Alirocumab therapy causing plantar bullae in a patient with hypercholesterolemia

Hiba Basheer, MD, Heather Tucker-Bjorum, APRN, MSN and Ishwarlal Jialal, MD, PhD*

VA Northern California Healthcare System, Mather, CA, USA *(E-mail: kjialal@gmail.com).

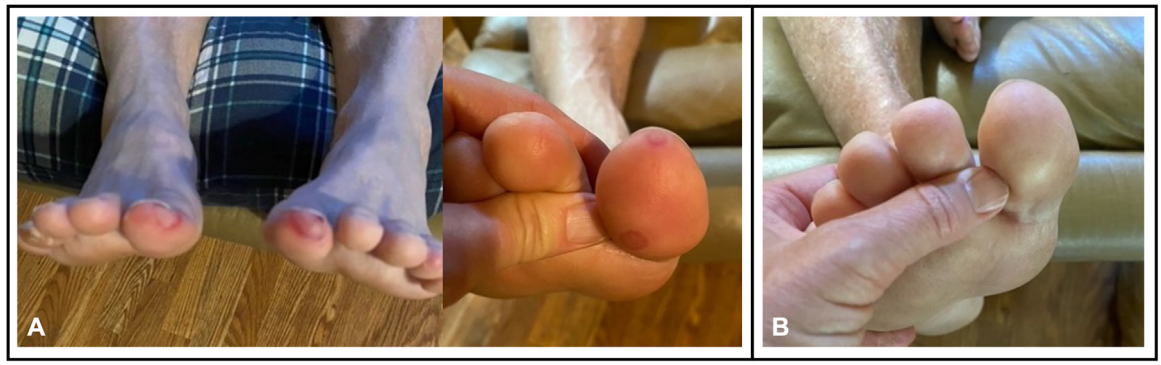

FIGURE 1.

CASE PRESENTATION

A 70-year-old Caucasian male with a past medical history of hypertension, hyperlipidemia, atherosclerotic cardiovascular disease (ASCVD) manifesting as two myocardial infarctions requiring three stent placements, gastroesophageal reflux disease (GERD) and obstructive sleep apnea (OSA) was seen in the endocrine clinic for management of his hyperlipidemia. He had a positive family history for hyperlipidemia in both his mother and sister. The latter having premature ASCVD since she had a myocardial infarction in her forties. He denied smoking cigarettes, ingesting alcohol and any substance abuse. In 1993, the patient was found to have elevated lipids and was placed on different cholesterol lowering agents over the years including fluvastatin, lovastatin, pravastatin, atorvastatin, niacin, fenofibrate, ezetimibe and colestipol. He could not tolerate statin therapy because of myalgias and experienced gastro-intestinal side effects with both niacin and colestipol. Following his initial evaluation at the endocrine clinic and his high risk for ASCVD, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor therapy was considered based on the most recent AHA/ACC Multi-society Cholesterol Guidelines.[1] He did not have tendon xanthoma or diminished pulses. His-lipid profile at this visit revealed a total Cholesterol 330 mg/dl (all reference ranges provided in parentheses, <200 mg/dl); Triglyceride 121 mg/dl (<150 mg/dl); LDL-C-247 mg/dl (<100 mg/dl); HDL-C-59 mg/dl (>40 mg/dl). Other pertinent laboratories revealed a creatinine 1.26 mg/dl (0.5–1.1); albumin 4.5 g/dl (3.3–4.8), TSH-1.53 uIU/mL (0.34–5.60), HBAIC 5.9% (<6.5%).His-urine was negative for protein. Alirocumab was recommended by the VA pharmacy and was initiated at a dose of 75 mg subcutaneous injection every 2 weeks in addition to ezetimibe.

Follow up labs after five months revealed an excellent response with lipid panel revealing Cholesterol 200 mg/dl; LDL 107 mg/dl; HDL 65 mg/dl; TG 144 mg/dl. Patient stopped alirocumab 5 months later after worsening of blisters on his toes that started shortly after using this medication. Dermatology was consulted and they concurred with our diagnosis that the skin lesions were due to alirocumab. At that point, patient had been off the alirocumab for eight weeks and had no new blisters. Eight months later, alirocumab was retried and again patient developed new blisters on his toes. Eventually alirocumab was stopped permanently. A request for bempedoic acid has been made. The figures show the blisters on his toes on alirocumab (Fig. 1A) and absence of blisters (Fig. 1B) when the drug was stopped.

The PCSK9 inhibitors are an excellent addition in patients with high risk ASCVD with a LDL-C > 70 mg/dl on maximum tolerated statin therapy.[1] These drugs appear to be well tolerated with injection site reactions being the commonest side effect. However, a review of the literature reveals 2 case reports of skin lesions.[2,3] Kanda and Okajima in 2019 reported an atopic dermatitis like rash in a patient treated with evolocumab.[2] Ghernauten et al. reported a maculopapular exanthema in a 60-year-old patient on evolocumab.[3]

Our case study contributes to the literature by reporting the novel adverse reaction of a blistering skin lesion

on alirocumab (which contains polysorbate) that resulted in discontinuation of therapy.

In conclusion, health care providers should be aware of other skin lesions on PCSK9 inhibitors other than injection site reactions.

SOURCE OF FUNDING

None

DECLARATION OF COMPETING INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

We thank the patient for consenting to publish his case report.

REFERENCES

1. **Virani SS, Akeroyd JM, Smith SC, et al.** Very high-risk ASCVD and eligibility for nonstatin therapies based on the 2018 AHA/ACC cholesterol guidelines. *J Am Coll Cardiol*. 2019;74(5):712–714.
2. **Kanda N, Okajima F.** Atopic dermatitis-like rash during evolocumab treatment of familial hypercholesterolemia. *J Nippon Med Sch*. 2019;86(3):187–190.
3. **Ghernautan V, Amini M, Sachmechi I.** Maculopapular exanthema after the second dose of evolocumab. *Cureus*. 2021;13(5).