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Serial Misdiagnosis of Erythromelalgia in Bilateral Lower Extremities as Cellulitis

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Abstract

Objective

The purpose of this case report is to describe the presentation and initial misdiagnosis of erythromelalgia in a 61-year-old woman in an urgent care and outpatient clinic.

Clinical Features

The patient's chief complaint was rapid-onset pain and erythema of the right foot following a fall, with initial presentation to a rural urgent care. A plain film radiograph of the right foot was negative for acute fracture or dislocation. A diagnosis of cellulitis of right foot was suggested based on the presentation of frank erythema, pain and pruritus of the right foot. This diagnosis was assumed despite a lack of comorbid diagnosis of diabetes mellitus or history of gout in the patient, denial of penetrating trauma to the extremities, and lack of fever or other systemic symptoms.

Intervention and Outcome

The patient was suspected to have cellulitis of the right lower extremity with an unknown inciting factor. The patient was given oral cephalexin 500 mg three times daily (TID) for seven days; and was advised to return to the clinic if resolution was not achieved. The patient was adherent with outpatient treatment yet returned to the urgent care 1 week later with symptoms of left toe redness, edema and pain. She was suspected to have resistant cellulitis of bilateral feet and was treated with sulfamethoxazole-trimethoprim 800-160 mg twice daily (BID) for fourteen days. The patient did not seek further medical attention until a routine visit with her primary care physician five months later. At this time, she described the episodes which her provider believed were misdiagnosed, and erythromelalgia was considered.

Conclusion

The incident revealed that for this female patient with suspected erythromelalgia of the feet, serial misdiagnosis of her condition as cellulitis, and treatment with antibiotics was insufficient to resolve symptoms. Considerations to improve care are patient education and routine follow-up with a primary care physician. This would establish continuity and identify a lack of response to treatment requiring more extensive investigation. Failure of symptom resolution despite treatment with antibiotics and instead, successful resolution with time, temperature change and elevation suggest an alternative diagnosis of erythromelalgia for the patient.

Keywords: Erythromelalgia, Cellulitis, Autoimmune Disease, Infectious, Skin Infection, Erythema

Introduction

Erythromelalgia is a rare, often-underdiagnosed condition affecting the skin [8]. It is classically recognized based on the triad of erythema, warmth, and pruritus. Skin findings can occur anywhere on the body but are typically found on bilateral extremities. Erythromelalgia can be suspected in patients presenting without a history of trauma or prior infection to an area. There are primary and secondary and causes, though limited data is available. Classification of erythromelalgia is based on relation to myeloproliferative disorders, inherited disorders, or response to aspirin. Primary erythromelalgia is thought to occur within the first two decades of life and may be idiopathic or inherited. Suspected pathophysiology includes sodium channel dysfunction [5, 6, 8]. In contrast, secondary erythromelalgia typically occurs later in life, and may be related to myeloproliferative disorders or autoimmune disease. Suspected pathophysiology includes platelet dysfunction and other, unknown mechanisms. Many researchers believe erythromelalgia has a female predominance, and children, though rarely affected, have a poor prognosis [2, 3]. In terms of cases by gender, a 3:1 female to male ratio was observed in a New Zealand study [3]. The diagnosis is rare, with 0.36–2 cases per 100,000 people estimated to occur each year in both the United States and Europe [1, 8].

Most incidents occur in bilateral feet and are related to triggers such as heat, standing, tightly fitting clothing and exercise. Diagnosis is largely history-based, and treatment includes avoidance of inciting factors, decreasing activity, extremity elevation and cooler temperatures. Myeloproliferative variants may be responsive to aspirin and topical therapies such as lidocaine or capsaicin [8].

The misdiagnosis of erythromelalgia as cellulitis is not commonly reported in the literature, possibly because erythromelalgia is rare itself. The purpose of this case report is to describe the serial misdiagnosis of erythromelalgia as cellulitis in a 61-year-old female at an urgent care clinic.

Description of the case report

A 61-year-old female presented to a rural urgent care clinic with an initial chief complaint of "itchy, painful swelling" and erythema of her right foot for two days. She noticed that the redness began suddenly after wearing sandals outdoors in the summer heat and falling. She denied any fever, chills, or systemic symptoms. She denied penetrating trauma to the region or a history of infection.

Her past medical history revealed no allergies and no changes in food or topical creams. Current medications taken by the patient included Celecoxib 200 mg BID, Omeprazole 20 mg DR daily, and Fluoxetine 40 mg daily. She denied recent hospitalizations. Her only medical conditions were chronic back pain, osteoarthritis, and hypertension.

The physical examination findings at her first visit were as follows: vital signs: temperature: 99.1 °F, pulse: 95 beats per minute, respirations: 24 per minute, oxygen saturation: 94% on room air, blood pressure: 114/73. Her musculoskeletal exam was grossly normal, with intact ROM and strength. Examination of her extremities revealed: 2+ pitting edema of the right foot, 2+ distal pulses, erythema, and increased warmth of the dorsal aspect of right foot. A negative Homan's sign was appreciated. In addition, there was no evidence of open wounds, evidence of trauma, purulence, or skin-breaks.

Despite lack of penetrating trauma, fever or comorbid diabetes mellitus, the patient's rapid-onset, painful condition was suspected to be cellulitis. Differential diagnosis included: gout, Raynaud's phenomenon, local trauma, vasculopathy and complex regional pain syndrome. The patient remained in the urgent care under observation until a random glucose sample collected revealed 104 mg/dL. Patient's hemoglobin A1c two months ago had fallen in the prediabetic range <6.0%.

