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CLINICAL VIGNETTE

Hot and Red: Erythromelalgia

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Case Presentation

A 31-year-old female with no significant past medical history presented to urgent care for swollen, red toes bilaterally. There was an associated “tingling” pain up to 5/10 in intensity which lasted from a few minutes to a few hours. The toes get numb and discolored during these episodes. Usually the toes become red in color, but sometimes gain a purple hue as episodes are resolving. Symptoms first began 3 months ago, but are occurring much more frequently now in mid spring. Interestingly, the patient believes these episodes are triggered by heat. In fact, she can no longer take hot showers because that will trigger an episode. Symptoms, at first, occurred daily, but then decreased to about once a week. She finally decided to get evaluated because the frequency had again increased to nearly daily.

She does not recall any inciting events and tries to cool down her toes to improve symptoms. There are no skin changes and toes look normal when they are not turning red/purple or swollen. In fact, she has brought pictures of her toes at different stages. Her hands and fingers are never affected and no one in her family has had similar symptoms. Her mother has a history of hypothyroidism and father has a distant history of lung cancer. Review of systems is notable for dry mouth, and the patient chronically has dry eyes for the last 2 years. She also states that unless she sleeps 8 hours a night, she will be fatigued and have “foggy brain.” She takes ginkgo biloba, magnesium and a probiotic regularly, but no prescribed medications.

Physical Exam

Vital signs: Blood pressure is 110/68, heart rate 77, afebrile with RR of 18 and pulse ox of 97%. She is 5’6” and weighs 116lbs. The patient is pleasant, interactive, well-developed, well nourished, in no acute distress and with an overall unremarkable exam.

Lab Evaluation

Antinuclear Antibody: positive (1:80 nucleolar)
Unremarkable labs include: Urinalysis, Complete Blood Count with differential, Thyroid Stimulating Hormone, HIV, RPR, Erythrocyte Sedimentation Rate, C-Reactive Protein, Rheumatoid Factor DsDNA Antibody by EIA, nDNA (Crithidia) Antibody IFA, SSA/SSB, C3/C4 levels, Sm/RNP Antibodies, Scleroderma Antibody (SCL-70), DRVVT, Centromere B Antibody, Dilute Russel Viper Venom Test (DRVVT), Beta 2 Glycoprotein, and Cardiolipin Antibody

Case Summary

The pictures and description of symptoms were initially concerning for Raynaud’s phenomenon which occurs in 3-5% of the population. However, the patient’s symptoms are triggered by heat - not cold. Thus, EM rose to the top of the differential.

The patient was referred to a rheumatologist who agreed with the above diagnosis especially since the extensive lab evaluation was unrevealing. The patient’s chief complaint in addition to her other symptoms of dry eyes, dry mouth and fatigue in the setting of a mildly positive ANA could be an evolving presentation for a connective tissue disorder. However, it has now been over 15 months since the patient first presented to my office and no other progressive symptoms have arisen and labs have remained unchanged.

Discussion

Erythromelalgia is a rare clinical syndrome affecting less than 2 per 100,000 people per year from population-based studies involving the US, Sweden, and Norway.²⁻⁴ It is characterized by redness, heat, and pain in the extremities. Episodes of pain are intermittent with either days or years between the crises, and episodes may last within the range of minutes to hours. For the remainder of the time, the extremities appear normal and may actually be purple (acrocyanotic) and cool to the touch during the recovery phase. At this time, there is no cure for EM.

Symptoms most commonly manifest in the feet, followed by the hands, and rarely in the face. Specifically, EM most frequently presents in the palmoplantar region.¹ In addition to the palmoplantar region, presentation is high in the toes and fingertips. A study of 168 patients, conducted by Davis et. al, showed that 88.1% of cases involved the feet and 25.6% of cases involved the hands. Only one or two of the patients were symptomatic in facial regions, such as the ears.⁵

Warm ambient conditions can either exacerbate or trigger an episode. For this reason, many patients may feel pain at night when in bed or during periods of physical exertion, such as running and exercising. In a study of 51 cases, Babb et. al reported most patients described a burning, sharp, or stinging pain. One patient described the feeling, “as if one’s toes had been hammered repeatedly.”⁶

Due to its rarity and similar clinical manifestations to other syndromes, EM can be difficult to diagnose. The above patient

was asymptomatic during her visits but had taken photos of her feet while symptomatic. The intermittent nature, redness, heat, pain, and response to warm ambient temperatures are the main telling factors. Skin biopsy would only be helpful in ruling out other conditions, but would not be helpful in diagnosing EM as the histopathologic findings are nonspecific.⁷

Differential Diagnosis

Differential diagnoses include other conditions that cause pain in the extremities. Large or small fiber neuropathy could be in the differential, but may also be comorbid with EM. Peripheral vascular disease, other forms of vasculitis, Fabry disease, lipodermatosclerosis, acrocyanosis, Raynaud phenomenon, cellulitis, and other metabolic diseases that cause a discoloration or redness of the extremities could be included in the differential.⁸ Raynaud phenomenon and acrocyanosis can also be comorbid with EM as patients may have other vascular manifestations in between flares of EM.⁹

Disease Associations

There may be an association between EM and myeloproliferative diseases such as, essential thrombocytosis, chronic myelogenous leukemia, polycythemia vera, and myelofibrosis.⁵ The rates of association vary widely in the literature with some studies stating as that as many as 65% of patients who have essential thrombocythemia or polycythemia vera may present with EM.¹⁰ However, other studies report the incidence of EM between 3-20% amongst those suffering from myeloproliferative disorders.^{8,11}

Treatment

To date, there is no cure for EM. Thus, most treatment strategies revolve around symptom relief. Taking into account the association with myeloproliferative disease, it is advisable to obtain a complete blood count with differential to assess the potential of underlying myeloproliferative diseases that might necessitate treatment.

Conservative management includes avoid precipitating factors, limb elevation, and short exposure to cool water and fans (5-10 minutes every 2 hours). Some case reports and smaller studies have tried topical therapies and even systemic treatments with variable results. Topical options include lidocaine patches, capsaicin, amitriptyline, ketamine, and midodrine.¹²⁻¹⁴ Alternative systemic treatments include aspirin^{8,15} and treatments that target neuropathic pain such as: gabapentin,^{16,17} pregabalin,^{16,18} venlafaxine,¹⁹ oral amitriptyline,^{16,20} and steroids.¹⁸

Depending on the severity of the syndrome including the frequency of episodes, a patient's quality of life could significantly decrease. Patients may stop exercising or participating in physical activities. Even sleep can be affected as the warm ambience of a bed can precipitate an episode. Mental health services may need to be offered in addition to other treatment strategies.²¹

Conclusion

Overall, EM is an interesting and rare diagnosis. Clinicians should be aware of its unique and memorable presentation as it can cause a significant amount of distress and may be associated with an underlying vascular or myeloproliferative disorder. The key symptom: painful, red and inflamed extremities (usually feet) that are triggered by heat.

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