Vibrio Cholerae non-O1 non-O139: The first reported case of bacteremic cellulitis in Portugal.

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Abstract

Non-O1 non-O139 *Vibrio cholerae* can rarely cause severe extra-intestinal infections like skin and soft tissue infections, primary bacteremia or pneumonia. The authors describe a case of a 69-year-old man who developed a bacteriemic cellulitis after placing his legs in shallow water in the Cávado river estuary. This is the first reported case of a non-O1 non-O139 *V.cholerae* bacteriemic celluilitis in Portugal.

Keywords: *Vibrio cholerae* non-O1. Bacteriemia. Cellulitis. Portugal

Introduction

Vibrio cholerae is a gram-negative bacteria, from the family of Vibrionaceae, ubiquitous in aquatic environment[1]. Its growth in water environment is best in summer months and in estuaries or other brackish waters[2]. There are reports of *V.cholerae* in freshwater in central and northern Europe as well as in saltwater from the Mediterranean Sea[1].

V.cholerae is mostly known for the epidemic cholera, presenting with profuse watery diarrhea, associated with O1 and O139 serogroups that secret cholera toxin. However, there are more than 200 serogroups and the non-O1 non-O139 *V.cholerae* infections can cause mild cases of diarrhea but also, rarely, severe extra-intestinal infections like skin and soft tissue infections, primary bacteremia, pneumonia among others[1].

The following clinical case is presented to point out, that in an adequate epidemiological context, this diagnosis should be considered due to its severity and high mortality.

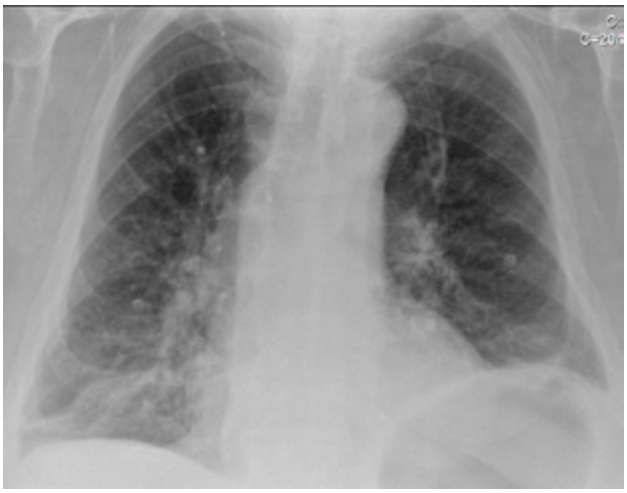
Case presentation

A 69-year-old French man with morbid obesity (IMC 37.2Kg/m^2) and venous insufficiency associated with venous eczema in the lower limbs, moved to Portugal in February 2016. He presented in July to the Emergency Department with a 7-day history of aggravated swelling and the appearance of redness and pain of the lower limbs associated with a 3-day history of cough with purulent expectoration and dyspnea. He was unaware of fever. Ten days before he had placed his legs in shallow water in the Cávado river estuary as part of a local treatment for venous eczema. He denied recent travel or the ingestion of raw seafood.

In the Emergency Department, he appeared ill, was sudoretic with a temperature of 39.0ºC, blood pressure of 104/80mmHg, heart rate of 151 beats per min, tachypneic with 32 breaths per min. On pulmonary auscultation, there was wheezing and rhonci bilaterally. The lower limbs showed exuberant edema up to the inguinal ligament, globally erythematous, warm, tender and with purulent exudation.

Electrocardiogram showed a sinus tachycardia; Arterial blood gases was abnormal with a hypoxemic respiratory failure: PaO2 73mmHg and PaCO2 45mmHg on a FiO2 28%, pH 7.46, HCO_3-28.5mmol/L, SatO2 93% and lactate 1.3mmol/L. Laboratory tests (Table 1) revealed a leukocytosis of 20450/mcL with 93% neutrophils, marked elevation of C-Reactive Protein (44.20mg/dL). The chest radiography (Figure 1) showed a consolidation in the right lung.

Fig. 1. Chest radiography at admission with consolidation in the right lung.



Three sets of blood cultures were drawn, a sample of sputum was sent for culture and empiric antibiotic treatment was initiated with intravenous levofloxacin 750mg q24h for a cellulitis and a community pneumonia.

In the Medicine Ward, the patient had a slow improvement. The respiratory failure resolved after 3 days and the blood work showed a decrease in the inflammatory markers (Table 1).

A *V.cholerae* was identified in all 3 blood cultures with 2 different methods. The *V.cholerae* isolate was susceptible to most antibiotics, including fluoroquinolones. The sample was sent to Instituto Ricardo Jorge to determine the serogroup and later revealed a non-O1 non-O139 *V.cholerae*.

