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CASE REPORT

Rash associated with Pregabalin: A case report

Pregabalin ilişkili döküntü: Olgu sunumu

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ABSTRACT

A 48-year-old man with erythematous, maculopapular rash localized to his extremities and lumbar region that he had been receiving oral pregabalin 300 mg per day for 2 months to treat his neuropathy was applied. The Naranjo probability scale indicates a probable relationship between the development of rash and use of pregabalin by our patient. Pregabalin was discontinued and antihistaminic treatment, oral methyprednisolone and topical steroid cream were given to treat the rash. The rash almost completely resolved one week after pregabalin was discontinued. Pregabalin-induced rash was rarely reported in Phase 3 clinical trials, and there is currently only one available report on the development of a rash coinciding with the use of pregabalin. No clear mechanisms reported for rash associated with pregabalin. It is usually recommended to start pregabalin with low doses and slow increases might prevent the incidence of side effects. *J Clin Exp Invest 2013; 4 (1): 107-109*

Key words: pregabalin, rash, multiple myelom

ÖZET

Kırksekiz yaşında ve 2 aydır nöropati tedavisi için 300 mg/gün oral yolla pregabalin kullanan erkek hasta, ekstremiteler ve lomber bölgesinde eritematöz, makülopapüler döküntü şikayeti ile başvurdu. Naranjo olasılık skalası döküntü ve pregabalin kullanımı arasında muhtemel bir ilişkiyi gösterdi. Pregabalin tedavisi kesilerek, antihistaminik tedavi, oral metilprednizolon ve topical steroidli krem başlandı. Tedavinin kesilmesinden 1 hafta sonra döküntü neredeyse tamamen düzeldi. Pregabalin ilişkili döküntü faz 3 klinik çalışmalarda nadiren rapor edilmiştir. Pregabalin kullanımına eşlik eden döküntü daha önce yalnızca bir vaka raporunda sunulmuştur. Pregabalin ilişkili döküntünün mekanizması tam olarak anlaşılamamıştır. Düşük dozlarda pregabalin tedavisine başlamak ve doz artımını yavaş yapmak yan etki insidansını azaltabilir.

Anahtar kelimeler: pregabalin, döküntü, multipl myelom

INTRODUCTION

Pregabalin is a new synthetic analog of γ-aminobutyric acid. The precise mode of action of pregabalin has not been fully elucidated; it possibly does interact with α2δ presynaptic voltage gated calcium channels and reduces the release of several neurotransmitters.[1] It's approved for the treatment of neuropathic pain associated with diabetic peripheral neuropathy, and postherpetic neuralgia.

Pregabalin is generally well tolerated. It's side effects are usually mild-to-moderate in intensity and are usually transient.[1] Dizziness and somnolence are the most frequent adverse reactions for drug withdrawal.[2] The discontinuation rate due to adverse events varies across studies, but it is approximately 17% for patients receiving pregabalin (depending on dose) compared to 6.3% for patients receiving placebo.[3]

The adverse effect profiles of most antiepileptic drugs include rash. Gabapentin, an antiepileptic drug used in neuropathic pain, may cause rash during treatment.[4,5] Because of the similar molecular structure with pregabalin, hypersensitivity reactions can possibly be observed during pregabalin treatment. However, we could find only one published report in describing the development of rash due to Pregabalin.[6] Herein, we present a second patient who developed an extensive rash one week after beginning pregabalin therapy for neuropathy.

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CASE

A 48-year-old man presented with malaise and backache. Anemia and increased erytrocyte sedimentation rate was noted. Bone scan showed osteolytic lesions on the clavicula, right radius and 9th-10th ribs. Evaluation for the suspicion of multipl myeloma showed light chain kappa in serum and urinary protein electrophoresis. Diffuse neoplastic plasma cell infiltration was documented in the bone marrow biopsy and aspiration. After the diagnosis of multipl myeloma, then the patient was treated with vincristine 0.4 mg, adriamycin 9 mg/m^2 and dexamethasone 40 mg (VAD) chemotherapy. After 2 cycles of VAD chemotherapy, he received bortezomib 1.3 mg/m2, adriamycin 9 mg/m^2, dexamethasone 40 mg (PAD). After 4 cycles of PAD chemotherapy, the patient received autologous bone marrow transplantation on October 2010.

