CLINICAL VIGNETTE

Erythromelalgia

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Case Report

A 60-year-old male presents to rheumatology with over 40 years of foot symptoms. He reports feelings of intense heat in his feet that turn red regularly. His feet can feel boiling hot and then transition to ice cold. There is no sweat or clamminess. There are no other color changes in the toes to white, blue or purple. The same symptoms do not occur in the hands. The symptoms are triggered with temperature changes, stress and physical activity and can sometimes be relieved with cooling measures. There was no clear preceding event to the onset of the symptoms. He had already seen multiple doctors over the years including vascular and neurology with unremarkable evaluations. He had also tried and failed multiple treatments including topical lidocaine, topical steroids, clonazepam, carbamazepine, gabapentin and pregabalin.

His past medical history was significant for Hashimoto's disease, excised melanoma, osteoarthritis with bilateral knee replacements and hyperlipidemia. His medications were atorvastatin, levothyroxine and zolpidem as needed. He quit smoking in his 30s and did not drink alcohol or use drugs. Family history was significant for a mother who had melanoma and a father with esophageal cancer.

Laboratory studies showed normal CBC, metabolic panel, sed rate and TSH. Vitamin B12 and folate levels were normal. He had a positive ANA serology at 1:640 homogenous as well as positive TPO antibodies consistent with his diagnosis of Hashimoto's disease. Additional serologies for dsDNA, SSA, SSB, Smith, RNP, centromere, Scl-70, RF, celiac, cryoglobulins, complement and cardiolipin antibodies were all normal. Serum protein electrophoresis and immunofixation were also normal. He had normal venous and arterial ultrasounds of the lower extremities as well as normal EMG and nerve conduction studies.

He was diagnosed with erythromelalgia of the feet and started on amitriptyline at night which was ineffective in managing his symptoms. A subsequent 3-month trial of aspirin 325mg daily was also ineffective. He was then started on duloxetine daily and within a month had 80% improvement of his symptoms overall with less redness, pain and improved quality of life.

Discussion

Erythromelalgia comes from the Greek: erythros "red," melos "limb" and algos "pain."

It is a rare disease where the prevalence is not well known.[1] It is more common in women and can present at any age with symptom onset commonly reported in the first two decades of life, although it is most often diagnosed in the fifth and sixth decades.[2] The pathophysiology of erythromelalgia is also not well known but vascular, neuropathic and genetic factors are thought to play a role.[1]

The disease has been classified as idiopathic, primary, and secondary. Primary erythromelalgia is an autosomal dominant inherited disorder associated with either a sporadic or familial mutation on the SCN9A gene that codes for voltage-gated sodium channels expressed mainly in dorsal root ganglia and the sympathetic ganglia neurons. The secondary form has been associated with underlying diseases including hematologic diseases, cancers, autoimmune diseases, infections, neuropathies, vascular diseases, medication reactions, and toxins. Myeloproliferative neoplasias, essential thrombocytopenia and polycythemia vera are the most commonly associated conditions thought to responsible for approximately 20% of secondary erythromelalgia cases. Erythromelalgia can precede or be present at the same time as the underlying disease.[1]

Erythromelalgia has no formal diagnostic criteria, and the diagnosis is typically based on the hallmark symptoms of erythematous, warm, painful limbs precipitated by heat and relieved by cold conditions.[2] The pain is typically described as a burning sensation, throb or an electric shock. The symptoms may be symmetric or unilateral and the extension is variable from the phalynx of the toes to the entire limb. Lower limbs are much more commonly affected than upper limbs and there have been reports of symptoms occurring in the face, ear and tongue as well. Symptoms are usually episodic lasting 2-3 hours at a time. Between episodes, the limb can be normal or cold with numbness. Symptoms can be triggered by heat exposure, pressure, standing for long periods of time, physical activity, emotions, stress, alcohol, spicy foods, vasodilator drugs or exposure to chronic vibration.[1] These symptoms and limitations can have a significant impact on quality of life.

Non-pharmacologic treatment of erythromelalgia include trigger management and cooling strategies. To avoid situations that may trigger pain, people may avoid heat, use air conditioners, avoid wearing footwear, move to colder environments and limit physical activity. Once the erythromelalgia symptoms are active, relief is often achieved using cooling strategies such as

immersion of limbs in ice-cold water, repeated ice packs, application of cold socks or gloves and decreasing ambient heat with ventilation or fans. However, complications from chronic cold exposure have been reported including maceration, ulceration, windburn, hypothermia, frostbite and secondary infections.[2]

Medical management of erythromelalgia is challenging as there are no guidelines for treatment, significant variability within the clinical population and varying responses to pharmacotherapy. No single therapy has been found to be effective. As a result, the treatment approach has been mostly trial and error. Aspirin has been considered a first line treatment and there is more evidence that aspirin is effective for patients with myeloproliferative diseases and polycythemia vera in particular.[2] Potential topical treatments include lidocaine patches, amitriptyline/ketamine gel and capsaicin.[1] Many other pharmacologic agents have been used to treat erythromelalgia including sodium channel blockers (lidocaine, mexiletine, carbamazepine, oxcarbazepine), sodium nitroprusside, antidepressants (fluoxetine, sertraline, venlafaxine, amitriptyline, duloxetine), anticonvulsants (gabapentin, pregabalin), high dose steroids and IVIG. Opioids were not found to be helpful in controlling pain. Procedural interventions have also been reported and range from injection of botulinum toxin, sympathetic blockade and implantation of spinal cord stimulators.[2]

The general approach to erythromelalgia is to establish the diagnosis clinically, rule out other potential etiologies, screen for an associated underlying disease process or genetic etiology, discuss trigger prevention and cooling measures, and then trial and error pharmacologic therapies to help manage symptoms.[2] In this case, the patient had years of symptoms prior to being diagnosed, had both underlying malignancy and autoimmune disease, and had tried and failed multiple treatments prior to finding a medication that helped with his condition. This just highlights the need to be able to recognize the disease, as well as the complexity of erythromelalgia and its management.

REFERENCES

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