Severe cutaneous reaction to the messenger RNA (mRNA) BNT162b2 (Pfizer–BioNTech) vaccine

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ABSTRACT

The pathway out of the COVID-19 pandemic has been reliant on uptake of vaccination. In New Zealand, we have access to the messenger RNA (mRNA) BNT162b2 (Pfizer–BioNTech) vaccine. In this case report we discuss a patient who presented to an acute general medical service with a severe cutaneous adverse reaction (SCAR) after the vaccine with features of both Stevens–Johnson syndrome and acute generalised pustulosis. Early recognition and management of SCARs is required to prevent morbidity and mortality.

The pathway out of the COVID-19 pandemic has been reliant on the uptake of vaccination. For the majority of the New Zealand population, we have access to the messenger RNA (mRNA) BNT162b2 (Pfizer–BioNTech) vaccine, which provides excellent protection from the most severe manifestations of COVID-19 infection.\(^1\) However, like any medical intervention, there are some patients who are affected by adverse reactions. In this case report we discuss a patient who presented with a severe cutaneous adverse reaction (SCAR) after the vaccine.

A 60-year-old woman presented to her general practitioner with a rash which began within 24 hours of her first dose of the Pfizer–BioNTech vaccine. She was usually independent with no prior admissions to hospital. She had a background of hypertension, dyslipidemia, impaired glucose tolerance, obstructive sleep apnoea, hepatic steatosis and high body mass index.

Her regular medications were chlorthalidone, losartan, atorvastatin and amlodipine. She had no known allergies and no prior history of drug reactions. There were no new or changed medications, including over the counter preparations, for at least two months prior to vaccination.

The eruption started on her right shoulder, chest and upper thighs with associated fever and fatigue. She had also noted some tiny pustules on the worst affected skin of the flexures, which would come and go from day-to-day. Five days later, when her symptoms did not abate, she presented to her GP. She was prescribed 40mg (0.5mg/kg) of morning prednisone, topical hydrocortisone butyrate (Locoid) and Pinetarsol solution for bathing. The rash continued to spread to involve much of her trunk and limbs. During phone consultation with her GP the following day, the patient reported worsening cutaneous pain and myalgia. She was referred to hospital on day six of her rash.

On admission she was alert and conversant, afebrile and haemodynamically stable. Her weight was 83.6kg. Blood pressure was 126/63mmHg, heart rate 105bpm, and oxygen saturations were 98% on air.

She had extensive confluent erythema involving approximately 70% of her body surface area. There were many areas of superficial peeling (Figure 1), but less than 10% deeper, full thickness epidermal loss. Nikolsky sign was negative. There were myriad scattered targetoid lesions over the trunk and limbs with vesicular and bullous areas on the proximal limbs (Figure 3). Notably her face was spared but her scalp was crusted. Three small 3mm diameter erosions were noted on her hard palate. Her lips were not crusted, but there were macules present on the vermilion. Two small vulvar erosions, 5mm in diameter, were also present. There was no conjunctival injection. At one stage early in her admission she had a few scattered, non-follicular superficial pinpoint pustules in the flexures.

Admission bloods showed haemoglobin 161g/L (115–155) and haematocrit of 0.46 (0.35–0.46). WBC 38.5xE9/L (4–11) and neutrophils 28.7xE9/L (1.9–7.5). Electrolytes revealed sodium 130 mmol/L (135–145), potassium 3.4mmol/L (3.5–5.2) and creatinine 127µmol/L (45–90). Fasting glucose was 10.4mmol/L (3–11). Liver function tests were
normal. Notably CRP was 129mg/L (0–5). Eosinophil count was 0.0xE9/L (0–0.5); this increased to 0.6xE9/L by day 3 of her admission.

The initial clinical impression was of Steven Johnson Syndrome (SJS) with minor mucosal involvement secondary to COVID-19 vaccination. The adverse drug reaction probability scale (Naranjo) score was 7, indicating a probable causal association between the rash and vaccination. Treatment was supportive, including intravenous fluid, careful fluid balance, topical betamethasone valerate (Beta) ointment, emollients and hydrating eye drops. Prednisone 40mg (0.5mg/kg) daily was continued. Assessment by the National Burns Service was sought and the patient was deemed appropriate for ward-based care initially, with ongoing burns unit remote monitoring.

