Lichenoid cutaneous skin eruption and associated systemic inflammatory response following Pfizer-BioNTech mRNA COVID-19 vaccine administration

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Abstract
The global effects of coronavirus disease 2019 (COVID-19) have driven unprecedented rapid development and mass deployment of vaccinations against the novel coronavirus. However, the short- and long-term adverse reactions following COVID-19 vaccinations are still under investigation as insufficient time has passed to fully explore these. The Pfizer-BioNTech COVID-19 mRNA vaccine has thus far shown a favourable safety profile in phase I–III studies. Although infrequent cases of generalized cutaneous reactions and systemic inflammatory response have been reported following other mRNA vaccines, these have not been reported following the Pfizer-BioNTech vaccine. We report a case of generalized lichenoid skin eruptions and systemic inflammatory response occurring together following the first dose of the Pfizer-BioNTech vaccine. Our case report adds to an accumulating body of literature connecting autoimmunity with the pathophysiology of the novel coronavirus disease.

KEYWORDS
COVID-19, COVID-19 mRNA vaccines, lichenoid skin eruption, systemic inflammatory response

INTRODUCTION
The devastating effect of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a worldwide effort to find an effective solution to control the pandemic. A number of vaccination options have been developed including the Pfizer-BioNTech BNT162b2 vaccine which was given emergency approval by the American Food and Drug Administration in December 2020. In New Zealand, this vaccine was licensed for use in February 2021, and national roll-out started in March of the same year.

Pfizer-BioNTech BNT162b2 is an mRNA vaccine that has been shown to provide 94.8% protection against COVID-19 in adults in phase III clinical trials.\(^1\) It is administered intramuscularly in two doses, 30 mcg each, at 21 days apart.\(^2\) Thus far, the rates of reported adverse events are low and predominantly mild. These include localized pain at injection site, fever, fatigue, headache, myalgia and arthralgia that occur mainly within 7 days of vaccination. Reported cutaneous reactions are predominantly limited to the injection site.\(^3\) A recent vaccine registry review found few cases of generalized skin reactions including maculopapular rash\(^4\) and morbilliform rash\(^5\) following Pfizer-BioNTech BNT162b2 vaccine administration. In another report, erythema multiforme, pityriasis rosea, erythromelalgia and petechiae, amongst others, were also documented.\(^3\)

Here, we report a case of generalized lichenoid skin eruption and associated systemic inflammatory symptoms following administration of the first dose of Pfizer-BioNTech vaccine.

CASE REPORT
A 53-year-old NZ European healthcare worker with no significant medical history or previous allergy presented 12 days following administration of the first dose of Pfizer-BioNTech vaccine with dermatographia and generalized papular erythematous skin eruptions involving her abdomen, chest, back and scalp. She also reported a history of light-headedness associated with nausea on days 1 and 2.
following the vaccine administration, for which she did not seek medical attention. A dermatology opinion at the time of presentation was pityriasiform skin reaction to vaccination and a punch biopsy was performed. She was treated with cetirizine 20 mg twice daily and topical steroid applications, and planned for outpatient phototherapy.

The patient represented acutely the following day to the local emergency department with generalized increased skin erythema in addition to the existing pityriasiform rash and associated sinus tachycardia (140/min), tachypnoea (25/min) and mildly elevated temperature of 37.6°C. Investigations showed slightly raised blood white cell count of $12 \times 10^9$/L and otherwise normal eosinophil count, C-reactive protein (CRP) and procalcitonin. She was treated with reducing doses of oral prednisone (40 mg and then 20 mg daily), oral famotidine 20 mg daily and admitted to hospital for further observations due to ongoing symptomatic episodes of sinus tachycardia.

Further transient episodes of sinus tachycardia (up to 160/min), tachypnoea (up to 30/min) and low-grade fevers (up to 37.8°C) lasting 20–30 min occurred over the next 5 days preceded by increased skin erythema and dysesthesia (Figure 1). Repeat investigations during these episodes showed normal inflammatory markers including a normal CRP, and repeat serial electrocardiograms showed sinus tachycardia (up to 150/min). She remained otherwise asymptomatic in between these episodes. Intravenous hydrocortisone 100 mg was administered during some of these episodes with complete rapid relief of symptoms.

