Lessons from practice

Toxigenic cutaneous diphtheria without recent travel, Sydney, Australia, 2022

Caitlin Swift[1]
Anthea L Katelaris[1]
Thea Briggen Tiqui[1]
Julie Smith[2]
Tracey Papa[1]
Estella Janz-Robinson[3]
Trang Nguyen[4]
Qinning Wang[4,5]
Jenny Draper[5,6]
Vitali Sintchenko[4,7]
Debbie JE Marriott[3]
Vicky Sheppeard[1,8]

1 Public Health Unit, South Eastern Sydney Local Health District, Sydney, NSW.
2 St Vincent de Paul Society, Sydney, NSW.
3 St Vincent's Hospital, Sydney, NSW.
4 Centre for Infectious Diseases and Microbiology – Public Health, Institute of Clinical Pathology and Medical Research, Sydney, NSW.
5 Microbial Genomics Reference Laboratory, Institute of Clinical Pathology and Medical Research, Sydney, NSW.
6 Sydney Medical School, University of Sydney, Sydney, NSW.
7 Sydney Institute for Infectious Diseases, University of Sydney, Sydney, NSW.
8 School of Public Health, University of Sydney, Sydney, NSW.

caitlin.swift@health.nsw.gov.au

doi: 10.5694/mja2.52190

Clinical record

A 58-year-old man attended a Sydney outpatient dermatology clinic in November 2022 for a lesion on the vertex of the scalp, enlarging over 3 years. On examination, elevated rolled edges with a large central haemorrhagic crust suggestive of basal cell carcinoma were observed; however, the mass was unusually boggy on palpation, raising the question of a superimposed infective process (Box). The patient was systemically well. Biopsy confirmed nodular basal cell carcinoma and the Public Health Unit was notified by a laboratory that *Corynebacterium diphtheriae* had been isolated from the tissue culture. This was accompanied by growth of *Staphylococcus aureus*. Polymerase chain reaction testing performed at the Institute of Clinical Pathology and Medical Research returned a positive result for diphtheria toxin gene 5 days later, and public health follow-up of toxigenic cutaneous diphtheria commenced in accordance with control guidelines.[1,2]

Further history was obtained. The patient was Australian-born, not Aboriginal or Torres Strait Islander, and reported receiving routine childhood vaccines and tetanus vaccination (which may have included diphtheria toxoid) following injuries. The scalp lesion had first appeared while living in Vietnam in 2019. Later that year, he moved to Uganda, before returning to Sydney in mid-2021. He had not travelled since this time. There was no prior treatment of the lesion apart from an unknown over-the-counter topical therapy obtained overseas.

Appearance of scalp lesion at initial dermatology review and biopsy site as indicated

The patient was managed with oral clindamycin 600 mg three times daily for one week and wound dressing, with good clinical response. Two throat swabs were culture negative for *C. diphtheriae* and a booster adult diphtheria–tetanus–pertussis (dTpa) vaccine was provided, as infection may not induce immunity.[2]

Contact tracing was complex. At the time of public health follow-up, the patient was living in a facility for people experiencing homelessness (facility A), after discharge from an unrelated 5-week hospital admission one day before the dermatology review. Before hospitalisation, he had lived for 5 months in a different, larger facility for people experiencing homelessness (facility B) and had worked briefly as a teacher for international students.

Booster vaccination was recommended for all close or household-like contacts if more than 5 years had elapsed since the last dose. At facility A, the patient's two roommates received clearance antibiotics, and all residents (n = 9) and staff (n = 11) underwent a throat swab. All were culture negative for *C. diphtheriae*. Booster dTpa vaccination was provided to seven residents and four staff, and opportunistically to 14 staff of an associated health service with possible exposure.

Hospital staff who had cared for the patient were considered low risk because of standard precautions and routine use of masks at that time due to COVID-19; ten staff were therefore provided opportunistic booster vaccination only. Other patients in shared hospital rooms and his students were not followed up due to low likelihood of direct contact with the lesion, negative throat swabs from the patient and his close contacts, and elapsed time since exposure.

A comprehensive public health response at facility B was conducted despite the elapsed time, due to concern about carriage and transmission of *C. diphtheriae* within the homeless community as a possible source of infection. Facility B had up to 50 residents plus 200 homeless community members visit each day. Both resident and day clients were targeted and a total of 118 nose and throat swabs were obtained; all were culture negative for *C. diphtheriae*. Booster dTpa vaccination was provided to 96 clients after reviewing the Australian Immunisation Register and facility clinical records, with 58% of those vaccinated aged 50 years or above. Facility staff were advised to be alert for skin lesions among clients; however, none were identified among those swabbed. Staff were recommended opportunistic booster vaccination.

Further analysis at Institute of Clinical Pathology and Medical Research identified the isolate as *C. diphtheriae* biovar mitis with reduced in vitro susceptibility to penicillin (minimum inhibitory concentration

0.25 mg/L). Whole genome sequencing confirmed toxin gene production and showed that the isolate was genomically distinct and not linked to available genomes from other cases in New South Wales, Queensland or Papua New Guinea, and not belonging to an assigned multilocus sequence type. The sequence most closely matched genomes reported in Europe in refugees from Africa.

We are not aware of any other diphtheria cases epidemiologically linked to this patient.

Discussion

Diphtheria is re-emerging in high resource settings due to migration from countries with poor vaccination coverage.[3] Within Australia, there were 29 cases of genomically linked toxigenic diphtheria with epidemiological links to North Queensland from 2020 to 2022,[4] and cases had also increased nationally over the previous decade.[5] Our unexpected case demonstrates the need for vigilance, including prepared public health systems to enable a prompt response.

