



Case Report

Vasculitic Skin Eruption Due To Rivastigmine Patch: A Case Report

Aslı F. KAPTANOĞLU¹, H. İlker İPEKDAL², Cem ÇOMUNOĞLU³, Amber EKER²

¹Near East University Hospital, Department of Dermatology, Nicosia, Cyprus ²Near East University Hospital, Department of Neurology, Nicosia, Cyprus ³Near East University Hospital, Department of Pathology, Nicosia, Cyprus

Abstract

Rivastigmine transdermal patches can provide non-invasive, continuous drug delivery, and offer significant potential advantages over oral treatments. However, the most common side effects of transdermal patch form is local skin reactions. A 75-years old female patient developed itching after the initiation of rivastigmine transdermal patch. Multiple, erythematous infiltrated annular plaques with significant borders (identical in shape with the patch) and generalised, excoriated erythematous papules, in addition to the lichenified excoriated plaques on both legs were detected in her physical examination. Histopathological examination of the skin biopsy which was performed from the lesions revealed leucocytoclastic vasculitis showing spongiosis and leucocyte deposition around the vessels. She responded to topical potent steroids and systemic antihistamines and recovered completely within a month. This is the first case of rivastigmine transdermal patch induced vasculitic skin eruption which was located in both application and non-application sites.

Keywords: Rivastigmine, drug eruption

Rivastigmine Transdermal Flastere Bağlı Vaskülitik Deri Döküntüsü: Bir Olgu Sunumu

Özet

Rivastigmine transdermal flasterler, ilacın sürekli ve non-invaziv verilmesini sağlamaları sayesinde ağız yoluyla verilen tedavilere nazaran önemli üstünlük sergilemektedirler. Bununla birlikte, transdermal flasterin en sık görülen yan etkisi lokal cilt reaksiyonlarıdır. 75 yaşındaki bir bayan hastada, rivastigmin flaster uygulamasının ardından kaşıntı gelişti. Fizik muayenesinde, keskin sınırları olan (flasterin şekli ile özdeş) yuvarlak, çok sayıda eritematöz plaklara ve bacaklardaki likenifiye ekskoriyasyonlu plaklara ek olarak jeneralize ekskoriyasyonlu eritematöz papüller tespit edildi. Topikal potent steroidlere ve sistemik antihistaminiklere cevap veren hasta, bir ay içerisinde tamamen düzeldi. Bu olgu, rivastigmin transdermal flasterin neden olduğu, hem uygulama bölgesinde hem de uygulama bölgesinin dışında lokalize olan ilk vaskülitik cilt döküntüsü olgusudur.

Anahtar Kelimeler: Rivastigmine, ilaç erüpsiyonu

INTRODUCTION

Rivastigmine is a second generation cholinesterase inhibitor which is approved for symptomatic treatment of mild to moderately severe Alzheimer's Disease and Parkinson's Disease dementia⁽⁵⁾. It can be

administered orally or via a transdermal patch. Difficulty in accessing therapeutic doses, poor patient compliance and gastrointestinal side effects have been identified as barriers to effective treatment with orally administered rivastigmine and other cholinesterase inhibitors. The

rivastigmine transdermal patch (RTP) provides steady delivery of drug through the skin into the bloodstream, and avoids the fluctuations in plasma concentration related with oral administration⁽⁷⁾. This pharmacokinetic profile of rivastigmine is associated with reduced adverse effects and well tolerability, however, transdermal administration of rivastigmine may result with dermatological complications. Itching, irritation, erythema and pruritus at site of patch have been the most commonly reported skin reactions for RTP^(4,8,13). This current case demonstrates a generalized vasculitic skin eruption as a complication of RTP application.

CASE PRESENTATION

A 75-years-old female patient admitted to dermatology department with a complaint of itching which started 2 months ago. It continued and increased since then. Severity of itching showed no difference between day and night. Her past medical history revealed that she was under the medication of metoprolol 25 mg once daily, lisinopril 20 mg once daily and amlodipine 10 mg once daily for hypertension and arrhythmia for the last 10 years. Additionally, she was prescribed rivastigmine with a diagnose of Alzheimer's disease 4 months ago. As she

couldn't tolerate the pills because of gastric intolerance, a new patch form of rivastigmine was initiated 2 months ago (rivastigmine 9.5 mg/24 h patch). After that, her itching started and aggravated day by day. At the beginning, skin lesions were located only at the application site but then itching got generalized. On her physical examination there were multiple, erythematous infiltrated annular plaques of 2.5 cm in diameter with significant borders and identical shaped with the RTP and generalised, excoriated erythematous papules of 0.5-1 cm in diameter, in addition to the lichenified excoriated plaques on both legs (Figures 1 and 2). Her systemic examination was normal. Slight elevation in Ig E was detected in her blood test. Her sedimentation rate, C-reactive protein level, liver enzymes, and complete blood counting, complement-3 and 4 levels were all normal. Antinuclear antibody was negative. Histopathological examination of the skin biopsy which was performed from the lesions revealed leucocytoclastic vasculitis showing spongiosis and leucocyte deposition around the vessels. She was consulted by neurology and her rivastigmin patch medication was stopped. She responded to topical potent steroids and systemic antihistamines and recovered completely within a month.

