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# Bullous fixed drug eruption following administration of the recombinant adjuvant Shingrix vaccine

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## SUMMARY

A 51-year-old woman with Crohn's disease presented with a bullous rash on her left arm and axilla 2 days after receiving her second dose of the recombinant adjuvant Shingrix vaccine. PCR for herpes simplex virus (HSV) 1, HSV 2 and varicella zoster virus was negative. Punch biopsy revealed changes that were consistent with a bullous fixed drug eruption. She was successfully treated with oral prednisone and topical triamcinolone cream. This is the first known case of a bullous fixed drug eruption due to the recombinant adjuvant Shingrix vaccine.

## BACKGROUND

The recombinant adjuvant Shingrix vaccine is now the preferred vaccination to prevent varicella zoster virus (VZV) reactivation and subsequent postherpetic neuralgia due to its favourable side effect profile and efficacy compared with the live Zostavax vaccination.<sup>1</sup> The Centers for Disease Control and Prevention currently recommends that all adults ages 50 and older should receive two doses of the Shingrix vaccine separated by 2–6 months. Overall, the vaccine is usually well tolerated by patients. Common side effects of the Shingrix vaccine include redness, swelling and pain at the injection site; myalgias; fatigue; and headaches.<sup>2</sup> We report the first known case of a bullous fixed drug eruption distant from the vaccination site following a second dose of the Shingrix vaccine. This case offers additional insight into the side effect profile of the Shingrix vaccine as it becomes more broadly used in the general population.

## CASE PRESENTATION

The patient is a 51-year-old woman with a medical history significant for Crohn's disease on infliximab, who presented to her primary care provider with a bullous rash on her left arm, axilla and lateral chest wall (figure 1) with associated subjective fever. Two days prior to presentation, she received her second dose of recombinant adjuvant Shingrix vaccine. She was not taking any new medications at the time, had not used any new topical products and did not have a similar rash in the past. She was taking infliximab for her Crohn's disease for 1 year and was due for her next dose the following week. She was experiencing intermittent loose stools at the time of examination, which was her normal baseline with the disease. On physical examination, the patient had diffuse erythema and swelling extending from the midchest to axilla and down the upper



**Figure 1** The patient's bullous rash on initial presentation.

arm with associated bullae, some of which had a central dusky appearance. There was no evidence of mucosal involvement on examination.

## INVESTIGATIONS

The patient was referred to dermatology, and a biopsy was performed. PCR from one of the bullae for herpes simplex virus (HSV) 1, HSV 2 and VZV was negative. Punch biopsy revealed epidermal necrosis leading to bullae formation along with a superficial and deep interstitial inflammation with numerous eosinophils and scattered neutrophils (figures 2 and 3). The clinical and histological changes were consistent with a bullous fixed drug eruption in response to the vaccine.

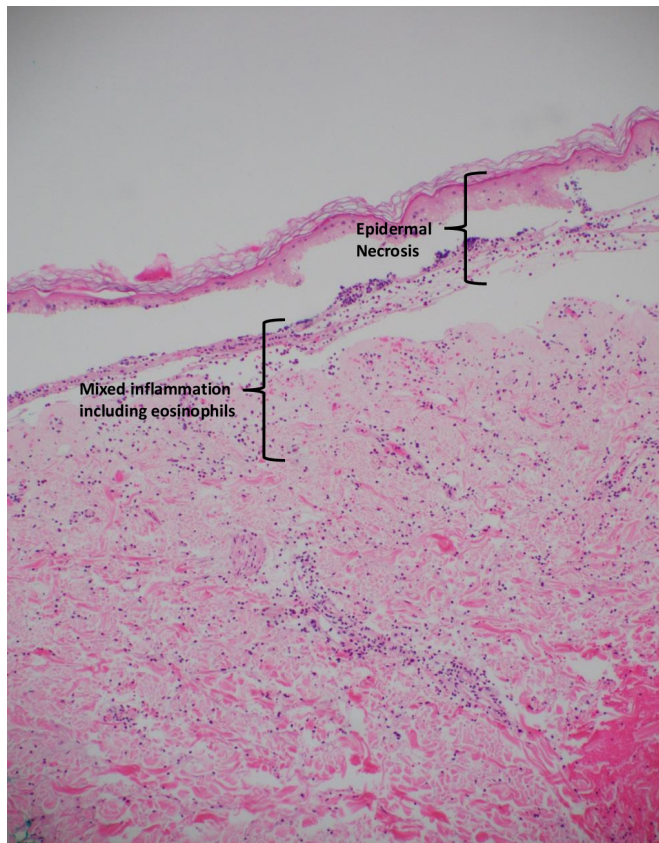
## DIFFERENTIAL DIAGNOSIS

Differential diagnosis at the time of patient presentation included VZV infection, HSV infection, bullous fixed drug eruption and contact dermatitis. Bullous pemphigoid was considered



