Correspondence

Pitfalls with Diphtheria-Like Illness due to Toxigenic Corynebacterium ulcerans

To the Editor—In a recent report about diphtheria-like illness due to toxigenic Corynebacterium ulcerans, Tiwari et al. [1] highlighted the importance of this emerging but often-neglected pathogen. Unfortunately, because of the pathogen’s novelty (the first valid molecular description of the species dates only to 1995 [2]), uncertainties related to diagnosis, therapy, and prevention of illness due to toxigenic C. ulcerans still exist. Two issues that were discussed by Tiwari et al. [1] are related to the sequence of C. ulcerans diphtheria toxin that we recently described [3, 4].

First, in our opinion, the efficacy of the commonly used diphtheria toxoid vaccine against diphtheria due to C. ulcerans is not known. For instance, among the 15 C. ulcerans–infected patients who had an obtainable vaccination history listed by Tiwari et al. [1] (including their own 2 patients), 4 and 7 patients were fully or partly vaccinated, respectively, whereas 4 patients had not received any diphtheria vaccination. More promisingly, although older, inconclusive studies were probably hampered by the presence of phospholipase D in C. ulcerans (reviewed by Wong and Groman [5]), more-recent laboratory studies that used toxigenic C. ulcerans and diphtheria antitoxin in cytotoxicity assays [3] or in an animal model [6] demonstrated a protective effect of diphtheria antitoxin, although the protective effect was determined on the basis of only 2 analyzed human-pathogenic strains. In conclusion, even if a protective effect of diphtheria toxoid vaccine against C. ulcerans is assumed (i.e., attenuated clinical symptoms are observed), one should remember from studies of Corynebacterium diphtheriae that vaccination probably does not prevent colonization by toxigenic corynebacteria but only prevents overt disease. Although we agree that, because of the lack of a proven vaccine against C. ulcerans, diphtheria toxoid vaccine might be a reasonable alternative, especially during revaccination, we feel that the evidence that “up-to-date immunization with a diphtheria toxoid vaccine will prevent diphtheria and diphtheria-like illness caused by C. ulcerans” [1, p. 399] is scanty.

Second, Tiwari et al. [1] reported that the real-time C. diphtheriae diphtheria toxin–encoding tox gene PCR, described by Mothershed et al. [7], revealed atypical amplification of subunit A and no amplification of subunit B. Similarly, another study reported that real-time PCR was insufficient for the detection of the C. ulcerans tox gene [8]. This is not unexpected, because a previous study revealed major nucleotide sequence differences between the C. diphtheriae tox and the C. ulcerans tox genes, as well as between tox genes from different C. ulcerans strains. Three more sequences of C. ulcerans diphtheria toxin have been published in GenBank, and an additional sequence was reported that was identical to 1 of our published strains [9]. Careful probe design is needed to detect the C. ulcerans tox gene by PCR, because considerable variations in the sequence of the gene have already been described.

Taken together, these 2 uncertainties in the diagnosis and the treatment of diphtheria-like illness due to toxigenic C. ulcerans highlight the need for a better understanding of the molecular epidemiology and characteristics of C. ulcerans and its diphtheria toxin–like toxin.

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References


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