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Original Article

Bacteremia caused by Aeromonas species in patients with cancer: Clinical manifestations and outcomes

Cynthia Pamela Alatorre-Fernández[1], Patricia Cornejo-Juárez[1], Consuelo Velázquez-Acosta[2], Patricia Volkow-Fernández[1]

[1] *Infectious Diseases Department, Instituto Nacional de Cancerología, Mexico City, Mexico*
[2] *Microbiology Laboratory, Instituto Nacional de Cancerología, Mexico City, Mexico*

Abstract

Introduction: Oncologic patients can have severe infections due to *Aeromonas*. This study aims to investigate the clinical characteristics and outcomes of cancer patients with bloodstream infections (BSI) caused by *Aeromonas.*

Methodology: We included patients with bacteremia caused by *Aeromonas* species from 2011 to 2018.

Results: Seventy-five BSI events in the same number of patients were identified. Forty patients were men (53.3%); the mean age was 49 years (IQR 28-61). *A. caviae* was the most frequent isolate (n = 29, 38.6%), followed by *A. hydrophila* (n = 23, 30.6%), *A. sobria* (n = 15, 20%), and *A. veronii* (n = 8, 10.6%). The most frequent underlying diagnosis was hematologic malignancy (n = 33, 44%), followed by breast cancer (n = 12, 16%) and gastrointestinal tract cancer (n = 8, 10.6%). The most frequent type of bacteremia was CRBSI in 32 cases (42.6%), followed by mucosal barrier injury-laboratory confirmed BSI (n = 20, 26.7%). Sixteen (26.2%) were hospital-acquired BSI. Attributable mortality occurred in 11 patients (14.6%). In univariate analysis *A. hydrophila* bacteremia, liver failure, skin/soft tissue infection, septic shock, inappropriate antimicrobial treatment, and relapse or cancer progression were associated with 30-day mortality. In multivariate analysis, only septic shock, inappropriate antimicrobial treatment, and relapse or cancer progression were associated with 30-day mortality.

Conclusions: *Aeromonas* species should be considered one of the causative pathogens of healthcare-associated bacteremia, especially in immunocompromised patients. In addition, it can be associated with high fatality, particularly in patients with severe clinical infections.

Key words: Bloodstream infection; *Aeromonas* species; mucosal barrier injury; cancer.

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Introduction

Bloodstream infections (BSI) are life-threatening events in patients with cancer; although the most frequent risk factors in these patients are the use of long indwelling central venous catheter (CVC) and severe neutropenia secondary to myelosuppressive chemotherapy, other factors are related to microorganism pathogenicity as in the case of *Aeromonas* infections.

The genus *Aeromonas* consists of 36 species of Gram-negative, non-spore-forming, facultatively anaerobic, oxidase, and catalase-positive bacilli, which are widely distributed in the environment [1]. These bacteria are native to aquatic environments of fresh and salt water, food such as fish, meat, dairy products, and fresh vegetable [2,3], and clinical samples of humans, in which they cause intestinal and extraintestinal infections [4–6].

Gastroenteritis is the most frequent clinical presentation in immunocompetent individuals [7]. Immunocompromised patients are susceptible to invasive *Aeromonas* infections such as bacteremia, meningitis, pneumonia, keratitis, osteomyelitis, hepatobiliary tract, and soft tissue infections [8,9]. Sepsis caused by *Aeromonas* is clinically indistinguishable from those caused by other Gram-negative bacilli. Due to bacteremic spread, invasive soft-tissue infections, such as necrotizing fasciitis, may involve more than one site [1,10]. Most cases of bacteremia are caused by *A. hydrophila*, *A. dhakensis*, *A. veronii*, or *A. caviae* [1,11].

The hospital environment constitutes an essential reservoir of microorganisms capable of generating infections. In many cases, there are no recommendations to prevent, monitor or control the presence of these pathogens, as is the case of the genus *Aeromonas* considered an emerging pathogen since it has been isolated in the drinking water system, food, detergents, and patients in the hospital environment [6,12] and has multiple putative virulence factors

associated with infection development [1]. Virulence factors include aerolysin, enterotoxins, hemolysin, protease, hemagglutinins, endotoxin, siderophores, Shiga-like toxin, secretion system type II, III, IV, and VI (TISS), polar and lateral flagella, pili and the ability to form biofilm [11].

