CASE REPORT

Leukocytoclastic vasculitis induced by Nateglinide

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Received: February 7, 2014 **Accepted:** April 18, 2014 **Online Published:** April 30, 2014
DOI: 10.5430/crim.v1n2p99 **URL:** http://dx.doi.org/10.5430/crim.v1n2p99

Abstract

Meglitinides, a class of drug used in type 2 diabetes mellitus, includes repaglinide and nateglinide and is associated with hypoglycemia, nausea, diarrhea and peripheral edema. We report a unique adverse reaction to nateglinide. A 55-year-old Caucasian male presented with a diffuse rash on his skin which started on his ankles bilaterally 3 weeks before presentation. Examination revealed a diffuse patchy maculo-papular rash, with some patches having pustules, purpura and eschar. Skin biopsy showed areas of fibrinoid deposition with wall thickening in superficial dermal blood vessels. The patient was recently started on nateglinide three months prior to admission at dose of 120 mg three times a day. During hospitalization, his nateglinide was stopped and started on oral prednisone 60 mg daily. His lesions improved over the next one week

Keywords

Leukocytoclastic vasculitis, Nateglinide

1 Introduction

Meglitinides, a class of drug used in type 2 diabetes mellitus, includes repaglinide and nateglinide and is associated with hypoglycemia, nausea, diarrhea and peripheral edema [1]. We report a unique adverse reaction to nateglinide.

2 Case presentation

A 55-year-old Caucasian male with a known history of Diabetes Mellitus, poorly controlled on metformin and insulin was started on Nateglinide 2 months before presentation. Three weeks after Nateglinide was started, he started having a rash which began as pinkish-red in color, with irregular boundaries and had multiple blisters around both ankles. The rash progressed over next one week to involve both lower legs. He took oral methylprednisone for 3 days without any effect on the progression of the rash. Over the ensuing 2 weeks, his rash progressed to involve both thighs, the abdomen, bilateral flanks and both arms, sparing chest and his face. He complained of itching in the rash, but no pain. His past history included diabetes mellitus type 2 for which he took insulin, metformin and nateglinide.

Examination revealed a diffuse patchy maculo-papular rash, with some patches having pustules, purpura and eschar. The lesions on his right leg are shown in panel 1. Initial complete blood count and metabolic profile were unremarkable except for hyperglycemia (glucose 260mg/dL) and HbA1c of 12.4%. Urinalysis and blood culture were unremarkable except for

glucosuria. ESR was 78mm/hr (normal 0-20mm/hr) and CRP was 11.2mg/dL (normal 0.0-0.9mg/dL). Anti-nuclear antibody, anti-neutrophilic cytoplasmic antibody, complement C3 level, C4 level and cryoglobulin level were unremarkable. Tests for HIV, hepatitis B, hepatitis C and syphilis were negative. Total IgM and IgG were normal. Skin biopsy showed areas of fibrinoid deposition with wall thickening in superficial dermal blood vessels. It also demonstrated perivascular and interstitial inflammatory infiltrates with neutrophils, occasional eosinophils, leukocytoclasis, extravasated red cells and endothelial cell enlargement consistent with leukocytoclastic vasculitis (now known as cutaneous leukocytoclastic angiitis [2]). The patient was recently started on nateglinide three months prior to admission at dose of 120 mg three times a day. There was no other identifiable predisposing factor for rash. During hospitalization, his nateglinide was stopped and started on oral prednisone 60 mg daily. His lesions improved over the next one week as shown in panel 2 (see Figure 1). The temporal association of nateglinide to his rash and no effect of the initial steroid (while on nateglinide) on its progression makes the nateglinide a most likely causative agent for the rash. We could not confirm the association of drug to rash as Nateglinide was not re-introduced and added to allergy list of patient. At discharge, his nateglinide was taken off from medication list, other home medications were continued and prednisone was tapered off. Since discharge, his rash has improved without any recurrence of lesions.

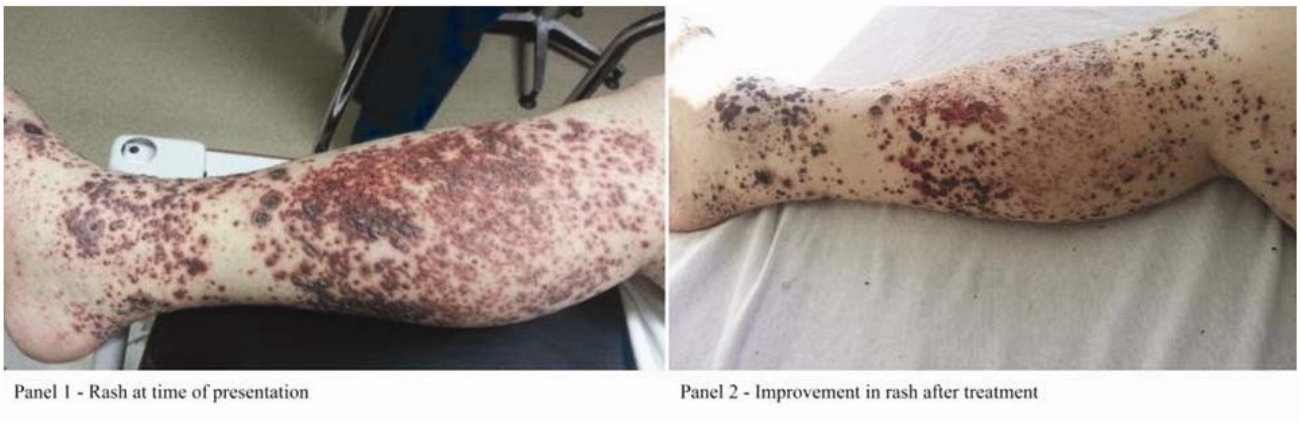

Figure 1. It reveals improvement in rash after discontinuation of drug and starting on steroid.

3 Discussion

LCV (also called hypersensitivity vasculitis) is associated with use of various drugs, including report on repaglinide 3, but to the best of our knowledge never by nateglinide. American College of Rheumatology has proposed that presence of three or more of following; age >16, use of a possible offending drug in temporal relation to the symptoms, palpable purpura, maculopapular rash and biopsy of a skin lesion showing neutrophils around an arteriole or venule; had a sensitivity and specificity for the diagnosis of hypersensitivity vasculitis of 71 and 84 percent, respectively [4]. Our patient had all the 5 criteria for the classification of vasculitis under LCV category. Biopsy of the skin lesion is helpful in diagnosis and immunofluorescence study should be done to rule out diagnosis of IgA vasculitis. Management includes stopping the offending drug and steroid therapy. Our patient was treated successfully with oral steroids. We recommend that clinicians should be vigilant for a new rash after starting nateglinide and have high index of suspicion for possible underlying leukocytoclastic vasculitis.

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