The patient was discharged after 7 days and continued oral levofloxacin for another 10 days in ambulatory. The patient was re-evaluated in consultation 2 weeks later with complete resolution of the symptoms.

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Table 1. Laboratory test results at admission and discharge.

	Normal range (units)	Emergency Department	7th day
Hemoglobin	13.2-17.2 (g/dL)	15.4	15.7
Leucocytes	4.0-10.0 (x10^9/L)	20.45	13.04
Neutrophils	55-75 (%)	93.3	84.2
Platelets	150-450 (x10^9/L)	220	348
INR	-	1.29	-
aPTT	30.6 (s)	38.0	-
Glucose	70-110 (mg/dL)	138	144
Urea	17-43 (mg/dL)	77	47
Creatinine	0.8-1.3 (mg/dL)	1.12	0.68
Sodium	136-145 (mmol/L)	132	140
Potassium	3.5-5.1 (mmol/L)	4.7	3.6
Total Bilirubin	0.3-1.2 (mg/dL)	1.27	-
Direct Bilirubin	<0.5 (mg/dL)	0.57	-
Alkaline Phosphatase	30-120 (UI/L)	75	-
Gamma-Glutamyl Transferase	<55 (UI/L)	36	-
Aspartate Aminotransferase	8-35 (UI/L)	37	-
Alanine Aminotransferase	10-45 (UI/L)	29	-
C-Reactive Protein	0.01-0.82 (mg/dL)	44.20	2.71
Myoglobin	1-147 (ng/mL)	1394	329
Troponin I	<34.2 (pg/mL)	70	-
BNP	<100 (pg/mL)	66.7	-

A *V.cholerae* was identified in all 3 blood cultures with 2 different methods. The *V.cholerae* isolate was susceptible to most antibiotics, including fluoroquinolones. The sample was sent to Instituto Ricardo Jorge to determine the serogroup and later revealed a non-01 non-0139 *V.cholerae*.

Discussion

Non-01 non-0139 *V.cholerae* (NOVC) extra-intestinal infection are rare but potentially fatal, similar to *V.vulnificus*[3]. The most frequent NOVC infection is an acute gastroenteritis but it can also cause biliary tract infections, primary bacteremia and in rare cases peritonitis, skin and soft tissue infection, urinary tract infection or pneumonia[4]. In a recent review of the literature, Maraki,S et al found 48 published cases of bacteremic skin and soft tissue infections from January 1974 to May 2015[1]. The host susceptibility is an important factor in NOVC infections and it have been associated with liver cirrhosis, diabetes mellitus, malignancies (particularly hematological) chronic kidney disease and immunosuppressed states[1,4,5]. In terms of clinical manifestation, it is not uncommon for NOVC infection to present without diarrhea[4]. On presentation, a significant amount of patients are diagnosed with shock which relates to the severity and therefore high mortality of extra-intestinal manifestations. Many require intensive car admission[4]. The mortality can reach 42% in cases of bacteremic skin and soft tissue NOVC infection and the presence of hemorrhagic bullae is associated with higher mortality[1,4].

Most cases originate from the ingestion of raw or undercooked seafood, by the ingestion of contaminated water or through the contact of a skin lesion with water[1]. In this case, in a warm month and involving shallow, brackish waters with an intermediate salinity that favor the development of *V.cholerae*[2], the discontinuity of the skin from the venous eczema allowed the *V.cholerae* to invade the lower limbs and the bloodstream.

Regarding the etiology of the pneumonia, the agent was not be identified in sputum culture. It is possible that NOVC was responsible since *V.cholerae* pneumonia has been described at least in two cases[6] and it could have been acquired

by hematogenous spread. On the other hand, a decreased immunity during the NOVC infection could have made the patient susceptible to a concurrent pulmonary infection.

There are no guidelines about the treatment of NOVC infections. Although *V.cholerae* isolates are susceptible to most antibiotics, some experts recommend, in the same way as in *V.vulnificus* infections, that an association of a third-generation cephalosporin and a tetracycline analogous or a fluoroquinolone alone are probably the most effective treatments[3]. The optimal duration of treatment is unknown[1].

To the best of our knowledge, this is the first case of a NOVC bacteremic skin and soft tissue infection in Portugal, whereas in Spain, there are at least 5 reported cases 1. There is a report of a NOVC bacteremia following a gastroenteritis in Portugal[7] and, in Portugal, the last known epidemic cholera occurred in 1974[8].

V.cholerae is a rare cause of infections, but in susceptible patients with epidemiological risk factors a high suspicion is needed and an early and appropriate antibiotic treatment is crucial.

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