



OPEN ACCESS

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

Hallie Thompson,¹ Laura Nichols,² Tania Gonzalez Santiago²

¹University of North Dakota, Edgeley, North Dakota, USA
²Sanford Health North, Fargo, North Dakota, USA

Correspondence to
 Hallie Thompson;
 hallie.b.anderson@und.edu

Accepted 31 July 2021

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.¹ 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.² 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



© BMJ Publishing Group Limited 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Thompson H, Nichols L, Gonzalez Santiago T. *BMJ Case Rep* 2021;**14**:e241293. doi:10.1136/bcr-2020-241293

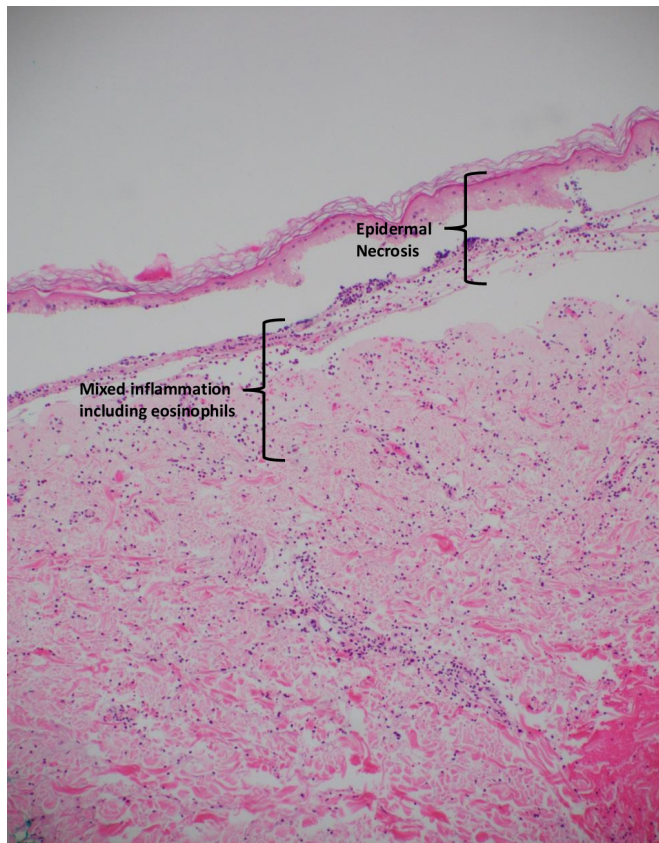


Figure 2 Punch biopsy from the patient's rash revealing epidermal necrosis leading to bullae formation.

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.

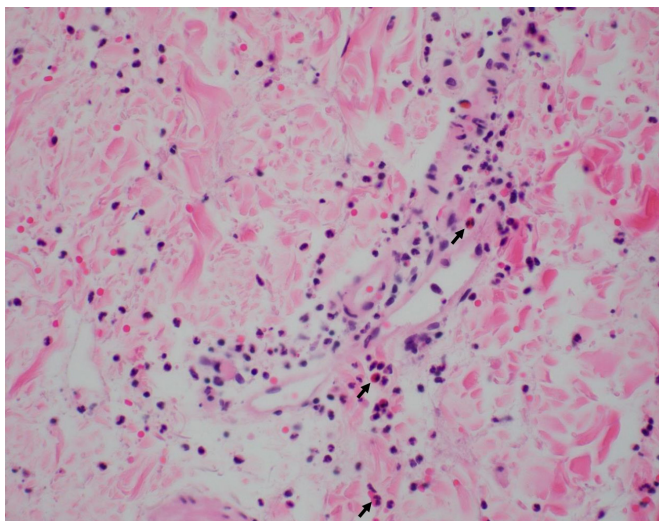


Figure 3 Higher power view demonstrating eosinophil infiltration.

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,³ and development of lichen planus, bullous pemphigoid and TEN has been reported following administration of the inactivated influenza virus vaccine.⁴ The live Zostavax vaccine has been shown to cause fatal disseminated VZV infections in both immunocompromised^{5 6} and immunocompetent patients,⁷ 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 mediate 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.⁸ Medications that have been shown to cause bullous dermatological reactions include non-steroidal inflammatory agents and antibiotics such as trimethoprim-sulfamethoxazole.⁹ The development of a bullous rash is likely due to a delayed-type hypersensitivity reaction, marked by T-cell hyperactivation.¹⁰ The reaction is generally self-limited and treated with discontinuation of the offending agent and corticosteroids. Bullous reactions can rarely occur with inflammatory bowel disease¹¹; 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,¹² 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.

Contributors I, HA, as first author was involved in collecting patient data and creating the case report draft. LN and TGS served as content experts by providing edits to the draft and obtaining patient consent.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

- 1 Symoniak MR, Farrokh P, Gandhi MA, Pejman F, Mona A, *et al*. Herpes zoster subunit vaccine for the prevention of herpes zoster. *Am J Health Syst Pharm* 2018;75:861–9.
- 2 James SF, Chahine EB, Sucher AJ, *et al*. Shingrix: the new adjuvanted recombinant herpes zoster vaccine. *Ann Pharmacother* 2018;52:673–80.
- 3 Pyl J, Aerts O, Siozopoulou V, *et al*. Bullous fixed drug eruption following human papilloma virus vaccination. *J Eur Acad Dermatol Venereol* 2020;34:e697–e698.
- 4 Sato NA, Kano Y, Shiohara T. Lichen planus occurring after influenza vaccination: report of three cases and review of the literature. *Dermatology* 2010;221:296–9.
- 5 Alexander KE, Tong PL, Macartney K, *et al*. Live zoster vaccination in an immunocompromised patient leading to death secondary to disseminated varicella zoster virus infection. *Vaccine* 2018;36:3890–3.
- 6 Ortiz-Brizuela E, Leal-Vega F, Cuellar-Rodríguez J, *et al*. Vaccine-Derived varicella zoster infection in a kidney transplant recipient after zoster vaccine live administration. *Vaccine* 2019;37:3576–9.
- 7 Harada K, Heaton H, Chen J, *et al*. Zoster vaccine-associated primary varicella infection in an immunocompetent host. *BMJ Case Rep* 2017;2:bcr-2017-221166.
- 8 Dharamsi FM, Michener MD, Dharamsi JW. Bullous fixed drug eruption masquerading as recurrent Stevens Johnson syndrome. *J Emerg Med* 2015;48:551–4.
- 9 Tavares Almeida F, Caldas R, André Oliveira Álvaro, Almeida FT, Oliveira AA, *et al*. Generalized bullous fixed drug eruption caused by ibuprofen. *Contact Dermatitis* 2019;80:238–9.
- 10 McNeil MM, DeStefano F. Vaccine-Associated hypersensitivity. *J Allergy Clin Immunol* 2018;141:463–72.
- 11 Pellicer Z, Santiago JM, Rodríguez A, *et al*. Management of cutaneous disorders related to inflammatory bowel disease. *Ann Gastroenterol* 2012;25:21–6.
- 12 Naranjo CA, Busto U, Sellers EM, *et al*. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30:239–45.

Copyright 2021 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-licensing/permissions/>
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

Customer Service

If you have any further queries about your subscription, please contact our customer services team on +44 (0) 207111 1105 or via email at support@bmj.com.

Visit casereports.bmj.com for more articles like this and to become a Fellow