Diphtheria can present as respiratory or cutaneous infection, and toxigenic *C. diphtheriae* accounts for most notifications in Australia.[5] Most cases reported in Australia are cutaneous diphtheria,[5] which typically presents as secondary infection of existing skin lesions or well demarcated ulcers.[1,2] Transmission of diphtheria is usually via respiratory droplets or direct contact with respiratory secretions or exudate from an infected person or carrier.[1,2]

Cutaneous diphtheria contact tracing aims to identify co-primary or secondary cases, as well as asymptomatic carriers to eliminate carriage.[2] Determining the extent of contact tracing for this case was challenging, as the source of infection and hence duration of infection or colonisation with *C. diphtheriae* was unknown. The whole genome sequencing findings suggest possible overseas acquisition in Uganda and therefore chronic carriage, but given low representation of genomes from diphtheria endemic countries in publicly available databases, more recent local acquisition from an unknown source is possible. The infectiousness of our case was also unclear; however, both respiratory and cutaneous infection can occur in cutaneous diphtheria contacts,[6,7] and there is some evidence that cutaneous diphtheria may be more transmissible than respiratory diphtheria, possibly due to greater environmental contamination.[8,9]

Our precautionary mass testing at facility B provided reassurance that respiratory carriage of *C. diphtheriae* was not present in that community, with limitations that carriage may be transient and not everyone was tested. However, this response involved significant resources which must be carefully weighed against potential benefits of mass testing of contacts. The benefits of mass opportunistic dTpa boosting remain high, particularly in vulnerable populations.

The potential delay in diphtheria toxin result (7 days from specimen collection in this case) poses a challenge for public health control of diphtheria given the usual 2–5-day incubation period.[1] Public health staff should consider this when conducting risk assessments before toxin status is known, and where possible, request expedited testing if there are high risk clinical or public health features.

Diphtheria vaccination protects against toxin-mediated severe disease. In Australia, a booster dose of diphtheria-containing vaccine is recommended at age 50 years because of waning immunity[10] but is not funded under the National Immunisation Program. The provision of age-appropriate booster dTpa vaccines for people experiencing homelessness could be considered by jurisdictional health departments, in conjunction with homeless health services, to increase protection of this population who would otherwise be unable to access this vaccine.

Lessons from practice

- Toxigenic diphtheria can arise in unexpected circumstances, and public health systems in Australia must be prepared.
- Widespread testing of contacts of a diphtheria case of unknown source requires careful consideration of potential benefits versus costs and is likely to be of low utility in most Australian settings, although opportunistic vaccination should still be considered.
- Maintaining high diphtheria vaccination coverage across all ages is crucial for protection against severe disease.
- The provision of age-appropriate diphtheria–tetanus–pertussis vaccine boosters by homeless health services could increase protection against vaccine-preventable diseases for people experiencing homelessness, who would otherwise be unable to access this vaccine.

Patient consent: The patient gave written consent for publication.

Acknowledgements: We thank the patient described in this report for his gracious cooperation with public health authorities and consent for publication, and all staff who assisted with this response, particularly Phillip Read, Cathy Macknight, Matt Larkin, Jose Vargas-Castillo, Lilia Graham, and laboratory staff at SydPath and NSW Health Pathology. We also thank our public health colleagues in North Queensland for sharing their insights and experience with us.

Competing interests: No relevant disclosures.

Provenance: Not commissioned; externally peer reviewed. ■

© 2023 AMPCo Pty Ltd.

1 NSW Health. Diphtheria control guideline. 2017. https://www.health.nsw.gov.au/Infectious/controlguideline/Pages/diphtheria.aspx (viewed Aug 2023).

2 Queensland Health. Diphtheria: Queensland health guidelines for Public Health Units. 2019. https://www.health.qld.gov.au/cdcg/index/diphtheria (viewed Aug 2023).

3 European Centre for Disease Prevention and Control. Increase of reported diphtheria cases among migrants in Europe due to *Corynebacterium diphtheriae*, 2022. 6 Oct 2022. https://www.ecdc.europa.eu/en/publications-data/increase-reported-diphtheria-cases-among-migrants-europe-due-corynebacterium (viewed Aug 2023).

4 Hempenstall A, Short J, Marquardt T, et al. Clinician alert: toxigenic diphtheria cases across North Queensland are on the rise. *Med J Aust* 2023; 218: 238. https://www.mja.com.au/journal/2023/218/5/clinician-alert-toxigenic-diphtheria-cases-across-north-queensland-are-rise

5 Winkler NE, Dey A, Quinn HE, et al. Australian vaccine preventable disease epidemiological review series: diphtheria 1999-2019. *Commun Dis Intell (2018)* 2022; 46: https://doi.org/10.33321/cdi.2022.46.42.

6 de Benoist AC, White JM, Efstratiou A, et al. Imported cutaneous diphtheria, United Kingdom. *Emerg Infect Dis* 2004; 10: 511-513.

7 Edwards D, Kent D, Lester C, et al. Transmission of toxigenic *Corynebacterium diphtheriae* by a fully immunised resident returning from a visit to West Africa, United Kingdom, 2017. *Euro Surveill.* 2018; 23(39).

8 Koopman JS, Campbell J. The role of cutaneous diphtheria infections in a diphtheria epidemic. *J Infect Dis* 1975; 131: 239-244.

9 Belsey MA, LeBlanc DR. Skin infections and the epidemiology of diphtheria: acquisition and persistence of *C diphtheriae* infections. *Am J Epidemiol* 1975; 102: 179-184.

10 Australian Technical Advisory Group on Immunisation (ATAGI). Australian Immunisation Handbook. Canberra: Department of Health and Aged Care, 2023. https://immunisationhandbook.health.gov.au (viewed Aug 2023). ■