PCSK9 inhibitor therapy: delayed-onset cutaneous reactions

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Introduction

Cutaneous side-effects have been associated following initiation of PCSK9 inhibitors.[1,2] We report two cases where there was a delayed onset of cutaneous side-effects.

Case report 1

A 64-year-old man with a history of type 2 diabetes mellitus (T2DM), probable familial hypercholesterolaemia and clinical atherosclerotic cardiovascular disease (previous coronary artery bypass grafting at age 58 years) was commenced on injectable proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitor therapy with alirocumab. He had a history of intolerance to four statin formulations. Alirocumab was initially given at a dose of 75 mg subcutaneously every fortnight. The dosage was subsequently increased following a non-ST segment elevation myocardial infarction to 150 mg fortnightly, 11 months after initiation.

The initial dose of alirocumab 75 mg fortnightly was associated with coryzal symptoms after each subcutaneous administration of alirocumab, which was reported as a minor concern. Following the increased dose of alirocumab to 150mg fortnightly the patient reported a cutaneous reaction at the tip of his nose 24-36 hours after the subcutaneous injection, lasting up to 48 hours. This cutaneous reaction involved erythema, pain and swelling of his nose, extending 3 cm from the tip (Figure 1). This reaction occurred on four consecutive occasions after administration of the higher alirocumab dose. The 150mg fortnightly dose was reduced to 75 mg fortnightly and the patient's symptoms improved.

It is unclear what the possible mechanism underlying this reaction might be at present: there is very little about this form of reaction documented in the literature.

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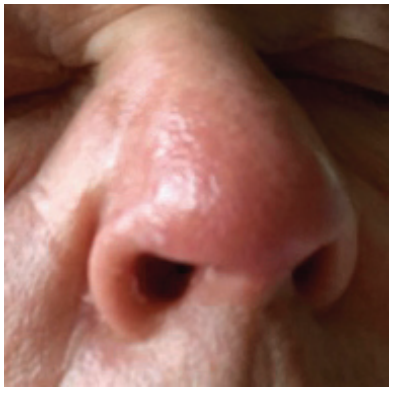
Figure 1. Cutaneous reaction (erythematous swelling) seen at the tip of the nose

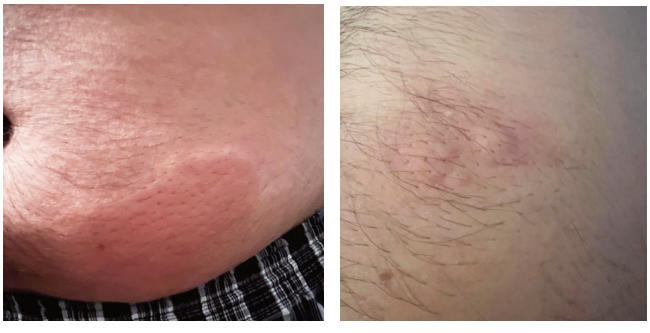


Case report 2

Delayed-onset urticaria at PCSK9 inhibitor injection site

A 48-year-old man with a history of familial hypercholesterolaemia, coronary artery disease, T2DM, dermographism and statin intolerance presented after two years of PCSK9 inhibitor therapy with new cutaneous changes. The skin changes occurred on the day of injection after a switch from alirocumab 150 mg fortnightly to the 300 mg monthly injection. Other (unchanged) medications included alogliptin, dulaglutide, aspirin, fenofibrate and ezetimibe. At lipid clinic review, new-onset torso erythema and urticaria were observed (Figures 2 a&b).

Figure 2. Two urticarial reactions appearing at the site of alirocumab injection on the abdomen



Dermatology clinic review confirmed an urticarial response at the site of injection, for which the patient has been prescribed topical steroids and oral antihistamines prior to alirocumab injection. Additional measures such as alternating the injection site were also considered. He was able to continue with injectable lipid-lowering therapy to achieve his treatment target.

Injection site reactions have been reported as an early, but not delayed-onset, side effect following PCSK9 inhibitor initiation. A proposed mechanism involves an immune-mediated urticarial reaction.[3]

Conclusions

Cutaneous reactions associated with PCSK9 inhibitor therapy have been reported as an early manifestation in the primary outcome trials for both currently used PCSK9 inhibitors: for alirocumab at a rate of 3.8% compared to 2.1% with placebo in the ODYSSEY OUTCOMES trial,[1] and for evolocumab at 2.1% compared to 1.6% with placebo in the FOURIER trial.[2]

The two cases described above did not have early-onset cutaneous reactions but had reactions several months or years after initiation of therapy. These findings highlight the importance of awareness of skin reactions (both immediate and/or delayed) after initiation of PCSK9 inhibitor therapy.

Conflict of interest None.
Funding None.

Key messages

- Early cutaneous reactions associated with PCSK9 inhibitor therapy have been reported in outcome trials
- We report two cases where cutaneous reactions developed several months/years after initiation of PCSK9 inhibitor therapy
- Skin reactions -either immediate and/or delayed)- may occur after initiation of PCSK9 inhibitor therapy.

References

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