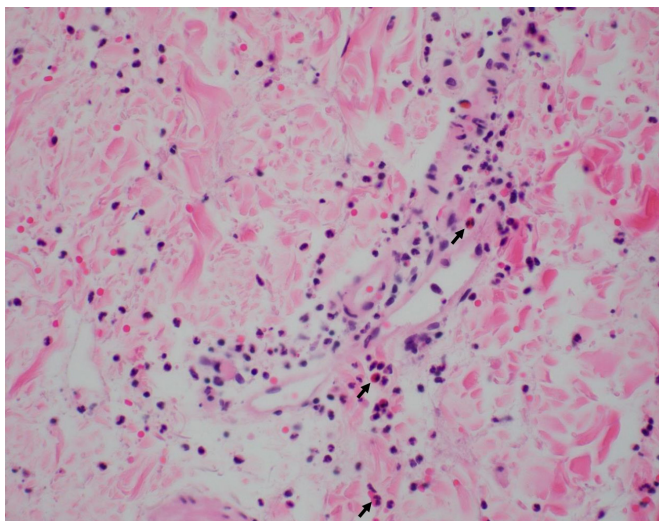
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**Figure 2** Punch biopsy from the patient's rash revealing epidermal necrosis leading to bullae formation.

less likely due to the patient's age at presentation and localised involvement; therefore, direct immunofluorescence was not performed. Aetiologies such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) were considered less likely due to the lack of mucosal involvement and severe systemic symptoms. With negative HSV and VZV PCR in conjunction with the biopsy findings, bullous fixed drug eruption was diagnosed.



**Figure 3** Higher power view demonstrating eosinophil infiltration.

## TREATMENT

The patient was prescribed prednisone 40 mg daily for 5 days with subsequent taper and triamcinolone 0.1% cream applied two times per day for 2 weeks. Because results of the viral PCR were not available at the time, the patient was also given a prescription for valacyclovir 1000 mg three times a day for 7 days.

## OUTCOME AND FOLLOW-UP

The patient's rash was successfully treated with oral and topical corticosteroids after 1 week of onset. She has not experienced a subsequent similar bullous reaction, but she continues to have some tenderness in the area.

## DISCUSSION

Dermatological reactions have been reported immediately following vaccine administration in previous cases, but this is the first known case of a reaction to the recombinant Shingrix vaccine. A bullous drug eruption following human papilloma virus vaccination was reported in an otherwise healthy 13-year-old girl,<sup>3</sup> and development of lichen planus, bullous pemphigoid and TEN has been reported following administration of the inactive influenza virus vaccine.<sup>4</sup> The live Zostavax vaccine has been shown to cause fatal disseminated VZV infections in both immunocompromised<sup>5,6</sup> and immunocompetent patients,<sup>7</sup> which is one of the factors that led to the development of an inactivated vaccine for the prevention of VZV reactivation. However, this case provides evidence that immunologically mediated reactions can occur with Shingrix vaccine administration despite its improved safety profile compared with the live vaccination. As in this case, patients with autoimmune disease may be at increased risk given the immune dysregulation associated with their underlying condition.

Development of a bullous fixed drug eruption to medications and vaccinations is a rare complication that can appear similar to bullous pemphigoid, SJS and TEN.<sup>8</sup> Medications that have been shown to cause bullous dermatological reactions include non-steroidal inflammatory agents and antibiotics such as trimethoprim-sulfamethoxazole.<sup>9</sup> The development of a bullous rash is likely due to a delayed-type hypersensitivity reaction, marked by T-cell hyperactivation.<sup>10</sup> The reaction is generally self-limited and treated with discontinuation of the offending agent and corticosteroids. Bullous reactions can rarely occur with inflammatory bowel disease<sup>11</sup>; however, the reaction in this case is more likely due to vaccination because the reaction occurred immediately following vaccination and has not recurred. The Naranjo Score, a tool used to determine the likelihood of adverse drug reaction,<sup>12</sup> in this case was 6, which indicates that the bullous reaction was likely an adverse reaction to vaccination.

This case highlights the possibility of an acute bullous reaction to the recombinant adjuvant Shingrix vaccine. The vaccine has

## Learning points

- ▶ This is the first known case of a bullous fixed drug eruption associated with the recombinant adjuvant Shingrix vaccine.
- ▶ Caution should be taken when administering the Shingrix vaccine to patients with autoimmune and/or immunocompromising conditions.
- ▶ Bullous fixed drug eruptions due to medications and vaccinations are self-limited and treated with discontinuation of the offending agent and corticosteroids.

been shown to be very effective at preventing VZV reactivation and postherpetic neuralgia and is well tolerated in most patients, so the benefits of receiving the vaccination outweigh the risks. Nonetheless, recognition of acute reactions associated with the vaccine such as the delayed-type immune dysregulation seen in this patient should be recognised and treated early.

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