Case report

First report of Central-line-associated bloodstream infection (CLABSI) due to Enterococcus raffinosus (ER) in a cancer patient

F. Angelini¹, L. Rossi², S. Taccogna³, A. Crisanti⁴, G. Borra⁵, E. Gozzi⁶

¹ Medical Oncology Unit, Regina Apostolorum Hospital, Albano, Rome, Italy; ² UOC of Oncology, ASL Latina, Distretto 1, University of Rome “Sapienza”, Aprilia (LT), Italy; ³ Department of Pathology, Ospedale Regina Apostolorum, Albano, Rome, Italy; ⁴, Medical Laboratory, Regina Apostolorum Hospital, Albano, Rome, Italy; ⁵ Medical Laboratory, Regina Apostolorum Hospital, Albano, Rome, Italy; ⁶ Medical Oncology Unit, ASL RM6, Polo Ospedaliero di Anzio, Rome, Italy

ORCID ID:
F. Angelini: 0000-0001-5964-4845; L. Rossi: 0000-0003-0635-6780; S. Taccogna: 0000-0002-5598-8963; E. Gozzi: 0000-0002-7570-3427

Abstract

Despite the advances made by therapeutic technologies, healthcare-associated infections (HAIs) are currently still a worldwide problem. Central-line-associated bloodstream infections (CLABSIs) are one of the most common causes of HAIs. The cost of CLABSIs is considerable, both for the increase in morbidity and financial resources expenses. Coagulase-negative staphylococci are the common pathogens responsible for CLABSIs, followed by Staphylococcus aureus, Enterococci, and Candida spp. The Enterococcus genus comprises of more than 50 species but E. faecalis and E. faecium are the most common causes of infections in humans. Enterococcus Raffinosus (ER) is a non-faecalis and non-faecium enterococcus even if ER has rarely been proven to be a human pathogen, recent reports of infections caused by enterococci that are relatively resistant to beta-lactam antibiotics by non-p-lactamase mechanisms have included strains of ER. Here we describe a first report of CLABSI due to Enterococcus Raffinosus in a cancer patient. Clin Ter 2023; 174 (6):469-472 doi: 10.7417/CT.2023.5010

Key words: Healthcare-associated infections (HAIs), Bloodstream infections, Central venous catheter (CVC), Central-line-associated bloodstream infection (CLABSI), Catheter-related bloodstream infection (CRBSI), Enterococcus raffinosus (ER), Cancer patient

Introduction

HAIs are largely responsible for morbidity and mortality in hospitalized patients. In the United States (US), up to 15% of patients, about 1.7 million people, develop HAI that causes 99,000 deaths annually (1).

The five most common HAIs are: CLABSIs, catheter-associated urinary tract infections (CAUTIs), ventilator-associated pneumonia, surgical site infection, and Clostridium difficile infection (1).

Central venous catheter (CVC) is an intravascular catheter that terminates at or close to the heart or in one of the great vessels which is used for infusion, withdrawal of blood, or hemodynamic monitoring (1).

CVC is often used in the care of (ill) patients and compared to peripheral intravenous access, CVC have considerable advantages: they allow safe administration of intravenous medications that cannot be given peripherally; they can stay in up to several years and only need to be flushed about once a month to prevent clotting.

However, despite the undeniable benefits of CVCs, they also can represent a potential entry way for bloodstream infections.

CLABSI is defined as a primary bloodstream infection in a patient who brings a CVC within 48-hour before the development of the infection itself that must not be related to an alternative cause (2).

CLABSIs are one of the most common causes of HAIs.

The most serious consequences of CLABSIs are: increased mortality rates, a significant morbidity in addition to significant increases in health costs, both in developed and developing countries (3).
In the US, CLABSIIs account for a range between 84,000—204,000 infections per year, resulting in up to 25,000 preventable deaths at a cost of up to 21 billion dollars per year (2).

In order to be diagnosed as a laboratory-confirmed CLABSI (LCBI), a central venous catheter needs to have been in place for more than 2 calendar days from the date of diagnosis itself. If the central venous catheter is in place for more than 2 calendar days and then removed, the date of diagnosis of LCBI may be the day of the device removal or the next day (1).

The most commonly reported causative pathogens remain coagulase-negative staphylococci, Staphylococcus aureus, enterococci, and Candida spp.4.

