

Phototoxic Rash during Therapy with Pramipexole in a Patient with Restless Legs Syndrome

طفح عند التعرض لضوء الشمس خلال علاج المريض بمتلازمة قململ
الساقين

Sir,

Drug-related phototoxic reaction is a well-established clinical entity. Historically, antineoplastic cytotoxic agents such as actinomycin C, doxorubicin, and fluoroquinolones are the most common drugs to cause phototoxic reactions in humans.¹ Dopamine agonists, ropinirole, and pramipexole are considered the first line of treatment for restless legs syndrome (RLS) in current evidenced-based guidelines, and to the best of our knowledge, no dermatological side-effects have been described in association with its use.² We describe a case of a man with RLS who developed a rare photosensitive rash due to pramipexole.

A 57-year-old male presented to the Department of Dermatology at San Cecilio University Hospital, Granada, Spain, with a 3-day history of itchy, erythematous rash and swelling on his face and arms. Other complaints included breathlessness and dysphonia. He had a past medical history of thyroidectomy and subsequent hypothyroidism, for which he took daily thyroxine. Two weeks before the rash had started, he had been diagnosed with RLS in the Neurology Department of our hospital, and a nightly dose of 0.3 mg of pramipexole had been prescribed.

On clinical examination, patchy macular erythematous plaques were noted [Figure 1]. The reaction was isolated to the photo-exposed aspects of his arms. Maculopapular erythema with oedema was observed on his face [Figure 2]. Blood tests revealed high C-reactive protein levels, an elevated erythrocyte sedimentation rate, and eosinophilia. His level of immunoglobulin E was also elevated. Biopsy of one lesion showed necrotic keratinocytes, an infiltration of lymphocyte associated with oedema, and vasodilation. A drug-induced phototoxic reaction was considered and pramipexole was discontinued. Intravenous hydration, steroids, and antihistamines were started. Symptoms and lesions cleared in the first 6 hours and resolved completely in 3 weeks with oral prednisone (1 mg/kg/day) and the use of strict photoprotection. Prednisone was gradually



Figure 2: Maculo-papular erythema with oedema as observed on eyelids.



Figure 1: Phototoxic reaction involving arms in a patient under treatment with pramipexole for his restless legs syndrome.

reduced and eventually discontinued. Upon follow-up, the patient began treatment with gabapentin (200 mg/day) for the RLS. He is free of lesions and no recurrence has been observed.

Drug-induced photosensitivity may be photoallergic or phototoxic. Phototoxic reactions do not require prior exposure and are dependent both on the drug dosage and the amount of the patient's ultraviolet light (UVL) exposure. Thus, a high dose of a photosensitising medication combined with prolonged and/or intense UVL exposure may result in erythema and oedema, resembling acute sunburn.³ Pramipexole is a non-ergoline dopamine agonist with a high selectivity for D2 and D3 receptors whose efficacy for RLS has been confirmed in different studies.⁴⁻⁶ It is usually well tolerated. In all the studies examined, the discontinuation rate (~20%) was similar, and the incidence of adverse events was not clearly dose-related. The most frequent adverse reaction was nausea, followed by fatigue, dizziness, headache, diarrhoea, nasopharyngitis, orthostatic hypotension, and increased body weight. While uncommon, the dermatological side-effects are described by the makers of pramipexole in the drug manufacturers' documents and on the European Medicines Agency's website.⁷ According to this information, hypersensitive reactions like exanthema and pruritus have been associated with the use of pramipexole. However, no clinical reports regarding photosensitivity or phototoxic reactions associated with pramipexole have been found. It is suggested that the prevalence of side-effects decreases significantly in long-term treatment (2.6%) as compared with early treatment.⁴⁻⁶ However, in our patient we decided to discontinue the therapy because of the severity of his rash. Systemic re-exposition to the offending drug remains the gold standard for diagnosis, but that was not considered in this case due to the possibility of a life-threatening adverse reaction. Instead, because our patient had been on pramipexole within the two weeks prior to the start of his rash, we suspected that pramipexole was the culprit in this patient's skin reaction. A photo patch test was suggested to confirm our clinical suspicion, but it was declined by the patient. Finally, while in our case there was a definite cause-effect correlation between the onset of rash and the initiation of pramipexole, we were not able to confirm this diagnosis; thus, our hypothesis is more probabilistic than direct. To the best of our knowledge, this is the first case of phototoxic reaction induced by pramipexole.

Husein H. ElAhmed

Department of Dermatology, San Cecilio University Hospital, Granada, Spain

E-mail: huseinelahmed@hotmail.com

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