

## Unexpected outcome (positive or negative) including adverse drug reactions

## Adverse skin reactions following intravitreal bevacizumab injection

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## Summary

The authors describe two separate cases of skin eruption following intravitreal bevacizumab injection with evidence to suggest that these were adverse drug reactions to bevacizumab. The authors also discuss how each case was treated and report on the final outcome.

## BACKGROUND

The manifestation of skin rash as a side effect of intravitreal bevacizumab treatment is a very rare complication.<sup>1 2</sup> But, as intravitreal injections are becoming more common, we feel this is an important adverse effect to be discussed with the patient when considering treatment. Also, there has been some suggestion that the development of the skin rash may correlate with the effectiveness of the treatment<sup>3</sup>, which would be worth exploring in the future once more evidence becomes available.

## CASE PRESENTATION

## Case 1

A 69-year-old man with diet controlled diabetes routinely presented in September 2007 to the eye clinic through the diabetic screening service with a query of central retinal vein occlusion in the right eye. His only other medical history was a small transient ischemic attack. He was booked for treatment with three intravitreal bevacizumab injections. However, 3 days after the first uneventful injection, the patient developed eczematous pruritic plaques and small discrete folliculitic lesions on the forearms and legs that lasted for a few weeks (figures 1–3). The skin changes regressed without any treatment. Following the second injection 1 month later, the patient reported reoccurrence of the skin changes on the initial areas as well as on new areas on his back and hips.

## Case 2

A 89-year-old man presented with sudden reduction of vision in the left eye. He had a history of mild acne but no other past medical history and was on no medication. Funduscopy revealed left central serous retinopathy, which was confirmed on optical coherence tomograph. It was decided to treat the patient with intravitreal bevacizumab. Following the first injection, the patient developed a skin eruption.

## INVESTIGATIONS

Skin swabs taken from case 1 showed no bacterial pathogen. A skin biopsy was also taken from one of the eczematous

looking plaques on the left hip of case 1. Histology showed mild acanthosis and perivascular chronic inflammation with occasional eosinophils. There was no evidence of spongiosis. These histological features were reported to be compatible with a drug reaction.

A skin biopsy taken from one of the acneiform lesions of case 2 showed folliculitis.

## DIFFERENTIAL DIAGNOSIS

The differential diagnosis was an allergic skin reaction to drug treatment.

## TREATMENT

Case 1 was prescribed potent topical corticosteroids.

Case 2 was prescribed conventional acne treatment and an emollient cream.

## OUTCOME AND FOLLOW-UP

The skin reaction subsided in case 1 and, as vision improved after the second injection, the third injection was omitted as it was felt the side effects outweighed any possible further benefits.

The skin of case 2 gradually improved and was almost completely clear after 6–8 weeks.

## DISCUSSION

The manifestation of skin rash as a side effect of intravitreal bevacizumab treatment is a very rare complication.<sup>4 5</sup> Only two cases have been reported in the literature. However, the incidence of skin rash with intravenous treatment of bevacizumab has been well documented and reported to be as high as 46% and seems to be dose dependent.<sup>6 7</sup> Acneiform rash is very common with other growth factor inhibitors. It can occur in over 90% of patients receiving cetuximab and panitumumab (both epidermal growth factor receptor inhibitors).<sup>8</sup>

The reported presentations of skin rash are mild and tend to be self-limiting and spontaneously improve as the treatment is withdrawn. There is also a suggestion that the rash is indicative of a positive treatment response.<sup>3 9</sup>



**Figure 1** Rash on the forearms of patient 1 after the first intravitreal injection.



**Figure 2** Rash on the leg of patient 1 after the first intravitreal injection.

No such correlation has been reported with intravitreal use.

Ladas *et al* report the case of a patient who developed a maculopapular rash on the forehead and the temporal

regions around both eyes 12 days after a bevacizumab intravitreal injection. The rash subsided with topical corticosteroid treatment but reoccurred in the same pattern following repeated intravitreal bevacizumab injections.



**Figure 3** Rash on the shin of patient 1 after the second intravitreal injection.

They followed up the patient for 13 months and, as with our case, the rash did not reoccur after intravitreal bevacizumab injections were omitted. Their patient was also male and 50 years of age and they also could find no other cause for the rash.

#### Learning points

- ▶ Skin rash should be considered as a rare complication when contemplating intravitreal bevacizumab treatment.
- ▶ The rash seems to be self-limiting and responds well to topical treatment.
- ▶ There could be a possible link between the development of the rash and response to the intravitreal treatment, which could be investigated in the future.

**Competing interests** None.

**Patient consent** Obtained.

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