An Unusual Skin Reaction after Bexsero® Vaccination in a Paediatric Patient: A Case Report

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Abstract

Bexsero® is a multicomponent vaccine protecting against *Neisseria meningitidis* serogroup B, a major cause of meningococcal disease. Common side effects include injection site reactions (pain, redness, swelling) and systemic symptoms (fever, irritability, fatigue), while rarer complications like febrile seizures and Kawasaki disease occur in less than 1%. This case report describes a previously undocumented reaction in a twelve-week-old infant who developed immediate pale spots on the leg after vaccination, later progressing to a necrotic lesion. Possible hypotheses, including an immune response, intra-arterial injection with embolization, and vasospasm, are discussed.

Introduction

In 2023, Belgium recorded 104 cases of invasive meningococcal disease, with 83 confirmed by the National Reference Centre. The overall incidence was 0.71 cases per 100,000 inhabitants, with the highest rates observed in children between zero and four years (3.4 per 100,000), particularly infants under one year (8.8 per 100,000), as well as adolescents aged 15-19 (1.0 per 100,000) and adults over 80 (1.7 per 100,000). For the first time, serogroups W and Y were dominant (51.8%), followed by serogroup B (43.4%). Although serogroup B was the most prevalent in most age groups, serogroups W and Y were more common in adults aged 25-49 and those aged 65 and older. Among people over 65, serogroup Y was the most frequent. Among infants under one year, serogroup B accounted for six out of nine cases. Three deaths were reported, two from serogroup B and one from serogroup W (1).

Bexsero® is a vaccine given to individuals aged two months and older to protect against invasive disease caused by *Neisseria meningitidis* serogroup B. This bacterium is a gram-negative, aerobic microorganism responsible for severe illnesses such as meningitis and sepsis, collectively known as meningococcal disease. *N. meningitidis* is transmitted from person to person through aerosols or direct contact with the respiratory secretions of infected individuals or asymptomatic carriers, typically via coughing or sneezing (2).

Bexsero® is a multicomponent, recombinant, non-live vaccine specifically targeting meningococcal group B. To stimulate an immune response, it includes four antigenic proteins from the *N. meningitidis* bacterium: Neisseria Heparin Binding antigen, Neisserial adhesion A, factor H binding protein and outer membrane vesicles from Neisseria meningitidis group B strain NZ98/254 measured as amount of total protein containing the PorA P1.4. Apart from these proteins, it also contains inactive ingredients, such as aluminium hydroxide, histidine, sodium chloride, sucrose and water for injection (3).

In Belgium Bexsero® is not part of the routine immunization schedule, but it is advised at individual level (4). The vaccine is administered via intramuscular injection. For children until two years of age, it is injected into the anterolateral thigh muscle (musculus vastus lateralis), while for older children and adults, it is given into the deltoid muscle region of the upper arm (5).

