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LETTER TO THE EDITOR

Insulin allergy manifesting soon after COVID-19 vaccination (BNT162b2)

Insulin allergy is well known to cause not only local skin reactions but also systemic anaphylaxis, and can produce life-threatening effects[1]. Recently, with the increasing number of COVID-19 vaccinations, various types of skin reactions have been reported[2]. Such symptoms are assumed to be host immune responses to substances included in the vaccines,

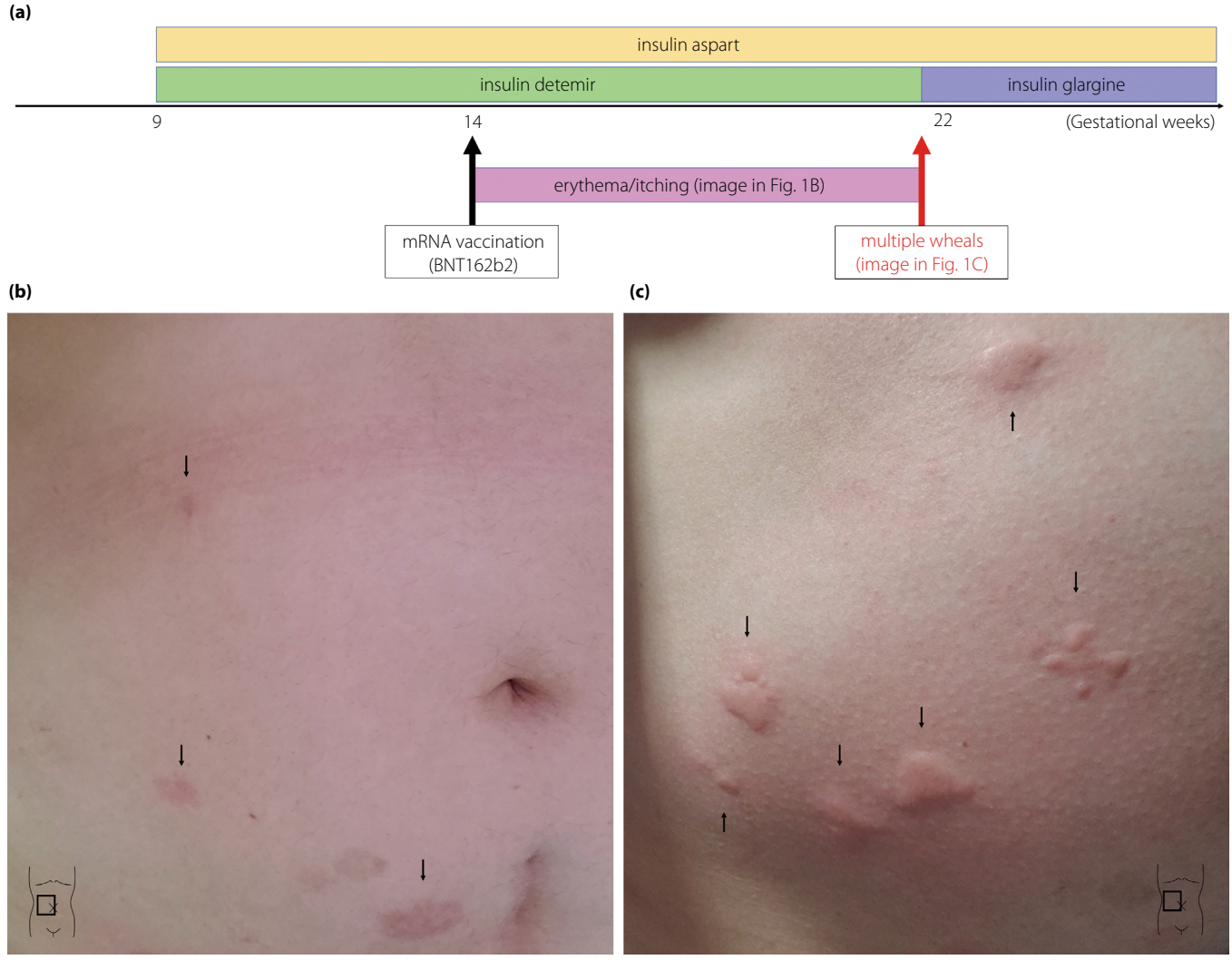

Figure 1 | (a) The time course of skin rashes. (b) An image showing erythema at 2 weeks after the COVID-19 vaccination. Erythema (arrows) appeared repeatedly at the injection sites of insulin detemir. (c) Multiple wheals over the entire abdomen (arrows) manifested rapidly after insulin detemir injection on day 53 after the vaccination.