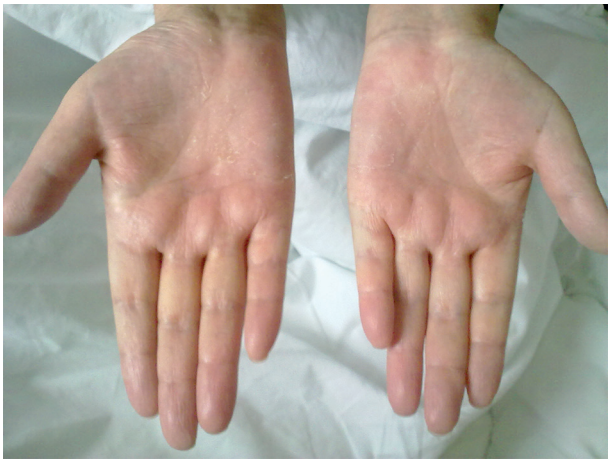

Figure 1. Bilateral palmar eritematous rash

After his chemotherapy regimen, the patient developed palmar-plantar pain and hypoesthesia. In neurological evaluation, electromyography showed mild polyneuropathy with axonal involvement of the sensory neurons. The polyneuropathy was probably associated with vincristin therapy and the patient was than treated with pregabalin (Lyrica, Pfizer). The starting dose was 150 mg po daily and increased gradually to 300 mg daily. Initially there were no adverse effects. However, on the 7th day of treatment, a maculopapular rash, without itching, has started, then increased, and spread over his wrist and progressed to the proximal arm and palms (Figure 1). Rash also occured over the lumbar region and proximal thigh (Figure 2). No mucosal lesion was seen. After dermatological evaluation, the rash was associated with recently started drug, pregabalin. Pregabalin was then discontinued and systemic antihistaminic treatment, methylprednisolone (20 mg/day, for 10 days) and topical steroid cream 2-3 times daily were initiated. His rash over the lumbar region and proximal arm abruptly disappeared. Rash over the wrist completely resolved over one week period. After symptomatic relief, as an alternative therapy for the ongoing neuropathic pain, gabapentin was initiated 300 mg po daily. During 1 month follow-up, similar allergic reactions were not encountered and neurological visit showed clinical improvement.

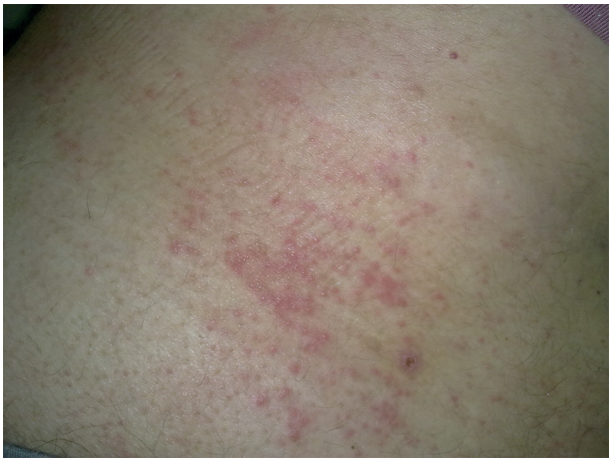

Figure 2. Maculopapular rash on the trunk and lumbar area

DISCUSSION

Numerous factors that may increase the propensity of an individual to develop a drug-induced rash have been identified. These factors are, being a woman of child-bearing age, the initial dose selected, concomitant viral infection, immune-mediated disorders, pharmacogenetic variability, and age.[7,8] Arif et al. emphasized that the only non-drug predictor of antiepileptic drug (AED) related rash was rash to another AED, with an odds ratio of 3.1.[4] This patient had a hematologic malignancy which at least in partly may have contributed to the development of rash via immune mechanisms. As a precaution, pregabalin treatment was started with lower doses (150 mg) and increased to recommended dose (300 mg). Due to his medications for multiple myeloma including, prophylactic antibiotics (levofloxacin, trimethoprim/sulfamethoxasole), calcium plus vitamin D3, zoledronic acid and proton pump inhibitor, it's difficult to definitively attribute the rash to pregabalin treatment. The Naranjo Adverse Drug Reaction Probability Scale is a simple questionnaire including[10] parameters for determining the likelihood of whether an adverse drug reaction is actually due

to the drug rather than the result of other factors. Probability is assigned via a score termed definite, probable, possible or doubtful.[9] Using the Naranjo Scale, a ‘‘probable’’ reaction (Score: 6) was attributed to pregabalin.