Phenotypical methods show important limitations for characterizing *Aeromonas* spp. since many commercialized methods tend to confuse different species. In recent years, techniques such as Matrix-Assisted Laser Desorption/Ionization-Time Of Flight Mass Spectrometry (MALDI-TOF MS) [13], 16S ribosomal ribonucleic acid (rRNA) sequencing multilocus phylogenetic analysis (MLPA) allow is to identify the different species [14,15]. At present, molecular identification uses the information included in the genome for genome comparison. Several techniques have been used, such as the Average Nucleotide Identity (ANI) or the *in-silico* DNA-DNA Hybridization (*isDDH*) [16,17].

Beta-lactams are considered adequate antibiotics in non-immunocompromised, non-bacteremic patients. However, due to the risk of selection of the resistant subpopulation in *Aeromonas* with

chromosomally encoded beta-lactamases, the use of a beta-lactam agent (except for fourth-generation cephalosporins) for bacteremia with a high bacterial burden should be discouraged [9].

The objectives of our study were to assess the clinical features, resistance patterns, and outcomes of cancer patients with *Aeromonas* BSI at an oncologic hospital in Mexico City.

Methodology

We conducted a retrospective study at Instituto Nacional de Cancerologia (INCan), México, a 135-bed tertiary referral medical center for cancer patients. Between January 2011 and December 2018, all episodes of bacteremia due to *Aeromonas* species occurred in hospitalized or ambulatory patients were recorded. The clinical and laboratory information was retrieved from medical charts. The following data were recorded: baseline characteristics, cancer diagnosis, the status of the disease, chemotherapy regimen used, clinical features, antibiotic therapy, and outcome (alive, death due to infection, death due to other condition) at seven- and 30 days after *Aeromonas* bacteremia diagnosis.

Comorbidities included were: diabetes mellitus, high blood pressure, hypothyroidism, other neoplasms, renal or liver failure, HIV infection, and Charlson's comorbidity index. Severe neutropenia was defined as an absolute neutrophil count (ANC) < 500/mL. Lymphopenia was defined as an absolute lymphocyte count < 200/mL. Liver failure was considered when there was a 5-fold increase in alanine aminotransferase or aspartate aminotransferase, or a two-fold increase in bilirubin levels (Grade 2-3 toxicity according to the Common Terminology Criteria for Adverse Events) [18]. Bacteremia events were classified as: A) Secondary bacteremia; when there was another source of infection with the same bacteria isolated from another clinical site of infection; B) Catheter-related bloodstream infection (CRBSI); when a patient with a long-indwelling catheter and fever or shiver after catheter use had a positive blood culture drawn from the catheter and from peripheral vein puncture taken the same day consecutively with a different time to positivity of >2 hours with no other source of infection; C) Mucosal Barrier Injury Laboratory Confirmed Bloodstream Infection (MBI-LCBI) that was bacteremia caused by a group of organisms known to be commensals of the mouth or gastrointestinal (GI) tract in patients with neutropenia (neutrophils < 500 cells /mm^3 at least in two measures, or < 100 cells/mm^3 in one), or receptor of hematopoietic stem-cell transplantation, or grade 3-4 graft versus host disease, or diarrhea 1L in 24 hours within seven days prior, or on the day of collection of positive blood culture. Although *Aeromonas* was not included in the microorganisms listed as causing MBI-LCBI we recorded those who met the other criteria of MBI-LCBI [19]; D) Primary bacteremia; considered in those patients with positive blood cultures who presented clinical sepsis and no underlying infection was diagnosed despite intense clinical and radiological workout.