Skin biopsies were taken from multiple sites. Histopathological evaluation showed a spongiotic epidermis containing subcorneal and intraepithelial pustules with abundant neutrophils (Figure 4). No epidermal necrosis was present. There was prominent papillary dermal oedema (Figure 5) forming vesicles in places. The vesicles contained neutrophils and some lymphocytes. There was a mild perivascular lymphocytic infiltrate in the superficial dermis. Lymphovascular spaces appeared somewhat ectatic and there was swelling of endothelial cells. The histological features were those of acute inflammation with pustules, favouring acute generalised exanthematous pustulosis (AGEP). Direct immunofluorescence was negative. Histologic features were not typical of erythema multiforme, SJS or toxic epidermal necrolysis (TEN). In SJS/toxic epidermal necrolysis, one would expect epidermal necrosis and subepidermal bullae with minimal inflammatory infiltrate, which was not the case here. Therefore, while histology was much more characteristic of AGEP than SJS, clinical appearances were arguably more consistent with SJS. A diagnosis of SCAR to COVID-19 vaccination with features of both AGEP and SJS was made.

During the patient’s hospital stay there was some extension of the rash onto the face and lower legs, but slow overall improvement. On day 4 of her admission, her prednisone was increased to 60mg daily (0.75mg/kg) and betamethasone valerate ointment was continued. Epidermal loss remained below 10% and was predominantly in flexural areas. The patient had inpatient monitoring from the ophthalmology service; there was no

**Figure 1:** Confluent erythema with superficial peeling.

**Figure 2:** Targetoid lesions becoming confluent by admission.
Figure 3: Targetoid lesions on thighs with confluence displaying bullous character and deeper erosive peeling.

Figure 4: Pustules, papillary dermal oedema and perivascular lymphocytic infiltrate.

Figure 5: Re-epithelialisation, dermal papillary oedema, but no epidermal necrosis as would be seen in SJS/TEN.
evidence of conjunctivitis and there were no corneal erosions but esterified hyaluronic acid (Hylofast) eye drops were advised.

The patient improved and was discharged after 11 days to continue a weaning course of prednisone and topical treatment. Her complete cutaneous recovery took many months. A report was filed with the Centre for Adverse Reactions Monitoring (CARM). In this case we found no triggers to explain this patient’s SCAR except recent vaccination with Pfizer–BioNTech vaccine.

Discussion

Both AGEP and SJS are considered SCARs. AGEP is usually a drug eruption characterised by superficial pustules and associated with eosinophilia, which was present in this patient (0.6xE9/L by day 3) despite high dose corticosteroids. The onset of AGEP is usually within 2 days of exposure to the culprit medication and it may overlap clinically with other CD8+ T cell hypersensitivity reactions such as SJS. Other differentials include generalised pustular psoriasis, which has recently been reported after the Pfizer vaccine, as well as small vessel vasculitis and cutaneous lupus. These were thought to be less likely clinically as the rash was not psoriasiform and resolved with no sequelae. Histology was also more in keeping with AGEP as discussed. It is worth noting that immunofluorescence was negative, as were other features of a systemic connective tissue or vasculitic disease.

SJS is often a more severe mucocutaneous reaction usually triggered by medications, particularly antibiotics and anticonvulsants. Onset can occur within a few days but is frequently delayed by a week or two, even up to a month after starting a medication. Targetoid lesions are a feature. It is on a spectrum with toxic epidermal necrolysis (TEN) which has the same underlying pathology but is defined as detachment of >30% of the skin surface.

In this case, the clinical diagnosis of SJS did not match with the histological findings, which favoured AGEP. Clinically and temporally this case is consistent with a severe form of AGEP. However, due to the features of SJS with risk of progression to TEN, early multidisciplinary input was requested. Often, as in our patient, SJS skin eruptions have a prodromal phase of malaise and fever followed by worsening cutaneous lesions and mucosal involvement, including genital mucosa. This can be significant, resulting in scarring and morbidity. There can be ocular lesions, but fortunately early ophthalmological assessment during the patient’s inpatient stay confirmed no ocular involvement; this was monitored closely and outpatient follow-up confirmed no ocular sequelae. Liver derangement is also common and renal impairment can occur. Evolving cutaneous lesions can lead to fluid loss due to breakdown of the skin barrier and thus increased risk of sepsis. Treatment is ideally managed in a specialist unit with multidisciplinary input. However, access to such units remains an issue in New Zealand, where burns unit beds are limited.

While in this case the cause of SCAR has been attributed to the BNT162b2 vaccine, reactions due to vaccination are rare. A recent report outlined a case of SJS after a patient received his first dose of the recombinant ChAdOx1 nCoV-19 (AstraZeneca’s Covishield, manufactured by the Serum Institute of India). The patient recovered after a short course of cyclosporin.

Timely recognition and treatment of SCARs is required to minimise patient morbidity and mortality. This requires adequate training of healthcare staff to appreciate the urgency of diagnosis, obtaining early dermatologist input and liaison with a burns unit. Finally, early dermatology input is reliant on a funded and effective public dermatology service.
COMPETING INTERESTS
Nil.

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