The nature and etiology of a drug-induced rash may vary depending on the patient and the agent. The most common drug-induced rash is erythematous and is usually a result of delayed cell-mediated hypersensitivity. This occurs after the first or second week of therapy.[10] In our patient, more common complaints such as dizziness and somnolence were not encountered. On the sevent day of pregabalin treatment, erythematous rash located on his upper extremities, lumbar region and proximal thigh. Withdrawal of drug and symptomatic medication led to dramatic reduction of the mentioned lesions. Smith et al.[6] reported that, in their patient, the onset of the rash was approximately 2 days after beginning of pregabalin treatment, which was much earlier than our patient.

The efficacy and safety of pregabalin in the treatment of neuropathic pain was assessed in three large randomized controlled trials. In a six week study of 246 patients receiving pregabalin 150 mg, 600 mg, or placebo; overall pregabalin was found to be well tolerated.[11] The most common side-effects reported in both pregabalin treatment arms were dizziness and somnolence. Two other large clinical trials reported similar side-effect profiles.[12,13] More recently, a randomized, double-blind, placebo controlled trial showed that pregabalin (600 mg/day) was well-tolerated, and the adverse events were higher in the pregabalin arm. The most common adverse events due to pregabalin were, peripheral edema, dizziness, weight gain and somnolence.[14]

In this patient, after noting rash, pregabalin treatment was stopped immediately. After resolution of symptoms, gabapentin was started at lower doses and followed cautiously. However, no adverse effects were observed with gabapentin treatment. This may be due to the fact that, the S-isomer of the pregabalin has approximately 10 times higher affinity for the alpha-2-delta site which is required for anticonvulsant activity of pregabalin in vivo than the R-isomer.[15]

Like other numerous drugs, adverse effects can also be seen with pregabalin treatment. Rash, relatively a rare complication of pregabalin treatment, must be further investigated for its nature and cross reactivity with other drugs.

REFERENCES

1. Gajraj NM. Pregabalin: its pharmacology and use in pain management. Anesth Analg 2007;105:1805-1815.
2. Mula M, Pini S, Cassano GB. The role of anticonvulsant drugs in anxiety disorders: a critical review of the evi-dence. J Clin Psychopharmacol 2007;27:263-272.
3. Lozsadi D, Hemming K, Marson AG. Pregabalin add-on for drug-resistant partial epilepsy. Cochrane Database Syst Rev 2008;1:561-562.
4. Arif H, Buchsbaum R, Weintraub D, et al. Comparison and predictors of rash associated with 15 antiepileptic drugs. Neurology 2007;68:1701-1709.
5. Rowan AJ, Ramsay RE, Collins JF, et al. New onset geriatric epilepsy: a randomized study of gabapentin, lamotrigine, and carbamazepine. Neurology 2005;64:1868-1873.
6. Smith TL, Baldwin A, Cunningham LL Jr, et al. Rash Associated with Pregabalin Use. Ann Pharmacother 2008;42:1899-1902.
7. Pushkin R, Frassetto L, Tsourounis C, et al. Improving the reporting of adverse drug reactions in the hospital set-ting. Postgrad Med 2010;122:154-164.
8. Alvestad S, Lydersen S, Brodtkorb E. Rash from antiepileptic drugs: influence by gender, age, and learning disability. Epilepsia 2007;48:1360-1365.
9. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-245.
10. Valeyrie-Allanore L, Sassolas B, Roujeau JC. Drug-induced skin, nail and hair disorders. Drug Saf 2007;30:1011-1030.
11. Richter RW, Portenoy R, Sharma U, et al. Relief of painful diabetic peripheral neuropathy with pregabalin: A randomized, placebo-controlled trial. J Pain 2005;6:253-260.
12. Lesser H, Sharma U, LaMoreaux L, et al. Pregabalin relieves symptoms of painful diabetic neuropathy: A randomized controlled trial. Neurology 2004;63:2104-2110.
13. Rosenstock J, Tuchman M, LaMoreaux L, et al. Pregabalin for the treatment of painful diabetic peripheral neuropathy: A double blind, placebo-controlled trial. Pain 2004;110:628-638.
14. Arezzo JC, Rosenstock J, Lamoreaux L, et al. Efficacy and safety of pregabalin 600 mg/d for treating painful diabetic peripheral neuropathy: A double-blind placebo-controlled trial. BMC Neurol 2008;8:33.
15. Ben-Menachem E. Pregabalin pharmacology and its relevance to clinical practice. Epilepsia 2004;45:13-18.