

CAS CLINIQUE / CASE REPORT

CENTRAL VENOUS ACCESS DEVICE - ASSOCIATED BLOOD STREAM DUAL INFECTION WITH *VIBRIO ALBENSIS* AND *AEROMONAS HYDROPHILA*

Case Report and Review of the Literature

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ABSTRACT • Non-O1 and non-O139 *Vibrio* species such as *Vibrio albensis*, as well as *Aeromonas hydrophila* are marine inhabitants that can cause intestinal and extraintestinal infections such as bacteremias. Concurrent blood stream infection with both pathogens are rare. Herein, we present the first case of central venous access device associated blood stream simultaneous infection due to *V. albensis* and *A. hydrophila* in a patient with acute lymphoblastic leukemia.

Keywords : *Vibrio* ; *Aeromonas* ; bacteremia ; access device

INTRODUCTION

Vibrio species are rod shaped, gram-negative bacteria that inhabit fresh water, marine and estuarine environments [1]. Non-O1 and non-O139 *V. cholerae* strains cause sporadic cases of gastrointestinal and extraintestinal manifestations, such as skin and soft tissue infections, external otitis and bacteremias [2]. Ocular infections [3] and urinary tract infections [4,5] have also been reported. Blood stream infections with *V. cholerae* species are quite rare. As for the non-O1 and non-O139 *V. cholerae* serotypes, the literature regarding bacteremias caused by these organisms is limited to case reports and case series. For example, a literature review that consisted of a search period ranging from 1974 to 2014 enlisted 128 articles describing 350 cases of non-O1 and non-O139 *V. cholerae* bacteremias worldwide, with few cases attributed to *V. albensis* [2]. In Lebanon, *V. albensis* has been described as a causative agent of UTI in only one case report [4].

The other bacteria involved in our case belong to *Aeromonas* spp. These pathogens belong to the Aeromonadaceae family which are characterized as Gram-negative bacilli that are oxidase and catalase positive, and are glucose fermenters. They are also inhabitants of

fresh water environments and are infrequently associated with human infection, causing gastroenteritis, wound infections and bacteremias, whereby *A. hydrophila* is responsible for most of the human infectious cases described in the literature [6].

The usual modes of transmission of both *Vibrio* and *Aeromonas* species consist of either ingestion of food – mainly animal products – contaminated by either bacteria, or exposure of skin wounds to contaminated water [1,6].

In this report, we present the first case of central venous access device associated blood stream simultaneous infection due to *V. albensis* and *A. hydrophila* in a patient with acute lymphoblastic leukemia.

CASE PRESENTATION

A 65-year-old woman, known to have B-cell acute lymphoblastic leukemia (ALL) treated with multiple lines of chemotherapy and recurrent episodes of febrile neutropenia presented to the emergency department of the American University of Beirut Medical Center in June 2020. She was suffering from high grade fever and chills while being on a continuous infusion of blinatumomab through an implantable port. The patient was diagnosed with ALL in March 2020 and was in complete remission at the time of the admission. She was receiving blinatumomab (a bispecific T cell engager) as continuous infusion through her central venous access device. She reported fatigue since one week prior to presentation and mild productive cough of two weeks' duration that was not worsening. She denied any other respiratory, gastro-intestinal or urinary symptoms, and had no close sick contacts. Her implantable port insertion site did not appear infected with no tenderness to palpation. Her physical examination was significant for crackles heard over the lung bases bilaterally and for right costo-vertebral angle tenderness. The complete blood count showed leukocytosis with white blood cell count of 34,653 cells/mm³ (70% neutrophils and 16% eosinophils). Her procalcitonin level was 0.95 ng/mL (normal < 0.05 ng/mL). The urine analysis

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was significant for the presence of numerous white blood cells per high power field, and a positive leukocyte esterase ($500/\mu\text{L}$). Other laboratory tests including creatinine, electrolytes and liver enzymes were within normal ranges. Chest X-Ray showed clear lungs with atelectatic changes.

She was admitted to the hematology floor after blood and urine cultures were collected and she was first started on ceftazidime-avibactam and vancomycin. Peripheral and central blood for the patient were drawn into BACT/ALERT bottles and put in VIRTUO blood culture system (bioMérieux, Inc., Durham, NC, USA). Both central and peripheral blood cultures signaled positive after 4.5 and 8 hours of incubation, respectively. The cultures revealed bacterial growth of a non-lactose fermenting organism when sub-cultured on sheep blood, chocolate and MacConkey agars. The organism was identified by the Matrix-Assisted Laser Desorption/Ionization Time of Flight (MALDI-TOF) system (Bruker Daltonik, GmbH, Bremen, Germany) as *Aeromonas hydrophilia* with a green flag. The antimicrobial susceptibility testing for *A. hydrophilia* indicated susceptibility to amikacin, aztreonam, cefepime, ceftazidime, ciprofloxacin, gentamicin, imipenem, piperacillin/tazobactam, trimethoprim/sulfamethoxazole, and resistance to ampicillin. Urine culture showed growth of *Klebsiella pneumoniae*, which was Extended Spectrum Beta-Lactamases (ESBL), but was susceptible to carbapenems. Ceftazidime-avibactam and vancomycin were stopped and she was switched to ertapenem.