Polymicrobial bacteremia was defined as the simultaneous growth of an *Aeromonas* spp., and other bacteria from a blood culture. Appropriate antimicrobial treatment was considered when the antimicrobial therapy was initiated within 48 hours of the blood culture was obtained and if the strain was susceptible. Inappropriate antimicrobial treatment was considered when the *Aeromonas* was resistant to the antibiotic administered and/or when it was initiated > 48 hours after the blood culture was obtained. Attributable mortality was defined as death related to the episode of bacteremia without other causes of death.

Microbiological studies

Blood-culture samples were processed by the BACTEC 9240 System (Becton-Dickinson Microbiology Systems, New Jersey, USA). The

inoculated bottles were incubated for five days at 35 °C. Identification of microorganisms and susceptibility testing was performed by Phoenix automated system (Becton-Dickinson Microbiology Systems, New Jersey, USA). Clinical and Laboratory Standards Institute (CLSI) criteria defined susceptibility or resistance to antimicrobial agents [20]. MALDI-TOF was used since 2014 for the identification of species. The laboratory resources at INCan identified *A. caviae, A. sobria*, *A. hydrophila* and *A veronii*.

Statistical analysis

Descriptive analysis was performed for continuous and categorical variables. Continuous variables were analyzed using independent samples with the student´s t-test or ANOVA. For categorical variables, the Chi-square test or the Fisher exact test were used. Variables with p values < 0.1 were included in multivariate regression analyses. Odds Ratios (OR) with 95% Confidence Intervals (95% CI) were calculated. A *p value* of ≤ 0.05 was considered statistically significant. Data was analyzed employing SPSS (ver. 23) statistical software.

The Institution's Ethics Committee approved this study (number 2021/081).

Results

During the seven years of study, 28,105 blood cultures were taken; 4,267 (15.18%) were positive. In 3,035 (74.1%) Gram-negative rods were identified. Phoenix automated system identified 75 strains as *Aeromonas* spp., (2.4%); *A. caviae* (38.6%) was the most frequently isolated, followed by *A. hydrophila* (30.6%), *A. sobria* (20%), and *A. veronii* (10.6%). Forty patients were men (53.3 %); the mean age was 49 years (IQR 28-61). The most frequent underlying diagnosis was leukemia (n = 22, 29.3%), followed by breast cancer (n = 12, 16%) and GI tract cancer (n = 8, 10.6%). Baseline characteristics are presented in Table 1.

Fourteen patients were treated on an outpatient basis. Sixty-one patients required hospitalization (81.3%), with a median length of eight days (IQR 4-14.5). The blood culture was positive in 12 patients (19.7%) before hospitalization (in ambulatory evaluation). In 33 (54%), it was positive within the first 48 hours, and in 16 (26.2%), it was positive after more than 48 hours of hospital admission. This last group was considered hospital-acquired BSI. The most frequent cause of hospitalization was febrile neutropenia in 17 cases (22.7%). Forty-seven patients (63%) received chemotherapy during the 30 days prior to the BSI, and 5 (6.7%) during the same hospitalization.

The most frequent type of bacteremia was CRBSI in 32 cases (42.6.3%); 28 CVCs (87.5%) were removed, and four remained in place because of treating physicians' decisions (these patients received intravenous antibiotics). They had a negative blood culture control before hospital discharge; no recurrence was documented. Two CVCs were removed in patients with other types of bacteremia: one with MBI-LCBI who had persistent fever without other foci, and the other no longer needed the catheter because he had finished chemotherapy. Fourteen cases (18.6%) occurred in outpatients, all were CRBSI, and one had an infection of the catheter insertion site. In all the cases of CRBSI in ambulatory patients, the CVCs were removed, and patients were treated with oral antibiotics; none died.

Twenty-four catheter tips were cultured; 17 had a negative result, one was positive for *A. caviae*, six were positive for other microorganisms. The second most frequent type of bacteremia was MBI-LCBI (n = 20, 26.7%); all were hematological malignancy patients with fever and neutropenia, ten had diarrhea, and nine had mucositis.

Twenty patients (26.6%) had polymicrobial bacteremia, being related, in most cases, (n = 14, 18.6%) to CRBSI. *Klebsiella oxytoca* was the most common co-pathogen in five cases.

