

## ***Clostridium perfringens* bacteremia in an 89-year-old man with COVID-19 infection: Case report and brief literature review**

Siasios Panagiotis\*; Zaires Aristidis; Karapiperis Dimitrios; Antoniou Dimitra; Kachrimanidou Melina

**\*Corresponding Author: Siasios Panagiotis**

Microbiology Department, 424 General Military Hospital, Thessaloniki, Greece.

Email: panossiassios@gmail.com

### **Abstract**

We present the rare case of bacteremia caused by *Clostridium perfringens* in an 89-year-old rehabilitation center resident with COVID-19 infection and we review the literature regarding *C. perfringens* bacteremia, as well as the association between SARS-CoV-2 and *C. perfringens*.

**Keywords:** *Clostridium perfringens*; Bacteremia; SARS-CoV-2; COVID-19 infection.

### **Introduction**

*Clostridium* species are spore-forming anaerobic gram-positive rod bacteria, that are considered important constituents of the human microbiome, but also important agents in invasive infections, including bacteremia. Clostridial bacteremia is the second most frequent anaerobic bacteremia, ranging from 0.12-2% of all blood culture isolates [1-5]. Among clostridium species, *Clostridium perfringens* is the most common species isolated from blood cultures [1-4]. *Clostridium perfringens* is normally part of the human gastrointestinal, genitourinary, and skin microbiota [6] but also a causative agent of skin and soft tissue infections, gas gangrene, myonecrosis, and liver abscess [7,8]. *C. perfringens* bacteremia is a rare clinical syndrome, accounting for less than 1% of all bloodstream isolates [1,9]. Although rare, *C. perfringens* bacteremia may be accompanied with high mortality rate, making it one of the most severe types of bacteremia [10].

### **Case Presentation**

A 89-year-old male with a past medical history of atrial fibrillation and benign prostatic hypertrophy transferred to our hospital from a rehabilitation center, with an episode of atrial fibrillation with rapid ventricular response and COVID-19 infection. A day after the admission he presented with acute nausea and diarrhea, up to 3 green watery stools daily.

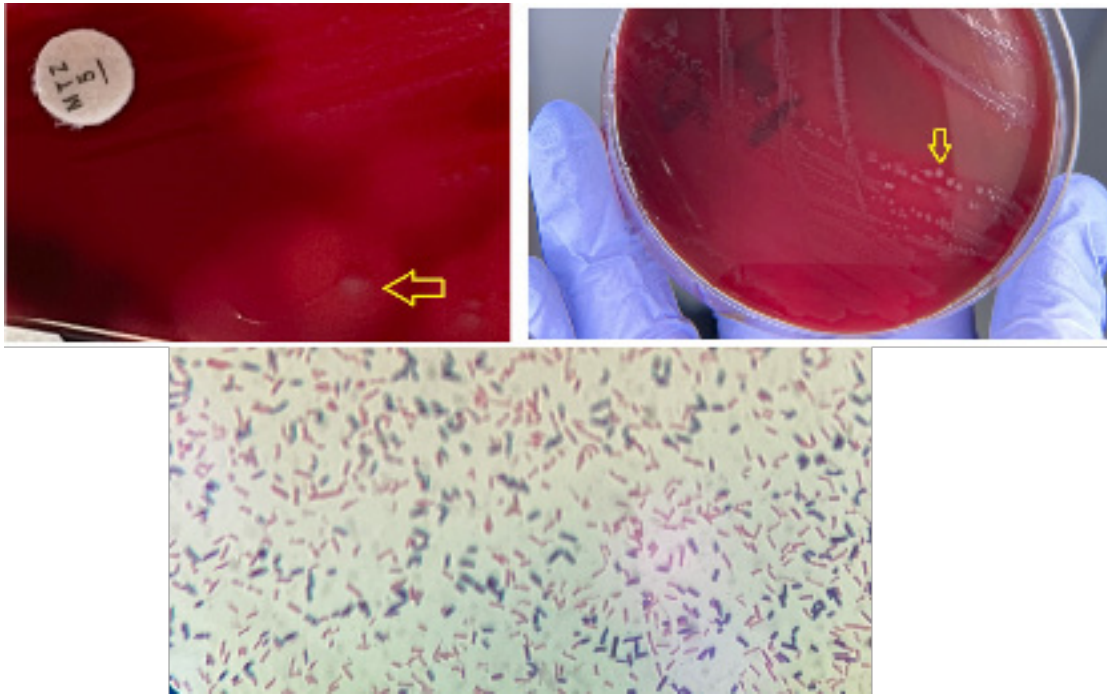
On admission, physical examination revealed him looking sick, emaciated and sometimes drowsy. He was oriented to place and to person but not to time. Vital signs demonstrated a blood pressure of 120/95 mm Hg, heart rate of 170 beats/minute, temperature of 37.4°C and oxygen saturation of 97% on room air. The cardiac examination revealed tachycardia, with normal heart sounds and no murmurs. His abdomen was soft and nondistended. The remainder of physical examination findings were normal. The performed ECG revealed an atrial fibrillation with rapid ventricular response, thus placing the patient under continuous electrocardiographic monitoring and later a decrease in heart rate was achieved pharmacologically with Digoxin and Lopressor in the emergency department. Because of the patient's impaired level of consciousness, a brain CT scan was performed without pathological findings.

