

## Cutaneous Diphtheria in a German Man with Travel History

Azadeh Orouji<sup>1</sup>, Alexander Kiewert<sup>1</sup>, Thomas Filser<sup>2</sup>, Sergij Goerdts<sup>1</sup> and Wiebke K. Peitsch<sup>1\*</sup>

<sup>1</sup>Department of Dermatology, <sup>2</sup>Medical Department II, University Medical Centre Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1–3, DE-68135 Mannheim, Germany. \*E-mail: wiebke.ludwig@umm.de  
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Cutaneous diphtheria is still endemic in many tropical regions, but rarely seen in developed countries, where it is most commonly related to a history of travel. It is caused by infection with *Corynebacterium diphtheriae* or, with increasing frequency, *C. ulcerans* (1, 2). *C. diphtheriae* and *ulcerans* occur in non-toxicogenic and toxicogenic strains, the latter producing the toxin responsible for the diphtheria disease and systemic toxic complications, such as neuritis and myocarditis. Both non-toxicogenic and toxicogenic strains may be harboured in the nasopharynx, skin, and other sites on asymptomatic carriers. They enhance in pre-existing skin lesions, commonly as co-infections with other pathogens (1, 2).

### CASE REPORT

A 55-year-old German man presented with a cutaneous ulcer of the knee, lasting for 4 weeks, which had developed from a painful nodule with purulent secretion. Extracutaneous symptoms, including fever, arthralgia, myalgia, headache and sore throat, were denied. The patient's medical history was otherwise unremarkable. He was a social worker, spending most of the year in Nepal and Indonesia in close contact with local children and adolescents, and he had returned from Indonesia 3 weeks prior to referral. He had received all recommended vaccinations with regular boosting. Clinical examination showed an ulcer with firm brownish crusts and undermined margins sized 5 × 5 cm on the left knee (Fig. 1). There were no signs of lymphadenopathy, no lesions of the oropharyngeal mucosa, and no pathological find-



Fig. 1. Ulcer with firm brownish crust and haemorrhage on the left knee.

ings of other organ systems. Laboratory tests revealed leucocytosis ( $17.7 \times 10^9/l$ ; normal:  $4.2\text{--}10.2 \times 10^9/l$ ) with neutrophilia (75.9%) and elevated C-reactive protein (50.3 mg/l; normal: 0–5 mg/l).

In cultures of swabs from the lesion on blood-agar, masses of *C. diphtheriae var gravis* were identified, together with Group C haemolytic streptococci. Both strains were sensitive to penicillin and erythromycin. Diphtheria toxin gene PCR was negative. Cutaneous diphtheria caused by non-toxicogenic *C. diphtheriae var gravis* was diagnosed. The patient was admitted to the infectious disease department and isolated. Treatment was initiated with penicillin 4 × 5 mega infusions and disinfection with polyhexanide, leading to rapid improvement. Later, when penicillin-resistant *Staphylococcus aureus* was also identified oral levofloxacin 250 mg 2/day was added.

The patient had received his last booster vaccination for tetanus and diphtheria 6 months prior to presentation. When enzyme-linked immunoassay (ELISA) was performed to determine *C. diphtheriae* antitoxin concentration, an adequate amount of antibodies was found (0.64 U/ml). As the isolated strain was non-toxicogenic, diphtheria antitoxin injection was not required.

### DISCUSSION

Primary cutaneous diphtheria lesions can range from a pustule, to an initially painful chronic non-healing ulcer with an adherent membrane and undermined margins. However, lesions may also be less distinctive. Therefore, a high index of suspicion is required to induce appropriate diagnostics, as *C. diphtheriae* cannot be isolated by routine culturing methods.

In Germany, nine cases of cutaneous or pharyngeal diphtheria have been reported to the Robert Koch Institute in the last decade (3). As in other European and Northern American countries, most of these cases were imported (3–5). However, indigenous infections are also still observed, especially in homeless people and people with a history of alcohol or drug abuse (6, 7). Although diphtheria vaccination coverage is high in young Western European children, adolescents and adults have significant gaps in immunization, due to lack of adequate boosting (8, 9). Persistent occurrence of both indigenous and imported diphtheria cases highlights the importance of regular boosters, especially for travellers to endemic regions (10).

In recent years, non-toxigenic *C. diphtheriae* strains have been isolated with increasing frequency, both from skin lesions of individuals under poor hygienic conditions and from pharyngeal swabs of patients with throat infections (11–14). They can sometimes cause severe invasive infections, most frequently, endocarditis and septic arthritis (11, 12). Moreover, it has been discussed that they could mutate into toxigenic strains by acquiring the *tox* gene (15). Therefore, increased awareness and immediate treatment is warranted. Both toxigenic and non-toxigenic *C. diphtheriae* are usually susceptible to penicillin and erythromycin. Diphtheria antitoxin should be administered without delay in all cases with proven or suspected toxigenic strains (1).

Due to increased travel to endemic regions, the number of cases of cutaneous diphtheria may increase in the near future. As a result of the sometimes vague clinical appearance and common co-infection with other pathogens, the diagnosis is prone to be overlooked. Awareness among clinicians and microbiologists should be increased and appropriate swab specimens obtained from any non-healing skin lesion in patients with a history of travel.

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