Table 1. Baseline Characteristics.

Characteristics	N (%)
Oncologic diagnosis	
Leukemia	22 (29.3)
Breast Cancer	12 (16.0)
Lymphoma	9 (12.0)
Gastrointestinal cancer	8 (10.7)
Female reproductive system cancer	6 (8.0)
Germ cell tumor	5 (6.7)
Head and neck cancer	4 (5.3)
Sarcoma	3 (4.0)
Other blood abnormalities	2 (2.7)
Liver and bile duct cancer	1 (1.3)
Other	3 (4.0)
Stage of the oncologic disease	
Responding/Stable disease	26 (34.7)
Disease progression	23 (30.7)
Recent diagnosis	13 (17.3)
Recurrent cancer	8 (10.7)
Complete remission	5 (6.7)
Cause of hospitalization	
Febrile neutropenia	17 (22.7)
Fever and gastrointestinal symptoms	16 (21.3)
Fever after catheter manipulation	10 (13.3)
Fever	9 (12.0)
Surgery	3 (4.0)
Chemotherapy	2 (2.7)
Other	8 (10.7)

One patient had polymicrobial bacteremia due to two strains of *Aeromonas*: *A. caviae* and *A. hydrophila.* Thirty-five patients (46%) had GI symptoms; 17 (22.6%) with neutropenia. Diarrhea was the main GI symptom in 14 cases (18.7%); eight patients had stool cultures with no isolation of *Aeromonas*. No patient reported recent exposure to fish, fresh, or salt water.

Eight patients (10.6%), all with hematologic malignancy, developed skin and soft tissue infections (four necrotizing fasciitis, three cellulitis, and one subcutaneous abscess). Two cases with necrotizing fasciitis, *A. hydrophila was* isolated from skin lesions; one patient required an amputation with a favorable outcome, and the other died. Twenty-four patients (32%) had severe neutropenia, and 41 (54.6%) had lymphopenia. Twenty-two patients had hyperglycemia, 36 hypoalbuminemia, 14 acute kidney injury, and 15 liver failure (four had a previous hepatic failure, and 11 presented acute hepatic failure). A comparative analysis between *Aeromonas* species is presented in Table 2.

Thirteen (17.3%) patients developed septic shock, of these, four (30.7%) were admitted to the intensive care unit (ICU) and required mechanical ventilation; two of them died. In 11 patient's death was attributed to *Aeromonas* bacteremia, which represented 14.6% of the whole series and 18% of the hospitalized patients. Treatment and outcomes are shown in Table 3. None of the patients with *A. caviae* bacteremia died. None of the patients with CRBSI died. None of the patients with

Table 3. Treatment and outcomes.

	N (%)
Initial treatment by family	
None	6 (8.0)
Third generation cephalosporin	28 (37.3)
Fluorquinolones	15 (20.0)
Carbapenem	22 (29.3)
Ureidopenicillin	4 (5.3)
Days of antibiotic treatment *median (IQR)*	9 (7-12)
Appropriate initial therapy	66 (88.0)
Attributable death	11 (14.7)
Days from diagnosis to death *median (IQR)*	1 (1-2)
Outcome after 30 days	
Other cause of death	5 (6.7)
Attributable death	11 (14.7)
Alive	59 (78.7)
Total	**75**

Table 2. Different clinical presentations among *A. caviae, A. hydrophila, A. sobria, A. veronii.*

