

Treatment of primary erythromelalgia with cyclosporine.

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TO THE EDITOR: Erythromelalgia is a rare disease of unknown cause, characterized by redness of the skin, increased temperature, and pain in the extremities. Erythromelalgia is often primary, but it may also be secondary to disorders such as myeloproliferative diseases. Although a wide variety of therapies have been tried, no effective treatment is yet available.

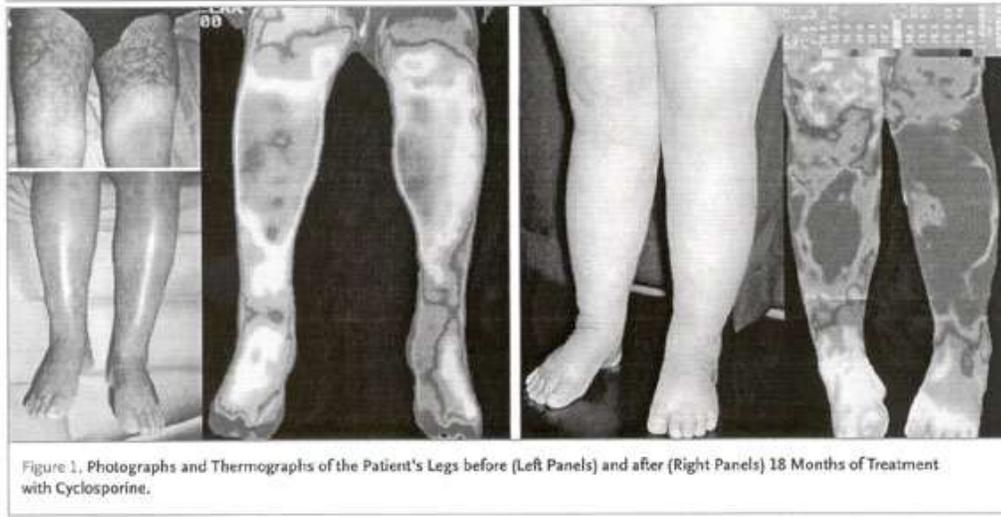
A 28-year-old woman presented with severe, persistent burning pain in the legs and feet, with marked erythema, swelling, and warmth (Fig. 1, left-hand panels). The erythema had begun at the age of four years, with no associated disorder. After adolescence, the symptoms became continuous, with erythema that extended to the thighs and the development of live do-like lesions. Burning pain during the night was relieved only by immersion of the affected areas in ice water. No treatment relieved her symptoms, which were due to autosomal dominant erythromelalgia. [1] Her older sister and eight year-old daughter also had this disorder.

We decided to treat the patient with cyclosporine at a dose of 5 mg per kilogram of body weight per day. Surprisingly, over a three-month period, the erythema and pain in her legs gradually subsided. The dose of cyclosporine was then tapered to 3 mg per kilogram per day, and after 10 months, her symptoms had further improved. Eighteen months after the start of treatment, the redness of her feet, lower legs, and thighs had subsided, with normalization of the surface temperature (Fig. 1, right hand panels). Her quality of life was remarkably improved.

A recent study of linkage analysis in families with hereditary erythromelalgia revealed that the susceptibility gene is on chromosome 2, although the candidate gene is still unknown.[2] Mork et al.[3] proposed that an increase in thermoregulatory arteriovenous shunt flow results in decreased perfusion of the superficial vascular plexus and, eventually, in tissue hypoxia, which accounts for the persistent pain. Although the mechanism by which cyclosporine ameliorates this disorder is unknown, it is likely that cyclosporine acts through pathways other than immuno-suppression. Cyclosporine may reduce nitric oxide production in vascular smooth-muscle and endothelial cells through down-regulation of inducible nitric oxide synthase [4] and stimulate endothelin-1 production,[5] resulting in an amelioration of the microvascular abnormalities in erythromelalgia. These actions may be involved in the mechanism underlying the most frequent side effects of cyclosporine-that is, hypertension and nephrotoxicity.

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