A paediatric case of lymphadenitis by toxigenic Corynebacterium ulcerans

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Introduction: Corynebacterium ulcerans, a potentially toxigenic zoonotic agent, may produce diphtheria toxin and causes varied types of infections in humans. Cases of infection due to toxigenic C. ulcerans infection have been increasingly reported.

Case presentation: A 6-year-old Japanese girl who had been vaccinated using diphtheria toxoid presented with fever and swelling in the left neck. Ultrasonography showed cervical lymphadenitis with cellulitis. C. ulcerans was isolated from the drainage specimen. The infection was cured with erythromycin administration. Her anti-diphtheria toxoid antibody level was at an adequate level for diphtheria prevention on admission and was significantly increased 3 weeks later. Zoonotic infection was considered likely, because a family cat had shown rhinitis and skin ulcers prior to symptom onset in the child.

Conclusion: In addition to the number of reported cases of infection in adults, C. ulcerans infection in previously vaccinated children should also be a subject of concern in Japan.
The isolates were identified as toxigenic *C. ulcerans* by biochemical differentiation as follows. Biotyping was performed using the API CORYNE system (SYSMEX bioMérieux). Diphtheria toxin production was confirmed by a modified Elek test (Engler *et al.*, 1997) and Vero cell cytotoxicity tests (Miyamura *et al.*, 1974). The anti-diphtheria toxoid antibody level was 0.757 IU ml$^{-1}$ at onset, increasing to 6.05 IU ml$^{-1}$ after 3 weeks.

The family cat had shown eye discharge, sneezing and skin ulcers before the onset of symptoms in the patient. Unfortunately, *C. ulcerans* was not able to be grown from swabs of the bulbar conjunctiva, pharynx or skin of the domestic cat, probably because antibiotics had been administered prior to specimen collection.

All other members of the patient’s immediate family had been immunized with diphtheria toxoid vaccine (DT) four times and showed no symptoms. Cultures of throat swab specimens from family members all showed negative results. DT was provided for the patient’s mother, because her anti-diphtheria toxoid antibody level was significantly below the protective level of $>0.1$ IU ml$^{-1}$.

**Discussion**

Reports of *C. ulcerans* infection have markedly increased in recent years (Wagner *et al.*, 2012). Most cases have involved older adults who were not up to date with immunization against *C. diphtheriae*. Paediatric cases of *C. ulcerans* infection are extremely rare, because children generally receive a routine series of DT injections. To the best of our knowledge, only four paediatric cases of *C. ulcerans* have been described in the literature (Table 1). Unfortunately, detailed descriptions about immunization histories and levels of anti-diphtheria toxoid antibody have been lacking (Hart, 1984; Pers, 1987; Kisely *et al.*, 1994; Public Health England, 2000). Illness occurred in our patient despite the presence of what was considered an adequately protective level of anti-diphtheria toxoid antibody ($>0.1$ U ml$^{-1}$), although symptoms were mild and pseudomembrane formation was not observed. *C. ulcerans* initially infects the throat, and the colonized bacteria subsequently produce diphtheria toxin and form a pseudomembrane that causes serious dyspnoea. Acquired anti-diphtheria toxoid antibody might be helpful in preventing formation of the pseudomembrane but may not prevent invasion through cervical lymphadenitis from the throat via the blood or lymphangion to allow early colonization by *C. ulcerans*. Furthermore, we have suggested the possibility of a partial immunity response due to differences between the DT produced by *C. diphtheriae* and some *C. ulcerans* strains (Sing *et al.*, 2005).

We should consider *C. ulcerans* as prevalent among animals (Katsukawa *et al.*, 2012; Hirai-Yuki *et al.*, 2013). It has been reported previously by Shimono *et al.* (2012) that surveillance of cats in Tokushima Prefecture, where the patient lives, found *C. ulcerans* colonizing 4.2 %, and anti-diphtheria toxoid antibody was present in 10.5 % of cats. We recommend that pet owners wash their hands after touching animals, and wear a mask and gloves if the animal shows signs of illness.

**Table 1. Paediatric cases of *C. ulcerans* infection**

<table>
<thead>
<tr>
<th>Year</th>
<th>Age/sex</th>
<th>Country</th>
<th>Symptom</th>
<th>Route</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>9 years/boy</td>
<td>Denmark</td>
<td>Respiratory diphtheria-like illness</td>
<td>Unknown</td>
<td>Pers (1987)</td>
</tr>
<tr>
<td>1994</td>
<td>9 years/girl</td>
<td>UK</td>
<td>Pharyngitis</td>
<td>Unknown</td>
<td>Kisely <em>et al.</em> (1994)</td>
</tr>
</tbody>
</table>

**Fig. 1.** Ultrasonography showing an unclear boundary and hypoechoic lymph with a maximal size of 9 × 7 mm. Blood flow is observed in the lymph nodes. The surrounding subcutaneous tissue appears hyperechoic.
In conclusion, we suggest that, while DT immunization might be effective in preventing severe respiratory disease caused by C. ulcerans, lymphadenitis may occur in children despite DT vaccination and having protective antibody titres because DT vaccination does not prevent colonization by corynebacteria. Close contact with sick animals should be avoided whenever possible.

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References