Characteristics	*A. caviae* N = 29	*A. hydrophila* N = 23	*A. sobria* N = 15	*A. veronii* N = 8	*p* value
Gender					
Male	11 (38)	12 (52)	11 (73)	6 (75)	0.088
Female	18 (62)	11 (48)	4 (27)	2 (25)	
Charlson CI ≥ 4	23 (79)	14 (61)	8 (53)	3 (38)	0.097
Type of bacteremia					
Catheter related	22 (76)	6 (26)	2 (13)	2 (25)	
MBI-LCBSI	1 (3)	6 (26)	9 (60)	4 (50)	
Secondary	3 (10)	7 (30)	3 (20)	2 (25)	0.062
Primary	3 (10)	4 (17)	1 (7)	0	
Polymicrobial	12 (41)	3 (13)	2 (13)	3 (38)	
Underlying cancer					
Solid tumor	23 (79)	12 (52)	5 (33)	2 (25)	
Hemato-oncologic	6 (21)	11 (48)	10 (67)	6 (75)	
Symptoms					
Fever	26 (90)	22 (96)	15 (100)	8 (100)	0.426
Diarrhea	3 (10)	4 (17)	4 (27)	3 (38)	0.234
Mucositis	2 (7)	1 (4)	5 (33)	3 (38)	0.01
Skin infection	0	6 (26)	1 (7)	1 (13)	0.013
Septic shock	2 (7)	8 (35)	0	3 (38)	0.004
Laboratory					
Neutropenia	2 (7)	7 (30)	10 (67)	4 (50)	0.001
Lymphopenia	5 (17)	10 (43)	9 (60)	5 (63)	0.018
Hypoalbuminemia	11 (38)	11 (48)	10 (67)	4 (50)	0.597
Hyperglycemia	14 (48)	13 (57)	7 (47)	3 (38)	0.901
Renal failure	2 (7)	7 (30)	3 (20)	2 (25)	0.181
Liver failure	0	8 (35)	5 (33)	2 (25)	0.003
Abnormal hepatic image	6 (21)	11 (48)	8 (53)	3 (38)	0.229
Outpatient	10 (66)	2 (9)	1 (7)	1 (13)	0.04
Inpatient	19 (34)	21 (91)	14 (93)	7 (87)	
Correct antibiotic	25 (86)	19 (83)	15 (100)	7 (88)	0.429
Attributable mortality	0	9 (39)	1 (7)	1 (13)	0.001
Global mortality	2 (7)	10 (43)	3 (20)	1 (13)	0.012

Table 4. Univariate and multivariate analysis for mortality at 30-day.

Characteristic	Univariate			Multivariate	
	Alive (n = 61, 81.3%)	Death (n = 14, 18.7%)	*p* value	OR (CI 95%)	*p* value
Male	29 (47.5)	6 (42.9)	0.751	-	-
Female	32 (52.5)	8 (57.1)			
Cancer complete or partial remission	40 (65.6)	4 (28.6)	0.01	9.23 (1.41 – 60.16)	0.02
Relapse or progression	21 (34.4)	10 (71.4)			
Solid tumor	36 (59)	6 (42.9)	0.372	-	-
Hematologic malignancy	25 (41)	8 (57.1)			
Non-severe neutropenia	44 (72.1)	7 (50)	0.124	-	-
Severe neutropenia	17 (27.9)	7 (50)			
Monomicrobial bacteremia	42 (68.9)	13 (92.9)	0.095	-	
Polymicrobial bacteremia	19 (31.1)	1 (7.1)			
Aeromonas hydrophila	47 (77)	5 (35.7)	0.007	3.31 (0.55 – 19.79)	0.189
Other *Aeromonas* spp	14 (23)	9 (64.3)			
Non-liver failure	54 (88.5)	6 (42.9)	0.0006	3.91 (0.51 – 30.11)	0.189
Liver failure	7 (11.5)	8 (57.1)			
Non-septic shock	56 (91.8)	6 (42.9)	0.0001	12.71 (1.28 - 126.04)	0.03
Septic shock	5 (8.2)	8 (57.1)			
Appropriate treatment	56 (91.8)	10 (71.4)	0.056	9.17 (1.13 – 74.4)	2.08
Inappropriate treatment	5 (8.2)	4 (28.6)			

responding disease or remission of cancer died. Only one patient with polymicrobial bacteremia died (with isolation of *Aeromonas hydrophila* and extended-spectrum beta-lactamase-producing *Escherichia coli*). Seven of the nine patients that died within 48 hours were due to *A. hydrophila*, one *A. veronii,* and one *A. sobria* BSI.

