Unusual Case of Necrotizing Fasciitis Caused by *Vibrio cholerae* O137\(^\dagger\)

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Received 9 November 2010/Returned for modification 19 November 2010/Accepted 8 December 2010

We report a case of necrotizing fasciitis caused by *Vibrio cholerae* O137 in an immunocompromised 49-year-old man. The infection was acquired following a minor traumatic injury and exposure to seawater during the summer of 2009 in Italy. Although highly immunocompromised, the patient survived. The strain was cytotoxic, invasive, and adhesive and contained a fragment of the El Tor-like hemolysin (El Tor *hlyA*) gene.

**CASE REPORT**

In July 2009, an HIV- and hepatitis C virus (HCV)-positive 49-year-old man with chronic liver disease and type 2 diabetes mellitus fell while walking in the sea (Apulian region, Italy) and succumbed to a minor abrasion of his left foot. Four days later, the patient was admitted to a hospital with fever, foot pain, lower-extremity swelling, and erythema on arrival. He was immediately empirically treated with intravenous daptomycin and levofloxacin (500 and 750 mg/day, respectively). Over the following days, hemorrhagic bullous lesions ascending the leg up to the knee and a severe soft tissue necrosis developed and a clinical diagnosis of necrotizing fasciitis was made (Fig. 1). The patient underwent extensive fasciotomy and soft tissue debridement. Samples of blood, biopsy tissue from the lesion, and feces were taken before treatment with antibiotics. Blood cultures were negative, and pathogenic microorganisms were not detected in feces. The tissue biopsy culture on 5% sheep agar and thiosulfate citrate bile salt (TCBS) agar (Oxoid Ltd., Basingstoke, England) yielded only a Gram-negative, oxidase-positive curved bacterium. The isolate was identified as *Vibrio cholerae* (confidence, 97.8%) by the API ID 32 GN commercial system (bioMérieux, Marcy-l’Etiole, France), and the species identification was also confirmed using a standardized biochemical protocol (9). The isolate did not react with polyvalent anti-O1 and anti-O139 antisera (Denka Seiken Co. Ltd., Tokyo, Japan) and was serotyped as *V. cholerae* O137 by the National Institute of Infectious Diseases, Tokyo, Japan (16).

PCR assays were used to detect the presence of toxin-coding genes (10). These included the cholera toxin (*ctx*), heat-stable toxin (*stn/sto*), hemolysin (classical *hlyA* and biotype El Tor *hlyA*), toxin-coregulated pilus (classical *tcpA* and biotype El Tor *tcpA*), and zonula occludens toxin (*zot*) genes. Cytotoxicity against Vero cells and adhesive and invasive properties on CaCo-2 and HT29 cells were also investigated (2). *V. cholerae* O1 classical biotype ATCC 9459 was used as positive control for PCR amplification of the classical *tcpA*, classical *hlyA*, *ctxA*, and *zot* genes. The *V. cholerae* classical biotype and *V. cholerae* O1 El Tor biotype from the authors’ collection were used as positive controls for PCR amplification of the *stn/sto* and El Tor *hlyA* and *tcpA* genes, respectively (Table 1). The strain was cytotoxic, adhesive, and invasive and had El Tor *hlyA* and classical *tcpA* genes (Table 1).

The susceptibility of the isolate to 14 antimicrobial agents (amoxicillin-clavulanic acid, ampicillin, cefoperazone, cephalaxin, cephalothin, ciprofloxacin, colistin, gentamicin, kanamycin, levofloxacin, meropenem, oxolinic acid, tetracycline, trimethoprim-sulfamethoxazole) was determined by the disk diffusion method, according to guidelines of the Clinical and Laboratory Standards Institute (CLSI) (1). The isolate was resistant to cephalaxin and colistin. Although the most current antimicrobial recommendation for invasive *Vibrio* infections includes treatment with doxycycline (5), the parenteral formulation of this antibiotic is unavailable in Italy. For this reason, after the results of antimicrobial susceptibility testing were obtained, treatment was changed to meropenem and levofloxacin (3 g/day and 750 mg/day, respectively).