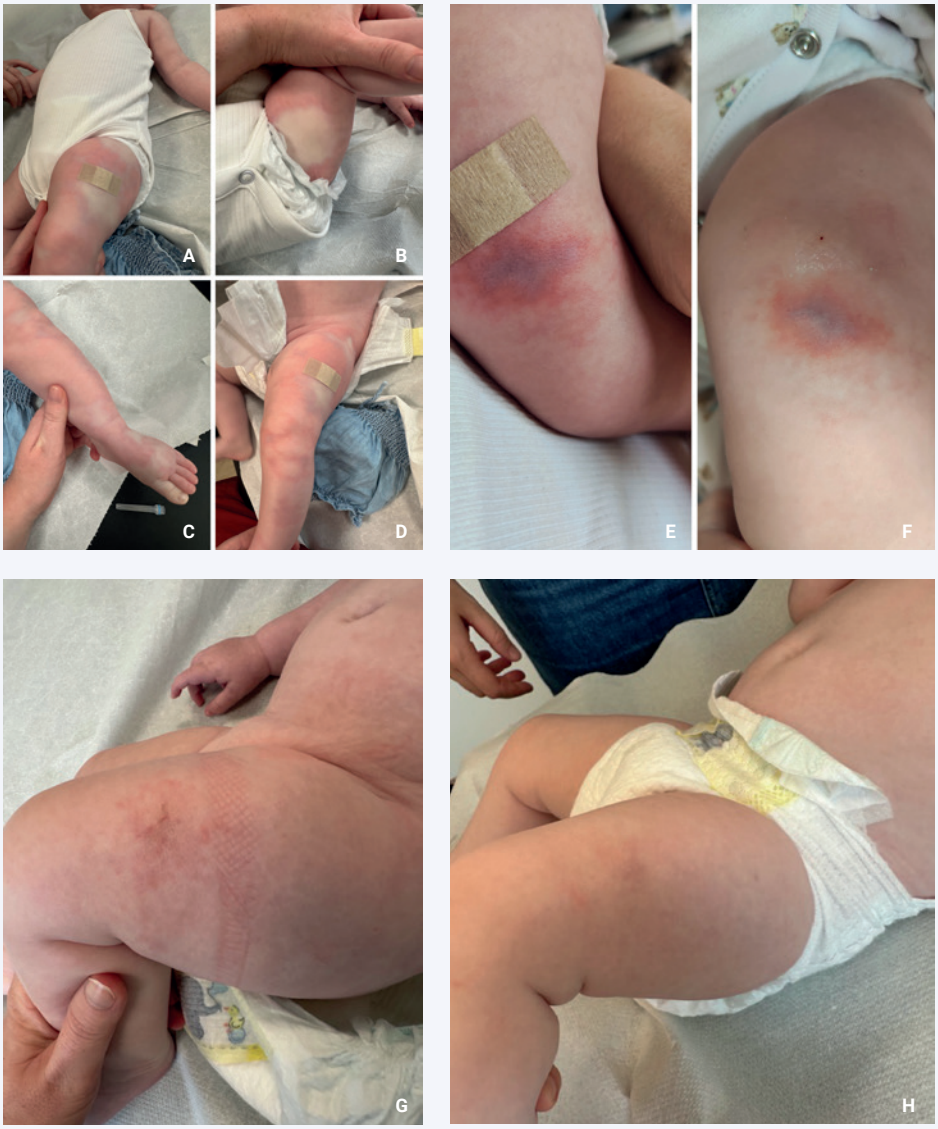
Skin reactions following Bexsero® vaccination, as documented in spontaneous suspected adverse vaccine reaction reports received up to and including 15/03/2022, range from mild and transient to more persistent and concerning manifestations. Common injection site reactions include erythema, swelling, induration and pain. More extensive skin reactions, such as rash, urticaria, pruritus, and dermatitis have also been reported. In some cases more severe presentations, like ecchymosis, skin discoloration, extensive limb swelling, necrosis or ulceration have been observed, though the exact causality remains uncertain (3,6).

Case report

A twelve-week-old girl (87 days) with an unremarkable medical history except for a one-day hospital admission for mild respiratory distress, visited the paediatric outpatient clinic to receive her first dose of the Bexsero® vaccine as a preventive measure. The vaccine was administered according to guidelines, intramuscularly in the anterolateral thigh of the left leg using a 23Gx1" needle. To ensure there was no intra-arterial placement, the paediatrician aspirated before administering the injection, and no blood was aspirated. Based on the latest studies, the Centres for Disease Control and Prevention state there is no evidence supporting the need for aspiration before intramuscular injections because no large blood vessels are present at the recommended injection sites (7).

Immediately after the vaccination unusual circular pale spots appeared on the girl's leg, without any apparent signs of discomfort.

FIGURE 1: Clinical presentation at the paediatrician (a-d), home on the same day (e,f), 5 days (g) and 2 months after onset (h).



Initially, a pale spot appeared directly distal to the injection site and spread down to the foot within seconds. A few minutes later, a purplish band formed around the various spots (Figure 1A). Several minutes after that, most of the spots disappeared, leaving only the initial one distal to the injection site.

Once stabilized, the child was sent home, with the mother sending pictures to monitor the progression of the leg. That same day, the pale spots completely disappeared, but a purplish area with surrounding redness developed at the injection site. While it appeared necrotic, this could not be definitively confirmed, as no dermatologist was consulted and no skin biopsy was taken (Figure 1B). Despite this, the girl remained otherwise healthy with no further complaints following the Bexsero® vaccination.

When the necrotic area appeared, a plastic surgeon was consulted for advice. She recommended treatment with a paraffin gauze dressing. Once the redness had resolved, a soothing and skin-repairing balm enriched with madecassoside, panthenol and antibacterial agents (Cicaplast®), was advised to support skin recovery (8).