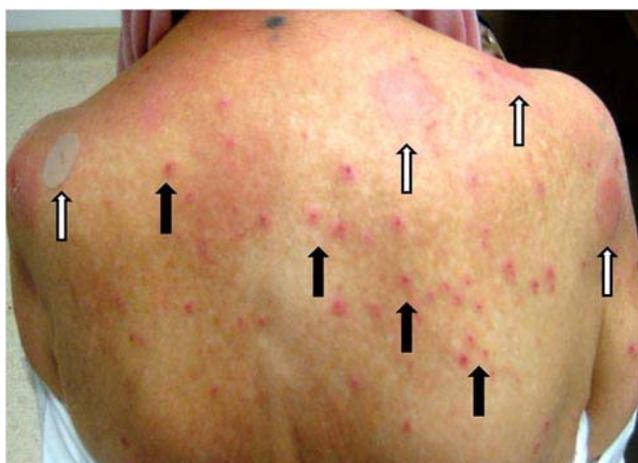


Figure 1: Erythematous infiltrated annular plaques (white arrows) and excoriated erythematous papules (black arrows).



Figure 2: Closer view of the erythematous infiltrated annular plaque (white arrow) and excoriated erythematous papules surrounded to this plaque (black arrows).

DISCUSSION

RTP was approved in July 2007 in US. In the patient information web site of RTP, it is recommended to apply to clean, dry, hairless, intact skin for every 24 hours at the same time of day and not to apply to skin that is red, irritated, or has cuts.

Clinical experience suggests that the most common form of skin irritation is erythema caused by removal of the patch, which normally resolves after a short period of time⁽¹⁷⁾. In order to reduce the frequency of skin reactions, daily rotation of patch has been recommended. In the IDEAL trial, the signs or symptoms that were most frequently reported as moderate or severe were erythema (redness; 8% for the 9.5 mg/24 h rivastigmine patch, up to 4% for placebo) and pruritus (itching; 7% for the 9.5 mg/24 h rivastigmine patch, up to 3% for placebo)⁽¹⁶⁾.

Drugs may elicit a considerable variety of clinical signs, often affecting the skin and the mucous membranes. The most common are maculopapular exanthemas and urticaria, more rarely pustules, vasculitic lesions, and lichenoid lesions may also be observed. Although these side effects are related with systemic

administration of drugs, topical drugs may also cause side effects.

Topical drug applications are developing by technologic developments. Patch applications are called transdermal therapeutic system (TTS). As TTS supply many advantages like drug delivery in a rate-controlled manner, sustained plasma concentrations and avoiding first pass metabolism⁽¹¹⁾. There TTS forms of many drugs such as hormones, nicotine, nitroglycerine and analgesics. By the increased use of this systems new drug reactions related to application site are reported^(10,11,14,15,18). TTS-treatment may induce contact allergies to pharmaceutical agents, as has already been described in other observations on allergies to haptens⁽⁶⁾. Also, TTSs can induce sensitisation in many ways. As long-time occlusion, irritation and repeated application of the allergen to the same skin location will maximize the development of hypersensitivity reaction. The mechanism of IgE-mediated reactions is well investigated, but the mechanisms of T-cell-mediated drug hypersensitivity are not well understood.

During the RTP treatment, our patient was also under the treatment of metoprolol, lisinopril and amlodipine for hypertension. No interaction with metoprolol, amlodipine or lisinopril has been reported for RTP. However, erythema multiforme associated with metoprolol succinate and amlodipine therapies and angioedema and erythroderma associated with lisinopril therapy have been reported^(1,2,3,9). Because of the potential skin side effects of these agents, it is controversial whether the skin lesions of our patient are related with antihypertensive treatment and/or RTP. It can also be argued that these antihypertensive agents may have caused hypersensitization to RTP. We think that histological and morphological characteristics, locations and the time of onset of the patient's lesions are suggestive for the skin reaction secondary to RTP. Although the lesions are not limited to the sites to where the RTP was applied, this may be the result of systemic effect of rivastigmine due to a specific sensitization in our patient. Grieco et al. have reported a 75-year-old male patient with recurrent lesions in previous application skin sites who was under the treatment of RTP⁽⁸⁾. They suggested this clinical condition as a specific sensitization to RTP.

The characteristic feature that differs our case from the previously reported RTP-induced skin reactions is that in our patient, the eruptions were occurred not only in the application sites but also in the non-application sites which were not under the direct effect of RTP. This condition also supports the specific sensitization to RTP and generalization of sensitization by continued contact with the antigen.

Although the data supports a favourable skin tolerability profile for the RTP, physicians must be aware of possible unexpected skin reactions after the application. To our knowledge, this is the first case of RTP induced vasculitic skin eruption which was located both in application and non-application sites.

Correspondence to:

Hüseyin İlker İpekdağ

E-mail: iipekdağ@yahoo.com

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