Repeated blood cultures two days after administering antibiotics did not show growth of any organism after 5 days of incubation. The patient then developed fever again on the sixth day after starting antibiotics and new blood cultures were collected, after which she was started on piperacillin/tazobactam and vancomycin. New peripheral blood culture did not show growth of any organism. However, the new central blood cultures showed growth of *A. hydrophila* in two culture bottles and *Vibrio albensis* in one culture bottle after 7 and 15 hours of incubation. *V. albensis* was also identified by MALDI-TOF (green flag) after growing on sheep blood and chocolate agars. The antimicrobial susceptibility testing for *V. albensis* indicated susceptibility to amikacin, amoxicillin/clavulanic acid, ampicillin, cefepime, ceftazidime, cefuroxime, ciprofloxacin, gentamicin, imipenem, piperacillin/tazobactam, tetracycline, and trimethoprim/sulfamethoxazole. The susceptibility testing of this pathogen was done based on CDC recommendation for *V. cholerae* [7]. What we tested and interpreted for the others was based on the Clinical and Laboratory Standards Institute (CLSI) disk diffusion results for Enterobacteriaceae, just for the interest of finding how this *V. albensis* reveals its susceptibility profile, as reported

earlier [4]. The quality control of susceptibility testing for both pathogens was controlled using the ATCC 25922 *E. coli* strain.

The implantable port was then surgically removed and she was discharged home on ciprofloxacin 500 mg twice daily for a full course of ten days. On follow-up after finishing the complete course of prescribed antibiotics, the patient was in stable condition and afebrile. Blood cultures were not repeated. The patient denied sea food intake and contact with water surfaces. Unfortunately, microbiological examination of her home water was not available.

DISCUSSION

An implantable port, also known as implantable venous access device, is a type of small-sized central venous access device that provides access to a large central vein leading directly to the heart [8]. Our patient had the implantable port inserted in order to receive the immunotherapy blinatumomab for her acute lymphoblastic leukemia (ALL). Hematological malignancies are associated with an increased risk for implantable venous access port infections [9]. Blinatumomab is a novel bispecific CD3 T-cell engaging antibody targeting CD19, approved for the treatment of relapsed or refractory B-lineage acute lymphoblastic leukemia. Treatment with blinatumomab has been associated with an immunosuppressive effect by inducing both B-cell aplasia with resultant hypogammaglobulinemia, and neutropenia [10]. Device related infections were reported in 4-20% of patients with relapsed or refractory ALL treated with blinatumomab [11].

The literature review done by S. Deshayes *et al.* [2] mentioning 350 cases of non-O1 non-O139 *Vibrio* reported worldwide reveals an association with a hematological malignancy and with liver cirrhosis in 12.9% and 54.2 % of cases, respectively. The causative source of infection was not found or not mentioned in 75% of cases. In Lebanon, three cases of bacteremias with non-O1 non-O139 *Vibrio* species (not further characterized or speciated) have been previously reported, in patients suffering from liver cirrhosis, premature birth and metastatic pancreatic cancer [12, 13]. Additionally, two cases of urinary tract infections with non-O1 non-O139 *Vibrio* species have been reported in Lebanon, one in a healthy young adult male (due to *V. albensis*) and the other in an adult woman (due to *V. fluvialis*) with history of recurrent urinary tract infections. Both these patients lived near coastal areas of Beirut, and *V. albensis* was identified from tap water sample from the house of the first patient, the tap water from the house of the second patient revealed mixed bacterial flora [4, 5].

Concerning the *A. hydrophila*, its simultaneous recovery with the *V. albensis* is an interesting finding as it has not been reported before in such a situation though it has been recovered from bacteremic patients [6].

Countries having a humid climate, like Taiwan in East Asia, have high incidence of *Aeromonas* and *Vibrio* infections, as these pathogens have ubiquitous presence in the humid marine environment and warmer weather in the area [14,15]. Such weather prevails in Lebanon, especially during the summer season, during which our patient was admitted.

Besides the microbiologic features mentioned above, *A. hydrophila* is characterized by its intrinsic resistance to ampicillin, which reflects the production of beta lactamases enzymes [6]. Moreover, false susceptibility to carbapenems has been reported in *A. hydrophila* isolates due to a newly emerging type of carbapenemase that is not accurately detected with conventional methods [16]. Such facts could explain why our patient's condition worsened after initial improvement, and why repeated blood cultures grew *A. hydrophila* again after being initially treated with ertapenem for six days although her first blood culture showed susceptibility of *A. hydrophila* to carbapenems. This bacteremic persistence could also be postulated to be due to colonization in biofilm formation at the implantable device [2,17].

The exact reason and explanation about how both unusual organisms inhabited the implantable portal device leading to bacteremia episodes remain to be determined. One possibility about the origin of her blood stream infection can be secondary to skin contamination from her home tap water as her implantable port was accessed when she was at home for a continuous administration of the chemotherapeutic agent blinatumomab. The tap water, and even drinking water in Lebanon have been previously reported to be contaminated with different types of bacteria including *Aeromonas* spp. and *V. albensis* as a result of wastewater contaminating the wells and underground water in Lebanon [4,18,19]. This is so, since no other possible source of infection could be identified given that the patient denied any sea food consumption and any contact to outdoor water surfaces prior to presentation.

CONCLUSION

Non-O1 and non-O139 *Vibrio cholerae* strains and *Aeromonas* spp. are potential causative organisms of serious infections including bacteremias, especially in immunocompromised individuals. The relatively infrequent number of reported cases of infection with these organisms could be due to underdiagnosis or underreporting, and thus should be made aware of and taken into

consideration when recovered from such patients. This case report suggests blood stream infection with *V. albensis* and *A. hydrophila* as a consequence of water contamination in a coastal area in Beirut. This raises the concern that water in this city is a potential source for infectious pathogens outbreaks in the absence of good sanitary measures. Such a situation, particularly if affecting immunocompromised patients, could be associated with high morbidity and mortality rates.

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