CASE STUDIES

Managing late onset primary erythromelalgia with oral pregabalin

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Abstract

Erythromelalgia, a rare vascular peripheral pain disorder characterized by erythema, warmth and severe burning pain of the distal extremities, more commonly affects the feet than hands. Generally, the worsening of the pain is noted with increase in temperature and exercise. In the absence of treatment, the disease episodes may last infinitely and are quite debilitating. Measures such as resting, elevation and cooling of involved extremities are typically adopted to relive pain. Previous case studies have reported symptomatic improvement with aspirin, vasodilators, beta-blockers, local anesthetics and gabapentin. Here we report the case of a 34-year-old army officer suffering from erythromelalgia for the 8 years, which was earlier misdiagnosed as plantar fasciitis. All previously described treatments were ineffective but oral pregabalin proved very effective in reducing the frequency and severity of pain episodes.

Keywords: Erythromelalgia, pregabalin

Introduction

Erythromelalgia (EM), a rare and chronic condition of unknown etiology, is characterized by recurrent intense burning pain in extremities associated with erythema and increased skin temperature. Warmth or heat intensifies the discomfort, while cold provides symptomatic relief.[1] The pathogenesis of erythromelalgia has been a matter of debate. The primary EM may occur due to mutation of voltage-gated sodium channel α-subunit gene *SCN9A* and the secondary may be associated with various disorders like thrombocytopenia, essential thrombocytosis, polycythemia, mushroom or mercury poisoning, myeloproliferative disorders, hypertension, vasculitis, systemic lupus erythematous, scleroderma, rheumatoid arthritis, Raynaud's disease, HIV and gout.[2] The disease is not associated with any sexual preponderance and is often intermittent in nature.

Primary EM, which can be of early or late onset, is most common in patients >20 years of age. The adult onset erythromelalgia is mostly idiopathic. The present study focuses on a case of late-onset primary erythromelalgia, which was earlier misdiagnosed as plantar fasciitis and the subsequent administration of oral pregabalin had contributed to a marked relief in symptoms.

Case report

A 34-year-old male who was a soldier by profession presented to the pain clinic with an 8-year history of painful recurrent erythema over bilateral hands and feet (Fig. 1 and 2) . A visual analogue score of 7/10 was noted. There was no history of trauma, fever or any infection. The pain aggravated with increase in temperature and exercise, and sometimes the pain impaired him from performing daily army conditioning drills. Soaking legs in cold water used to temporarily relive the pain. Drug history revealed no significant response of pain to NSAIDs (ibuprofen, aspirin), opiates, and amitriptyline. He was unable to bear weight on feet and had sleep disturbance. Pain used to get temporarily relieved by soaking legs in cold water. Patient also complained of occasional pain, redness and warmth over both hands, though it was not seen at the time of presentation. The evaluation of history indicated that the patient was misdiagnosed as plantar fasciitis and was on rehabilitation program for nearly 8 years. On examination, there was edema, localized grade II tenderness over erythematous area, normal range of motion, and he was afebrile with local warmth. Dorsalis pedis and posterior tibial pulses were all brisk bilaterally.

Evaluation for plantar fasciitis, malignancy, immune diseases and blood dyscrasia was negative. The patient

was non-diabetic, non-hypertensive, and euthyroid with no significant family history of similar pain.

Blood investigations were unremarkable. Anti-nuclear antibodies, CRP, ANA, RA factor, anti-CCP, uric acid, prothrombin time, activated partial thromboplastin time, serum fibrinogen, and platelet count were within the normal limits. There was no evidence of liver and kidney dysfunctions. There was no abnormal electrocardiographic pattern and history of radiation exposure.

Based on these findings, the diagnosis was concluded as late onset primary erythromelalgia of unknown origin. Treatment of the patient was initiated with a short course of oral deflazacort 6 mg twice daily for 1 week and oral pregabalin 150 mg daily in divided doses. From the ergonomic point of view, he was transferred from infantry division to administration. After 7 days, the patient reported a reduction in VAS score (from 7/10 to 2/10), and relief in erythema, swelling and tenderness. For the subsequent weeks, he was only on oral pregabalin 150 mg and his symptoms continued to improve, and within 1 month, the dose was reduced to 75 mg. For the past 4 months, the patient was receiving pregabalin 75 mg and it helped in reducing the frequency of duration and intensity of pain and erythema.

Discussion

Erythromelalgia (erythro = red, melos = limb, algos = pain) is characterized by burning discomfort, warmth and dermal erythema of the feet and/or the hands. Despite many proposed etiologies, the exact etiopathogenesis remains poorly understood. Drenth and Michiels classified the condition into 3 categories i.e, erythromelalgia (platelet-mediated and aspirin-sensitive), primary erythromelalgia, and secondary erythromelalgia.[3] Symptoms are often