A comparative analysis between patients that lived and died was done. In univariate analysis, risk factors related to death at 30 days was bacteremia due to *A. hydrophila*, liver failure, inappropriate antimicrobial treatment, and relapse or cancer progression. In the multivariate analysis, only inappropriate antimicrobial treatment and relapse or cancer progression were associated (Table 4).

The antimicrobial susceptibility pattern between species is presented in Table 5. Antibiotics used in neutropenic febrile patients were adequate in most isolates (susceptibility between 96-100%). Fluoroquinolones are an option for stable outpatient management when susceptible.

Discussion

We present a series of 75 patients with cancer and *Aeromonas* spp. bacteremia, none reported being exposed to fish, fresh, or saltwater recently, a previously described source of this kind of infection [21,22]. Most clinical reports of this infection come from Asia. To our knowledge, this is the first case series of *Aeromonas* bacteremia from Mexico, the largest in America, specifically in oncologic patients, and the first study to discuss the clinical presentations among different *Aeromonas* species in patients with cancer. Although it is recognized that patients with cancer have

Table 5. Antimicrobial susceptibilities of different *Aeromonas* species.

Antimicrobial agent	*A. caviae* (n = 29)	*A. hydrophila* (n= 23)	*A. sobria* (n= 15)	*A.veronii* (n = 8)	*p* value
	Susceptible/ tested isolates (%)				
Amikacin	27/27 (100)	23/23 (100)	12/12 (100)	7/7 (100)	
Aztreonam	23/24 (95.8)	22/22 (100)	12/12 (100)	4/4 (100)	0.657
Ceftazidime	26/27 (96.2)	23/23 (100)	15/15 (100)	6/6 (100)	0.647
Ciprofloxacin	25/27 (92.5)	19/23 (82.6)	14/15 (93.3)	6/7 (85.7)	0.645
Levofloxacin	27/28 (96.4)	22/23 (95.6)	15/15 (100)	5/5 (100)	0.841
Cefotaxime	26/27 (96.2)	23/23 (100)	14/15 (93.3)	6/6 (100)	0.63
Cefepime	26/27 (96.2)	23/23 (100)	15/15 (100)	5/5 (100)	0.656
SMX/TMP	24/28 (85.7)	19/23 (82.6)	12/15 (80)	6/7 (85.7)	0.965
Meropenem	26/26 (100)	23/23 (100)	13//13 (100)	6/6 (100)	
Imipenem	26/26 (100)	23/23 (100)	14/14 (100)	5/5 (100)	
Piperacillin/Tazobactam	26/27 (96.2)	21/23 (91.3)	14/14 (100)	5/5 (100)	0.586
Amoxicilin/clavulanic acid	20/20 (100)	17/19 (89.4)	13/13 (100)	3/3 (100)	0.413
Cefoxitine	11/27 (40.7)	6/23 (26)	4/15 (26.6)	2/5 (40)	0.728
Ertapenem	12/26 (46.1)	6/23 (26)	3/14 (21.4)	2/5 (40)	0.544

an increased risk for infection with this pathogen, at our institution, it represented only 2.4% of the blood isolates during the study period.

At our hospital, in all patients presenting with fever, blood cultures are drawn, empirical broad-spectrum antimicrobials are started, and results are closely monitored within the antimicrobial stewardship program. The bacteremia events are classified to determine therapeutic decisions, especially for CRBSI, where the conduct is to remove the CVC. Despite being a microorganism found in the water, *Aeromonas* was an infrequent cause of CRBSI. The above is derived from the strict care of the catheter that is carried out through the Intravenous Therapy Team (ITT) of the hospital, with a CRBSI rate of 1.1 per 1000 catheter days. There are some case reports in the literature about this type of infection due to *Aeromonas* that, in our series, represented 42.6% of the events [23]. At INCan, random monitoring of the hospital water is carried out to verify the quality of the water and identify pathogenic bacteria. During the study period, there was no isolation of *Aeromonas* in the hospital water.

In a Japanese case series with different underlying diagnoses, *A. caviae* was the most frequent isolate, with an unknown source of infection in 47.2% of the events [24]. In our study, *A. caviae* was also the most frequent cause of CRBSI ($p = 0.001$) with an OR of 12.9 (4.21-39.59), compared to other species of *Aeromonas*.