Enterococci are gram-positive cocci that are common residents of the gastrointestinal tracts of animals, including humans (5).

They are now the third most common nosocomial pathogens, causing 14% of HAIs in the US between 2011 and 2014, an increase from 11% in 2007 (5).

Their pathogenicity is mainly due to the increasing resistance to many antibiotics: they are intrinsically resistant to cephalosporins, aminoglycosides, lincomamides and streptogramins (5).

The Enterococcus genus comprises of more than 50 species but E. faecalis and E. faecium most commonly cause infections in humans.

In recent years, there has been increasing interest in unusual non-faecalis and non-faecium enterococci: they are able to cause serious infections like septicaemia, and they are also resistance to several antimicrobial agents, including β-lactams and glycopeptides (6).

Enterococcus Raffinosus (ER) is a non-faecalis and non-faecium enterococcus.

Phenotypic characteristics used for the identification of ER include acid formation in different carbohydrate broths, such as mannitol, sorbose, arabinose, raffinose, sucrose and sorbitol; utilization of pyruvate; acid production from MGP broth; resistance to erythromycin, but non hydrolysis of arginine (6).

ER has been described as occurring among the oropharyngeal flora of domestic cats and it has rarely been proven to be a human pathogen (6).

There is little evidence in the literature of infections caused by ER.

The present report is believed to be the first to report of a case of CLABSI due to ER in a cancer patient.

Case description

A 61-year-old man without a significant medical history, was referred to our Oncology Unit for further work-up and treatment of a rectal cancer.

Colonoscopy demonstrated a large tumor in the lower (intraperitoneal) rectum, which was diagnosed as adenocarcinoma on biopsy. We performed laparoscopic low anterior resection and histological examination of the tumor showed adenocarcinoma moderately differentiated with areas of solid growth G2 and with mucinous aspects (sec. WHO 2010), infiltrating the wall of the viscera to full thickness, coming to ulcerate the serous coating.

Two of the 14 retrieved lymph nodes contained malignant cells. pTNM results T3N1b R0.

According to the disease stage, the patient was recommended to receive adjuvant chemotherapy with 8 cycles of XELOX (Oxaliplatin 130mg/mq day 1, Capecitabine 2000mg/sqm/day, in two divided doses, for 14 days, every 3 weeks).

During the fourth cycle of chemotherapy, one hour after infusion of Oxaliplatin, he developed hypersensitivity reaction with generalized urticaria, which resolved with Benadryl. Chemotherapy infusion was immediately discontinued.

Patient completed the remaining cycles of adjuvant chemotherapy according to De Gramont schedule (bolus 5-Fluorouracil 400 mg/m2 iv with Leucovorin 200 mg/m2 iv and 1200 mg/m2 in 46-hour infusion of 5-Fluorouracil).

Two months after the end of adjuvant chemotherapy, computed tomographic (CT) showed a disease relapse with unresetable liver metastases.

Genetic analysis indicated the presence of the K-ras mutation. (Anti-angiogenetic therapy with bevacizumab, and chemotherapy with the FOLFIRI regimen irinotecan, 180 mg/m2 IV over 90 min; folinic acid, 400 mg/m2 IV over 2 h; 5-fluorouracil (5-FU), bolus of 400 mg/m2 IV; 5-FU, continuous infusion of 2400 mg/m2/6 h, and bevacizumab (5 mg/kg IV over 90 min) were administered.

After six cycles, patient was hospitalized because of abdominal pain, with severe diarrhea and hematochezia.

Physical examination demonstrated weakness with body temperature of 38.8 heart rate 97/min, blood pressure 125/77 mm Hg and respiratory rate 16/min.

Laboratory was remarkable for a white blood cell count of 10.5/mm3, C-reactive protein, lactate dehydrogenase and lactic acid were increased.

Re-assessment by CT showed disease progression (PD), multiple lung metastases.

The right subclavian tunneled CVC displayed erythema and purulent discharge at the exit site.

Three sets of blood samples for culture were drawn through the CVC (two sets) and a peripheral vein (one set).

Patient was empirically treated with cefazolin (1 g every 8 hr intravenously). Later, ciprofloxacin (200 mg every 12 hr intravenously) was added to cover gram-negative rods. On day 5 of hospitalization, all the blood cultures yielded gram-positive rods (Fig. 1).

The bacteria was identified as ER.