Fig.1: Dermal erythema of feet

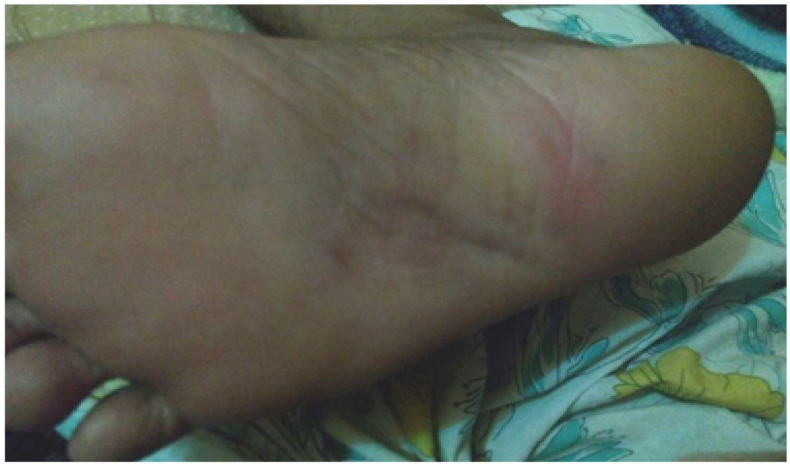
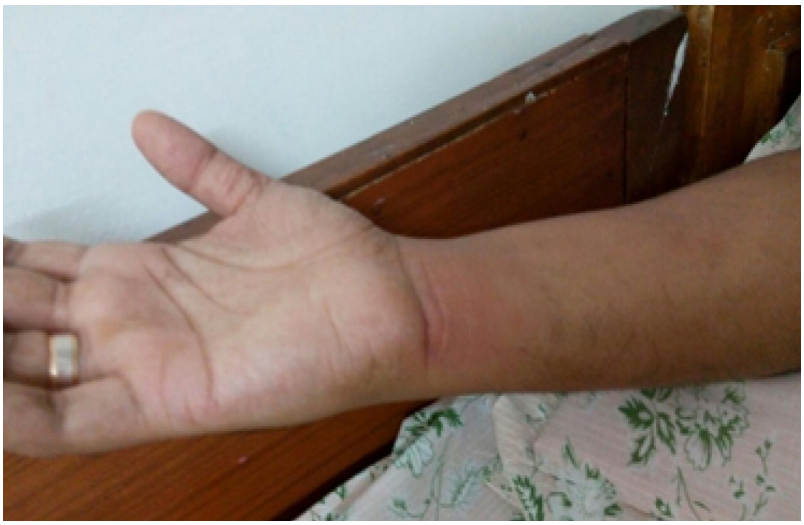


Fig. 2: Dermal erythema of hand



triggered by minor trauma, exercises or heat exposure and relieved by cooling and elevation of the limb. Pain due to erythromelalgia is often resistant to a range of analgesic therapies. Symptomatic responses have been reported to aspirin therapy (for erythromelalgia related to thrombocytosis), sodium nitroprusside, propranolol, high dose magnesium, lignocaine patch, amitriptyline and gabapentin.[4-8]

The involvement of secondary causes must be ruled out in cases with confirmed diagnosis. Erythromelalgia can be associated with SLE, Raynaud's disease, pernicious anemia, thrombotic thrombocytopenic purpura, infectious mononucleosis, metabolic, endocrine, and vascular origin and diabetic neuropathy. In the present case, appropriate testing was done to exclude all these conditions. Factors that may contribute to primary erythromelalgia include: postganglionic sympathetic dysfunction, hypersensitivity of C-fibers or/and maldistribution of skin perfusion caused by arteriovenous shunting.[9]

Presence of mechanical allodynia/hyperalgesia in affected area and ineffectiveness of opiate analgesics raised the suspicion of neuropathic pain mechanism. Pregabalin is a relatively safe anticonvulsant indicated for managing neuropathic and chronic pain conditions. The most common adverse events of pregabalin are dizziness, peripheral edema, weight gain and somnolence. The patients generally develop tolerance to these events.

The mechanism of action of pregabalin and gabapentin are almost similar, i.e inhibiting calcium influx and subsequent release of excitatory neurotransmitters. But pregabalin possess definite advantages over gabapentin. Bockbrader *et al.* have noted that pregabalin is found to have approximately 2.5 times greater potency than gabapentin based on plasma concentrations to treat neuropathic pain. The efficacy of pregabalin is comparable to gabapentin, however, at much lower doses. The probable reasons for the lower doses are much higher bioavailability (90% versus 33-66%) and rapid absorption (peak: 1 hr). Moreover, plasma concentrations increase linearly with dose. However, these do not hold true for gabapentin. The absorption rate of gabapentin is comparatively slower (peak: 3 to 4 hours post dose) and the association between plasma concentrations and increasing doses has been found to be non-linear.[10]

The present patient demonstrated immediate as well as long-term response to pregabalin administration in erythromelalgia. The initial and dramatic response to deflazacort and pregabalin might be due to placebo or steroid effect. However, long-term maintenance was achieved by pregabalin. The disappearance of tenderness over erythematous area (allodynia/hyperalgesia symptoms) shows that pregabalin is useful for managing neuropathic pain mechanism.

In conclusion, we report a successful management of erythromelalgia pain with pregabalin. Since the drug is relatively safe and well tolerated, it is better to initiate the treatment of erythromelalgia with pregabalin before considering more aggressive alternatives.

Competing interests

The authors declare that they have no competing interests.

Citation

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