Erythromelalgia: an underrecognized manifestation of small-fibre neuropathy.

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Erythromelalgia is characterized by intermittent heat, redness, and pain affecting the extremities.1 Exercise and increase in temperature are precipitating factors. During symptoms, blood flow and temperature increase without a concomitant increase in oxygenation.2 Severe sudomotor impairment and evidence of peripheral adrenergic dysfunction are also present.2 A recent study showed that a predominantly small-fiber neuropathy underlies most cases of erythromelalgia.3 The presence of intermittently increased blood flow and shunting suggests an associated vasculopathy.4 Erythromelalgia has been reported in association with myeloproliferative disorders, but the cause/effect relationship is not well established.5

A 43-year-old woman was evaluated because of a 6-month history of intermittent tingling in her feet accompanied by redness, warmth, and pain. Exposure to heat and exercise often precipitated her symptoms. Results of neurological examination, nerve conduction studies, and electromyography were unremarkable. Evaluation of the autonomic nervous system (heart rate response to deep breathing, tilt-table test, Valsalva maneuver, quantitative sudomotor axon reflex test) yielded normal findings. A thermoregulatory sweat test showed evidence of anhidrosis or hypohidrosis in patchy areas (shown in yellow) over the lateral aspects of the arms, fingers, and lower limbs (including distal aspects of the feet) in a pattern consistent with multifocal small-fiber neuropathy. Arterial Doppler studies showed no evidence of occlusive disease. Provocative vascular studies in the lower limbs revealed evidence of increased blood flow and temperature without an increase in oxygenation. Erythromelalgia as a manifestation of small-fiber neuropathy is not well recognized. Neuropathy and vasculopathy often coexist, and erythromelalgia may represent a predominant small-fiber neuropathy with disturbed control of vascular tone.3 Awareness of this entity will help ensure appropriate work-up and management of patients with small-fiber neuropathy. Erythromelalgia is the first inherited pain disorder in which a mutation has been linked with an abnormality in ion channel function. A mutation has been identified in the *SCN9A* gene.6 This gene encodes the voltage-gated sodium channel α subunit Nav1.7. Nav1.7 is expressed by nociceptive neurons, and recent evidence suggests that Nav1.7 plays a role in transmission of nociceptive information.7 Identification of erythromelalgia as a channelopathy suggests the possibility of rational therapies targeting the affected channel.

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