The patient was monitored by regular blood culture, line swabbing and testing of platelet levels and inflammatory markers.

Discussion

Bloodstream infections related to CVCs are usually defined as catheter-related bloodstream infection (CRBSI) and central line-associated bloodstream infection (CLABSI) (2).

CRBSI is a clinical definition based on clinical criteria related to a specific patient in which the diagnosis is being
considered. CRBSI requires specialized microbiological techniques to specifically identify the catheter as the source of bacteremia that may not be available in all hospitals (2).

In contrast, the diagnosis of CLABSI is a simplified definition based on surveillance criteria that identifies bloodstream infections in patients with CVCs in which there is no other obvious secondary source for bacteremia (2).

Even if introduction of the first widely adopted set of guidelines for the prevention of CLABSIs in 2002 has led to a substantial reduction in their incidence (4), they are still an important cause of morbidity and mortality in the intensive care unit, with increased costs to the healthcare system. Enterococci are one of the most common nosocomial pathogens (most notably E. faecalis and Enterococcus faecium).

Enterococci’s infections occur mainly among hospitalized patients, include urinary tract infections, bacteremia, intra-abdominal infections, and endocarditis (5).

ER was described as a new enterococcal species in 1989. ER has been isolated from: stasis ulcer dermatitis, clean-catch urine, abscess of Bartholini’s gland and rectal swab (1), and clean urine, rectal swab (6-8).

From January 1981 to September 1987, Sapico et al. 8 founded sixteen clinical isolates of ampicillin-resistant enterococci (ARE) from the microbiology laboratory of a 450-bed rehabilitation medical center 4/16 isolates were identified as ER.

Patients (PTS) were all female, with underlying diseases (venous stasis, alcoholic lower limbs liver disease with ascites; rheumatoid arthritis) and underlying diseases (venous stasis, alcoholic lower limbs liver disease with ascites; rheumatoid arthritis).

ER has been isolated from: stasis ulcer dermatitis, clean-catch urine, abscess of Bartholini’s gland and rectal swab (1), and clean urine, rectal swab (6-8).

Oster et al. 9 in a prospective review of all enterococcal isolated for 13 months showed that 9.0% were resistant to ampicillin. All were β-lactamase negative. Several isolated strains exhibited intermediate susceptibility to ciprofloxacin.

Nine (31.6%) of the isolated strain were E. raffinosus; Patients were predominantly male with underlying diseases (chronic urological abnormalities, wounds and cancer).

Authors described Ampicillin-resistant enterococci as appearing to be a growing clinical problem.

Sandoe J.T et al 10 described a vertebral osteomyelitis due to ER in elderly patient.

Freyaldenhoven B.S et al 11 reported the first case of a haematoma infected by ER in a elderly patient undergoing immunosuppressive therapy.

Savini V., Mann A. 12 et al reported the first case of vaginal infection caused by ER; the same authors also reported the first case of a wound ulcer infected with multidrug-resistant ER 13.

Mastroianni A. 6 described the first case of endocarditis due to ER in an 85-year-old man with a clinical picture suggestive of an indolent febrile illness.

Regarding antibiotic resistance, ER constitutes a relatively large proportion of enterococcal isolates resistant to ampicillin (6).

However, Kawalec M et al 14 also reported isolates in vancomycin-resistant enterococci (VRE).

Prakash V. P. et al 15 described multi-drug resistance among unusual species of enterococci:

- all six strains of ER showed resistance to ciprofloxacin, while 33.3% were
- susceptible to penicillin and ampicillin, and 66.6% were sensitive to gentamycin and streptomycin.
- None of the isolates were positive for β-lactamase, and all isolates were sensitive to vancomycin and teicoplanin (6-15).

The present report is believed to be the first to report a case of CLABSI due to ER in a cancer patient: future stud-
ies and observations are needed to clarify the role of this pathogen in the human species.

Declaration of conflicting interests

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Author contributions

Francesco Angelini was the primary editor and conceived the need to describe the case; Rossi Luigi wrote the manuscript; Silvia Taccogna reviewed the literature; Anna Crisanti and Giada Borra reviewed the manuscript according to the authors’ instructions; Gozzi Elisa coordinated the realization of the manuscript.

All authors read and approved the final manuscript.

Informed consent statement

Consent was obtained from the patient for publication of this report and any accompanying images.

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