Toxigenic Corynebacterium diphtheriae-Associated Genital Ulceration

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In October 2016, an adolescent boy sought care for acute genital ulceration in Cologne, Germany. We presumed a sexually transmitted infection, but initial diagnostic procedures yielded negative results. He was hospitalized because swab samples from the lesion grew toxigenic *Corynebacterium diphtheriae*, leading to the diagnosis of possibly sexually transmitted cutaneous diphtheria.

Members of the genus *Corynebacterium* colonize the upper respiratory tract and healthy skin and are frequently found in clinical specimens without clinical significance. Three species, *C. diphtheriae*, *C. ulcerans*, and *C. pseudotuberculosis*, can cause serious infections by acquiring the ability to produce the diphtheria toxin manifesting clinically as cutaneous or respiratory diphtheria. Because vaccination is widely used in industrialized countries, diphtheria is rare, but it remains endemic to several countries of Africa, Asia, the Eastern Pacific region, and Eastern Europe. During 2001–2016, a total of 80 cases of toxigenic *Corynebacterium* spp. infections were notified in Germany (1).

Case Report

In October 2016, a 16-year-old boy from Ethiopia sought care at the University Hospital of Cologne (Cologne, Germany) with 3 papules at the glans and a

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slightly bleeding, painful ulceration at the dorsal shaft of his penis. He complained about local pruritus and had swollen, painful inguinal nodules on the left side. On clinical examination, the ulcer appeared to have coalesced from a few smaller lesions with an erythematous base and a yellow to purulent exudate. The boy denied having lesions before the ulcer. Specific history could not be clarified satisfactorily: the boy had an undefined status of residence and lived in an accommodation facility for asylum seekers. Given that he was an unaccompanied minor refugee, the examiners considered traumatic sexual experiences when the boy was unwilling to share further details especially about his sexual history. General physical examination was unremarkable. Pubertal development was normal.

We presumed a sexually transmitted infection. Because we considered herpes simplex virus and chancroid as likely diagnoses, the boy started on empiric outpatient treatment with valaciclovir and azithromycin. Serologic screening for syphilis and herpes simplex virus PCR yielded negative results. Toxigenic C. diphtheriae was cultured from the ulcer, and the boy was hospitalized 7 days after initial consultation because of cutaneous diphtheria. Toxigenicity of the isolate was verified by real-time PCR for tox gene and the modified Elek test in the German National Consulting Laboratory for Diphtheria. On the day of hospitalization the lesions showed only minor signs of resolution. Blood test analysis did not detect any systemic inflammation. No other swab of the genital lesions or the uninflammed tonsils grew pathogens. Because the boy's vaccination history was unclear, we used an enzyme immunoassay to determine the serum level of diphtheria toxin antibodies, and the results indicated seroprotection (4.69 IU/mL).

The patient was isolated and treated with intravenous penicillin (6 million U/d). When susceptibility testing revealed penicillin resistance, his antimicrobial drug regimen was changed to ciprofloxacin (1,200 mg/d). After 4 days of inpatient treatment, the patient was discharged. Follow-up visits confirmed full recovery; repeat swab sample testing of throat and penis were culture- and PCR-negative. The patient completed antimicrobial drug therapy 10 days after discharge.

In contact tracing, initiated by the local health department, 2 persons were determined to be at risk because they shared a room with the patient at the accommodation facility. Swab samples from tonsils and suspicious skin lesions (including 1 penile wound) of the contacts were negative for *C. diphtheriae.* Consequently, we discussed public health actions with them; chemoprophylaxis or vaccination were not considered necessary.

Conclusions

Only few cases of cutaneous diphtheria are reported in Germany, and they are strongly associated with defined risk factors, especially contact, during endemic circulation, associated with traveling (2), migration (3), zoonotic reservoirs (4), or poor socioeconomic conditions (5). In this case, the clinical manifestion of the genital ulcer with typical symptoms of sexually transmitted infections, such as painful unilateral inguinal nodules, supports the likelihood of sexually transmitted diphtheria, although we were not able to verify the patient's medical or sexual history. We did not isolate any other pathogen, in contrast with another case of male urethritis in which toxigenic C. diphtheriae was part of a polymicrobial infection and sexual transmission was assumed (6). This case shows that unusual manifestations of diphtheria are conceivable on various body sites. Clinicians should consider this easily overlooked disease in the differential diagnosis for similar cases. This awareness might lead to an increase in confirmed cases, improve outcomes, and prevent disease through subsequent public health actions.

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References

- Robert Koch Institute. Infectious disease epidemiology annual report 2017 [in German] [cited 2019 Oct 10]. https://www.rki.de/DE/Content/Infekt/Jahrbuch/ Jahrbuch_2017.pdf
- Sing A, Heesemann J. Imported cutaneous diphtheria, Germany, 1997–2003. Emerg Infect Dis. 2005;11:343–4. https://doi.org/10.3201/eid1102.040560
- 3. Meinel DM, Kuehl R, Zbinden R, Boskova V, Garzoni C, Fadini D, et al. Outbreak investigation for toxigenic *Corynebacterium diphtheriae* wound infections in refugees from northeast Africa and Syria in Switzerland and Germany by whole genome sequencing. Clin Microbiol Infect. 2016;22:1003.e1-1003.e8.
- Berger A, Boschert V, Konrad R, Schmidt-Wieland T, Hörmansdorfer S, Eddicks M, et al. Two cases of cutaneous diphtheria associated with occupational pig contact in Germany. Zoonoses Public Health. 2013;60:539–42. https://doi.org/10.1111/zph.12031
- Lowe CF, Bernard KA, Romney MG. Cutaneous diphtheria in the urban poor population of Vancouver, British Columbia, Canada: a 10-year review. J Clin Microbiol. 2011;49:2664–6. https://doi.org/10.1128/JCM.00362-11
- Berger A, Lensing C, Konrad R, Huber I, Hogardt M, Sing A. Sexually transmitted diphtheria. Sex Transm Infect. 2013;89:100–1. https://doi.org/10.1136/sextrans-2011-050418

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