After five days, only a light spotty area and a palpable hard zone of induration remained (Figure 1C), but showed gradual improvement over time (Figure 1D).

On the same day as the Bexsero® vaccination, the girl did not receive any other injections. However, later on, she received additional injections in both legs, including the standard twelve-week vaccinations. She had also previously received her eight-week vaccinations, none of which caused a similar reaction. After discussing the situation with the parents, the paediatrician decided not to administer the second Bexsero® vaccination.

Discussion

This reaction to the Bexsero® vaccine has not been previously documented in medical literature or reported to the Federal Agency for Medicines and Health Products. To understand this phenomenon, the following hypotheses must be considered.

Peripheral vasoconstriction is a rare but documented adverse effect of the Bexsero® vaccine, likely caused by a reaction to one of its components (6). In this case, the unusual circular pale spots could indicate a temporary local vascular response, such as vasospasm. This narrowing of the blood vessels, caused by contraction of the vascular smooth muscle, restricts blood flow to specific skin areas and explains the observed discoloration.

A possible link can also be drawn with Raynaud's phenomenon, a condition characterized by episodic vasospasms and skin discoloration due to reduced blood supply. Raynaud's phenomenon has been reported as a rare side effect of various vaccines. Lisy et al. for instance, described its occurrence after COVID-19 vaccination, illustrating how vaccines can sometimes provoke vascular reactions through mechanisms that are not yet fully understood. The tissue necrosis observed in this case may have been caused by prolonged vasospasm, leading to ischemia and subsequent tissue damage (9).

While vasospasm remains the most plausible explanation, it is important to consider other potential mechanisms. One of these mechanisms is an acute local vasoconstriction, possibly triggered by an inadvertent intra-arterial injection of the vaccine, although the exact process remains unclear. Noradrenaline plays a central role in this response. When the injected substance enters the bloodstream, crystal formation may occur, which triggers the local release of noradrenaline. This release induces vasospasm, followed by thrombosis, impaired blood flow and potential tissue damage (10).

In terms of vascular anatomy, the descending branch of the lateral circumflex femoral artery is the artery most likely affected during a lateral thigh injection. This artery, which originates from the profunda femoris artery, supplies the vastus lateralis and rectus femoris muscles, as well as the overlying skin (11). Normally, penetrating a large artery like this would result in a positive

aspiration test, which was not observed in this case, making an unintended intra-arterial injection unlikely. Additionally, if a smaller artery had been punctured, the pressure required for an intramuscular injection would likely have caused arterial rupture and a subsequent hematoma. Since no hematoma was observed, the likelihood of intra-arterial injection is further reduced.

Another possible hypothesis explaining the pale spots is a rare immune-mediated reaction. While this hypothesis is unlikely, it is included to be complete. In this case, an overreaction of the immune system to one of the components of the vaccine might cause a localized inflammatory response and vascular damage, leading to both the initial pale spots and the subsequent necrotic lesion. According to Donaldson et al. aluminium salts, often used as vaccine adjuvants, can cause severe local reactions, including necrosis, particularly when injected incorrectly into subcutaneous fat. The case study describes an adult patient who developed a necrotic ulcer after receiving the Tdap and Pneumovax vaccinations, likely due to the inflammatory response triggered by these adjuvants (12,13).

However, this immune-mediated hypothesis is less likely in this case because of the timing of the reaction. Immune-mediated responses generally develop over several hours or days, while the symptoms in this patient appeared rapidly. The immediate onset of the pale spots and the quick progression to necrosis make this hypothesis highly unlikely (12,13). While it is important to consider all possibilities, the immune-mediated reaction does not align with the observed clinical timeline and therefore remains an unlikely explanation for the lesion.

Conclusion

Although the exact cause of this reaction remains unclear, these hypotheses suggest that both vascular and immune-mediated mechanisms could be involved. Further observation and research are necessary to understand this reaction better. This case highlights the importance of documenting and researching new and unusual reactions to vaccines to make sure the safety and effectiveness of vaccination remain guaranteed.

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Declaration of patient consent

The authors certify that they obtained all appropriate patient consent forms. The parents gave their consent to publish the photos and other clinical information in this article. They understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Conflicts of interests

The authors declare that they have no conflict of interest and no financial disclosures.

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