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mainly the lipid nanoparticle (LNP) components of mRNA COVID-19 vaccines[2]. We experienced a case with insulin allergy which manifested soon after COVID-19 vaccination.

The patient was a 36-year-old woman with type 2 diabetes. Her glycated hemoglobin (HbA1c) level had been maintained around 6.0% with metformin monotherapy (500 mg/day). With recognition of the pregnancy at gestational week 6, metformin therapy was discontinued. Thereafter, as self-monitoring blood glucose revealed gradual elevations in blood glucose levels, intensive insulin therapy administering insulin aspart (IAsp) before meals and insulin detemir (IDet) before bedtime was started at gestational week 9. During the first 5 weeks after the initiation of insulin therapy, her blood glucose levels were well controlled with no adverse effects, including skin symptoms. At gestational week 14, she received COVID-19 vaccination with BNT162b2 (Pfizer), an mRNA vaccine. The next morning, she recognized symptomatic erythema and itching at the abdominal site where the IDet had been injected the previous night. These symptoms recurred daily (Figure 1a,b) and each of the erythematous lesions persisted for 4 or 5 days. Notably, the lesions were found only at the IDet injection sites, not at those of IAsp. Although blood tests showed no abnormalities in levels of immunoglobulins, such as IgE, or white blood cell fractions, including that of eosinophils, based on her symptoms and the clinical course, our dermatologist diagnosed the local erythematous lesions in the present case as allergic reactions to IDet. On day 53 after the vaccination, multiple wheals over the entire abdomen suddenly appeared within a few minutes after IDet injection (Figure 1a,c), suggesting the allergic response to IDet had been exacerbated. IDet was switched to insulin glargine 100 U/mL (Gla100) the next night, and no skin rashes occurred thereafter.

Among the insulin preparations used, she experienced allergic reactions to IDet, but not to either IAsp or Gla100. IDet is a human insulin analog containing a myristoyl moiety (C(14:0)), while neither IAsp nor Gla100 contains such fatty acid moieties. The myristoyl moiety is regarded as an allergen candidate for the IDet allergy[3]. Intriguingly, the LNP components of mRNA COVID-19 vaccines, including BNT162b2, contain several fatty acid moieties[4]. Therefore, the LNPs contained in BNT162b2 could have sensitized host immunity against substances with the myristoyl moiety, although we cannot rule out the possibility that the allergic reactions observed in our patient were unrelated to the vaccination.

The case reported herein suggests that, in patients who are treated with analogue insulin or glucagon-like peptide-1 preparations containing fatty acid moieties and scheduled for mRNA vaccination, dermatological symptoms should be carefully examined, and, when skin reactions are detected, switching to preparations without fatty acid moieties should be considered.

DISCLOSURE

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Approval of the research protocol: N/A.
Informed consent: We informed the patient, and she gave her consent.
Registry and the registration No. of the study/trial: November 15, 2021, No. 23733.
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REFERENCES

1. Jacquier J, Chik CL, Senior PA. A practical, clinical approach to the assessment and management of suspected insulin allergy. *Diabet Med* 2013; 30: 977–985.
2. Corey KB, Koo G, Phillips EJ. Adverse events and safety of SARS-CoV-2 vaccines: what's new and What's next. *J Allergy Clin Immunol Pract* 2022; 10: 2254–2266.
3. Sola-Gazagnes A, Pecquet C, M'Bemba J, *et al*. Type I and type IV allergy to the insulin analogue detemir. *Lancet* 2007; 369: 637–638.
4. Schoenmaker L, Witzigmann D, Kulkarni JA, *et al*. mRNA-lipid nanoparticle COVID-19 vaccines: structure and stability. *Int J Pharm* 2021; 601: 120586.

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