A plain film radiograph of her right foot was negative for acute fracture or dislocation. Though the results were not strongly suggestive of acute infection, differentials were limited and therefore antibiotic therapy was initiated. The patient was sent home with oral cephalexin 500 mg TID for seven days and was advised to return should her condition deteriorate.

One week later, the patient returned to the urgent care with additional symptoms of left third-toe edema, erythema, and pain. The patient had been adherent to outpatient treatment, and therefore was suspected to have resistant cellulitis of bilateral feet. She was prescribed sulfamethoxazole-trimethoprim 800-160 mg BID for fourteen days.

The patient did not seek further care until a routine visit with her primary care physician months later. Though she did not take photos, at this time, the patient described the episodes to her physician and their eventual resolution. The patient stated that the redness and swelling improved after several months of non-pharmacologic treatment. She revealed experiencing relief after consistent interventions such ice baths, cold compresses, and elevation of the extremities. She also believed that the resolution correlated with the onset of a season change, as the colder winter temperatures helped reduce the pain and skin changes originally noted in the summer months. After a review of urgent care records and a detailed patient history, the primary care physician believed the patient had been misdiagnosed, and erythromelalgia was finally considered.

Discussion

As the etiology of erythromelalgia remains elusive in many cases, the treatment remains difficult as well. While the established link with myeloproliferative disease contributes to correction of the underlying illness for secondary erythromelalgia, the often-idiopathic cause of primary erythromelalgia hinders adequate medical management. The diagnosis of erythromelalgia is predominantly history-based without routine use of biopsy or other specific diagnostic criteria. The diagnosis is typically concluded based on erythema, pain and warmth of extremities which improves with cold and is exacerbated by heat.

Differential diagnoses which may cloud the accurate diagnosis and treatment of erythromelalgia include cellulitis, gout, Fabry's disease, autoimmune diseases, polyneuropathy or complications of diabetic nephropathy, and inflammatory processes due to local trauma [7]. Ruling out cellulitis includes careful history taking to evaluate traumatic, penetrating injury to the area and watching for resolution with an appropriate antibiotic regimen. The patient denied a history of penetrating wounds, and there was no evidence of skin breaking or purulence at the site of inflammation. In addition, she was afebrile, denied systemic symptoms and had bilateral erythema and edema, which would be a rare presentation for cellulitis. No laboratory work was drawn to measure a complete blood count in the patient, but she failed to improve with either antibiotic prescription. Inclusion of a complete blood count would have also helped rule out a myeloproliferative etiology. Ruling out gouty arthritis includes obtaining blood levels of uric acid, arthrocentesis, and analyzation of the joint fluid, and considering a history of gout. The patient in question did not have a history of gout flares, and her atypical presentation of redness in bilateral feet without pain and erythema of either great toe was not highly suggestive of gout. Fabry's disease would likely be accompanied by angiokeratomas and corneal opacities. To rule out complex regional pain syndrome (CRPS), it is important to note symmetry and location on a limb. In our 61-year-old female, symptoms were bilateral and more distal on the lower extremities. In contrast, CRPS is typically unilateral, proximal, and triggered by trauma to the area [4].

The consideration of autoimmune diseases was not entirely investigated and may be important in future workup, as one hypothesized etiology of erythromelalgia is suspected to be autoimmune in nature. However, the patient did not have a history of autoimmune disease, nor had she complained of any systemic symptoms, fatigue, or other joint pain. Possible laboratory workup might evaluate for the presence or absence of inflammatory markers such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), ANA, HLA-B27, or anti-cyclic citrullinated peptide (anti-CCP) antibody, among others. An investigation of rheumatoid arthritis or the seronegative spondyloarthropathies (ankylosing spondylitis, psoriatic, reactive or IBD-related arthritis), systemic lupus erythematosus, or other vasculopathies was not deemed clinically necessary and therefore, was not performed.

In terms of erythromelalgia treatment, pharmacologic interventions with uncertain evidence include trial of aspirin, opioids, immunosuppressants, NSAIDS, sodium-channel blockers, anticonvulsants, antidepressants among others. Studies continue to investigate patient response to multi-drug regimens. In addition, as evidenced anecdotally with this patient's case, non-medication-based therapy can be beneficial. Interventions include removing potential triggers such as exercise, excessive heat, and stress. Additionally, patients have tried cold therapy with measurable benefit [8].

More research needs to be done to clarify the pathophysiology behind erythromelalgia to enhance treatment options. Current areas include the genetic component, sodium channels, platelets and myeloproliferative disorders, and autoimmune and connective tissue diseases [1, 7]. The differential diagnoses of erythromelalgia should be ruled out prior to considering watchful waiting as a treatment option.

Conclusion

This presentation demonstrated that for this patient with suspected erythromelalgia of the feet, serial misdiagnosis of her condition as cellulitis and treatment with antibiotics was insufficient to resolve symptoms. Her bilateral involvement of symptoms is typical for erythromelalgia and exceedingly rare for cellulitis. Considerations to improve care are patient education, routine follow up with a primary care physician, more comprehensive lab workup, and referral to rheumatology when symptoms persist with first line, standard treatment. This would establish continuity, especially given the lack of response to treatment requiring more extensive investigation. Failure of symptom resolution despite treatment with antibiotics and instead, successful resolution with time, temperature change and elevation suggest a diagnosis of erythromelalgia for the patient.

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