The patient recovered gradually and was discharged after 50 days of hospitalization.

*V. cholerae* non-O1 non-O139 strains are globally distributed, common in coastal and estuarine areas, and more abundant during the warmer months (8). Self-limited gastroenteritis or extraintestinal infections occur, the former after the consumption of seafood and the latter after exposure to aquatic
El Tor-like hemolysin may be involved in the pathogenesis of invasive human diseases, even if its exact role remains to be clarified. However, it is also necessary to note that infection by pathogenic strains of \emph{V. cholerae} non-O1 non-O139 may not always lead to serious disease, due to factors such as host susceptibility and the level of exposure.

To date, cases of invasive infections by this group of microorganisms have been rarely reported in Italy (3, 13), and to our knowledge, this is the first report of necrotizing fasciitis caused by \emph{V. cholerae}. A recent study, however, documented the frequent presence of pathogenic \emph{V. cholerae} non-O1 non-O139 strains in the Italian marine environment in the warmer months (10), and satellite observations identified that the mean daytime seawater temperature in the area where the patient was exposed ranged between 25.5°C and 26.0°C. These are conditions favoring the proliferation of this group of microorganisms, and clinicians should be alerted to the potential hazard of invasive infections caused by \emph{V. cholerae} non-O1 non-O139 in Italy.

Previous studies demonstrated that liver diseases, diabetes mellitus, and hematologic malignancy are independent risk factors predisposing patients with invasive \emph{V. cholerae} non-O1 non-O139 infections, including necrotizing fasciitis, to have a fatal outcome (7, 11, 12). In the case reported here, despite having the majority of these underlying illnesses, the patient survived. We believe that the strain’s susceptibility to a wide range of antibiotics, together with timely and appropriate antibiotic and surgical treatments, contributed to a successful resolution of the infection.

In our opinion, the paucity of cases of necrotizing fasciitis caused by \emph{V. cholerae} non-O1 non-O139 reported worldwide, associated with the fact that the patient, although highly immunocompromised, survived his infection makes this case unusual.

In conclusion, this case demonstrates that, when the specific risk factors outlined above are present, even a minor skin abrasion can develop into a severe \emph{V. cholerae} infection. Public education programs on how to limit the risk of exposure to these microorganisms should be considered, in particular, for people in high-risk categories. Further investigations are required to clarify the exact role of the host, environment, and etiologic agent in the pathogenesis of invasive diseases caused by \emph{V. cholerae} non-O1 non-O139 in healthy and immunocompromised persons.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Serovar</th>
<th>Source</th>
<th>Origin</th>
<th>stn/sto</th>
<th>etoA</th>
<th>tcpA</th>
<th>zot</th>
<th>hlyA</th>
<th>Inv</th>
<th>Adh</th>
<th>Cyt</th>
</tr>
</thead>
<tbody>
<tr>
<td>\emph{V. cholerae} isolate</td>
<td>O137</td>
<td>Subcutaneous tissue</td>
<td>Patient with necrotizing fasciitis</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>\emph{V. cholerae} O1 classical biotype</td>
<td>O1</td>
<td>Stool</td>
<td>ATCC 9459</td>
<td>−</td>
<td>+</td>
<td>−</td>
<td>+</td>
<td>−</td>
<td>−</td>
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<tr>
<td>\emph{V. cholerae} O1 classical biotype</td>
<td>O1</td>
<td>Stool</td>
<td>Authors’ collection</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
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<tr>
<td>\emph{V. cholerae} O1 El Tor biotype</td>
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<td>Stool</td>
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* ET, El Tor; Class, classical; +, presence; −, absence; Inv, invasiveness; Adh, adhesiveness; Cyt, cytotoxicity.
We are very grateful to Eiji Arakawa, Department of Bacteriology, National Institute of Infectious Diseases in Japan, for complete serotyping of the bacterial isolate and to Jim McLauchlin, Health Protection Agency, London, United Kingdom, for helpful comments on the manuscript.

REFERENCES


