

Drug eruption associated with empagliflozin

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A 61-year-old man with a history of congestive heart failure, atrial fibrillation, chronic kidney disease and hypothyroidism presented to clinic with a painful, bilateral, nonblanching, lower extremity rash 2 weeks after starting empagliflozin (5 mg/d) (Appendix 1, Supplementary Appendix 1 and 2, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220934/tab-related-content). One month after starting the drug, we increased the dosage to 10 mg/d for ongoing heart failure management; his rash then worsened (Figure 1). Laboratory investigations showed that the patient was positive for antinuclear antibodies (1:160 titre), with no extractable nuclear antigen antibody. Test results for hepatitis B and C serology, antineutrophil cytoplasmic antibodies, cryoglobulins and rheumatoid factor were negative. Eosinophilia was absent and urinalysis was negative for blood with trace protein. The patient was started on 0.05% clobetasol cream, but was subsequently admitted to hospital owing to progression of the rash.

The differential diagnosis for the patient's rash included vasculitis, cellulitis, contact dermatitis, venous stasis and a cutaneous drug reaction. Our patient had a skin biopsy, which showed perivascular dermatitis with eosinophils and superficial excoriation, consistent with a drug eruption (Appendix 1, Supplementary Appendix 3). Empagliflozin was stopped and the patient completed a 5-day course of 30 mg prednisone with resolution of the rash (Appendix 1, Supplementary Appendix 4). Based on the temporal relationship between starting empagliflozin and the appearance of the rash — which worsened with an increase in dose and resolved when the drug was stopped — and with the exclusion of other medication culprits, we graded our patient's rash as 8 on the Naranjo algorithm and probable or likely on the World Health Organization Uppsala Monitoring Centre (WHO-UMC) causality system, indicating a probable adverse drug reaction to empagliflozin (Appendix 1, Supplementary Appendix 5).



Figure 1: Photographs of a 61-year-old man with bilateral lower limb distribution of drug eruption associated with empagliflozin, predominantly over the knees and feet.

Although sodium–glucose cotransporter-2 (SGLT2) inhibitors, including empagliflozin, are widely used in clinical practice, few cutaneous drug reactions have been reported. Ipragliflozin, which is not available in Canada, has some reports of association with a fixed drug eruption.^{1,2} Similarly, a postmarketing study using pharmacovigilance databases found a signal for skin toxicity with all SGLT2 inhibitors.³ Clinicians should be aware of this potential adverse event as usage of SGLT2 inhibitors continues to increase.

References

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