance.

References

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