A. caviae has poor cytotoxic enterotoxin production and polar flagellins Fla A and Fla B that promote bacterial adhesion [25]; this can explain why in our series, it caused mainly CRBSI and was not associated with a severe clinical presentation like necrotizing fasciitis. None of the patients with *A. caviae* died, 10 received ambulatory treatment, and in 21, the CVC was removed.

The most frequent clinical manifestation of *Aeromonas* infection is gastroenteritis; therefore, it is expected that it may cause MBI-LCBI, a common type of bacteremia described in cancer patients due to translocation from the gut to the bloodstream in the context of mucositis, diarrhea, and neutropenia in patients that received myelosuppressive chemotherapy; in this series, this type of BSI represented 26.7% of the total. We propose to consider *Aeromonas* as a cause of MBI-LCBI [26].

Febrile neutropenia was documented in 32.4% of our patients. In a case series of infections in adult febrile neutropenic cancer patients, only one case of *A. hydrophila* was reported, representing 0.72% of the total events [27]. *Aeromonas* are not represented in many studies which describe *Enterobacteriaceae* and antimicrobial resistance; nevertheless, multidrug resistance is rare [28]. Of note, 67.7 % of our isolates were resistant to ertapenem, which contrasts with 8% reported by Livemore *et al.* in 2001 [29].

Empirical antibiotic treatment usually recommended in neutropenic patients, such as antipseudomonal β-lactamic cephalosporin, piperacillin-tazobactam or a carbapenem (except ertapenem), is adequate to treat *Aeromonas* species in most of the cases [30,31]. At our institution, in high-risk patients with febrile neutropenia and septic shock, meropenem is the initial drug of choice. Four patients died despite initial therapy with meropenem.

Cancer patients can have liver disease secondary to malignant biliary obstruction, liver metastases, toxic effects of chemotherapy, and previous hepatic diseases. Liver disease is related to bacterial translocation of a high burden of *Aeromonas*, which has been reported in previous series, with a frequency of 30-60% [32,33]. We found that 23.4% of our patients had abnormal liver function now of the event.

Patients with *Aeromonas* BSI can develop soft tissue infections ranging from cellulitis to suppurative infections and necrotizing fasciitis. Four patients developed necrotizing fasciitis; three died, and one lived but required early amputation, achieving control of the infection. All of them had hematologic malignancy, as reported previously in the case series. Debridement of necrosis tissue is essential to improve survival [32,33]. *Aeromonas* should be considered in patients with hematologic malignancy with bacteremia that develops necrotizing fasciitis, and early aggressive management should be given.

Ciprofloxacin and levofloxacin can be good options for an oral antibiotic switch for ambulatory patients. No significant differences in antibiotic susceptibility between species were found in our study. Our results show that for patients with *Aeromonas caviae* and CRBSI, outpatient management with fluoroquinolones and removal of the CVC is appropriate therapy.

In previous reports, the case fatality rate of *Aeromonas* bacteremia ranges from 24% to 63% [19,34]. Underlying cancer, secondary bacteremia, nosocomial infection, immunosuppressant therapy, and higher severity of illness at presentation are associated with fatal outcomes. In this study, 21% of patients died in the first month, finding as risk factors related to attributable mortality were septic shock, inadequate antimicrobial treatment, and cancer progression.

Conclusions

Aeromonas species should be suspected as a cause of BSI in cancer patients to offer them adequate antimicrobial treatment in the first hours of the patient's arrival, considering the high number of patients who died within the first 48 hours. This group of bacteria should also be considered in cases of patients who present MBI-LCBI.

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Corresponding author

Pamela Alatorre Fernández. MD
Infectious Diseases Department, Instituto Nacional de Cancerología
Av. San Fernando No. 22, Col. Sección XVI,
Alcaldía Tlalpan, 14000, CDMX, Mexico.
Phone: (+52) (55) 5628-0447, ext. 12110
Email: drapamelaalatorre@gmail.com

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