The skin histology revealed lichenoid skin reaction and was deemed likely in reaction to the vaccine. The transient episodes of tachycardia, tachypnoea and fevers were thought to be due to an associated systemic inflammatory response syndrome (SIRS) as extensive work-up for infectious, autoimmune and vasculitic work-up was negative. This case was also reported to the Centre for Adverse Reactions Monitoring at the NZ Pharmacovigilance Centre. In addition, she was also referred to an immunologist who advised that a non-Pfizer vaccine should be administered for the second dose. This has thus far not been given due to potential future complications.

**DISCUSSION**

We report a case of generalized lichenoid skin eruptions and associated SIRS following the first dose of Pfizer-BioNTech COVID-19 vaccine.

Drug-induced lichenoid eruptions are a well-documented, although uncommon, entity resulting from type IV cell-mediated hypersensitivity response. They are characterized by dermal and perivascular infiltration of plasma cells, lymphocytes and eosinophiles, with resultant skin and mucous membrane manifestations. They are usually managed by removal of the offending drug, application of topical corticosteroids and, if extensive, systemic steroid therapy.

To our knowledge, generalized cutaneous adverse reactions following the Pfizer-BioNTech vaccine are uncommon (<1%) and SIRS is rare, with no documented case of both together. A recently published international registry comparing mRNA COVID-19 vaccines has shown overall low incidence of systemic cutaneous eruptions, with lower rates in the Pfizer-BioNTech compared to the Moderna vaccine. The risk of recurrence following a second dose was 26% and 6% for Moderna and Pfizer vaccines, respectively. There were no reported lichenoid skin reactions in this series.

Mild systemic inflammatory reactions following COVID-19 vaccinations, on the other hand, are well described and may be linked to recent reports of myocarditis and pericarditis. However, associated autonomic activation and SIRS are not well recognized post the Pfizer-BioNTech vaccine or the other mRNA vaccines. There is one published case report of SIRS following Moderna vaccine administration with generalized increased $^{18}$F-fluorodeoxyglucose uptake on positron emission tomography-computed tomography (PET-CT) and one further report of postural orthostatic tachycardia syndrome developing following the first dose of the Pfizer-BioNTech vaccine. Prior to COVID-19, viral infections and vaccinations have been implicated in precipitating autonomic dysfunction. Dysautonomia and a pro-inflammatory state are also well documented in severe COVID-19 infections. Furthermore, viral-mediated autonomic neuropathy is one of the postulated pathway leading to long COVID syndrome.

In our patient, each SIRS-like episode is associated with worsening skin eruptions suggesting a shared common pathological pathway. The risk and benefits of proceeding with the second vaccination dose, given our patient’s occupation as a healthcare worker in a high-risk area, are not clear and will require careful consideration.

Never before in human history have so many vaccines been developed and deployed so quickly to meet such an urgent need. The potential short- and long-term adverse reactions of COVID-19 vaccines will require ongoing surveillance. Exploring the pathophysiology of these adverse

**FIGURE 1** Generalized lichenoid pityriasiform rash on the abdomen and during a systemic inflammatory response syndrome episode
reactions may also provide insights into the long-term sequelae of COVID-19.

CONFLICT OF INTEREST
None declared.

AUTHOR CONTRIBUTION
Pei-Yee Onn acquired the clinical history, patient consent, drafted the manuscript, prepared the images and approved the final draft. Catherina L. Chang conceptualized the work, critically revised the manuscript and approved the final draft.

ETHICS STATEMENT
The authors declare that appropriate written informed consent was obtained for publication of this case report and accompanying images.

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How to cite this article: Onn P-Y, Chang CL. Lichenoid cutaneous skin eruption and associated systemic inflammatory response following Pfizer-BioNTech mRNA COVID-19 vaccine administration. Respirology Case Reports. 2021;9:e0860. https://doi.org/10.1002/rcr2.860