Complete blood count, comprehensive metabolic panel, urine, and blood cultures were done on admission. White blood cell was  $9.64 \times 10^3/\text{mm}^3$  (NR: normal range  $4\text{-}11 \times 10^3/\text{mm}^3$ ) with a left shift, while procalcitonin was slightly increased at 0.10 ng/ml (NR < 0.08 ng/ml). Lactate dehydrogenase was 331 U/L (NR 125-220 U/L), troponin was 46.2 pg/ml (NR < 34.2 pg/ml) and C-reactive protein was 9.5 mg/dl (NR < 0.5 mg/dl). Total and direct bilirubin were also elevated at 2.21 and 1.04 mg/dl respectively (NR 0.2-1.2 mg/dl and 0.0-0.5 mg/dl respectively), indicating mild jaundice. D-dimer was elevated at 6.92  $\mu\text{g}/\text{mL}$  (NR 0-0.5  $\mu\text{g}/\text{mL}$ ) and given the increased risk for thromboembolism a CT of the chest was obtained, which was negative for pulmonary embolism. The rest of his laboratory test results were within normal limits.

Empirical antibiotic treatment was initiated with intravenous piperacillin/tazobactam and remdesivir while the patient admitted to the infectious diseases clinic for further monitoring and treatment. The following days, a gradual and significant improvement of the patient's clinical picture was observed.

Stool and blood cultures were requested. Stool specimen was tested for both glutamate dehydrogenase and toxins A/B of *C. difficile* by an enzyme immunoassay (EIA; C. DIFF QUICK CHECK COMPLETE, Alere/TechLab, Blacksburg, USA), which was negative.

Both sets of aerobic and anaerobic blood cultures (BACTEC Plus Aerobic, BACTEC Lytic Anaerobic, BD BACTEC™ FX40) yielded positive in 24 hours, and the initial Gram stain directly from the bottle revealed Gram-variable rods. The blood culture broth was sub-cultured onto the surface of Columbia (Columbia agar + 5% sheep blood; bioMerieux), chocolate agar (Chocolate agar + PolyViteX™, bioMerieux), and MacConkey agar, which incubated under aerobic and anaerobic conditions. The occurrence of anaerobic growth of Gram-positive boxcar-shaped rods on Gram stain (Figure 1), with negative catalase reaction and the phenotypic characteristic of the presence of double-zone hemolysis indicated the presence of Clostridia species. The microorganism was identified by mass spectroscopy as *Clostridium perfringens* with a 99.0% confidence value using the Vitek® MS system (bioMerieux) and also by MALDI TOF (Brucker, MS system) with a score value of 2.31.



**Figure 1:** The colonies of *Clostridium perfringens* in Blood agar plate are surrounded by a double-zone haemolysis, which consists of an inner clear zone and an outer hazy zone (yellow arrows). Gram stain of *Clostridium perfringens*.

## Literature Review

A PubMed and Google Scholar search of the English- language literature was performed using the keywords “*Clostridium perfringens*”, “bacteremia”, “SARS-CoV-2” and “COVID-19”. The systematic review of the literature revealed 19 studies that have been published since 1969, describing cases of *C. perfringens* bacteremia (Table 1). The literature shows that *C. perfringens* is the most common species identified in the blood cultures of patients with clostridial bacteremia, representing between 21.7-71% of *Clostridium* species bacteremia [1-5,12,15,18-20]. According to the medical literature, the main risk factor for acquiring Clostridial bacteremia is malignancy [1-6,8,10,12-20] and male gender (summarized in Table 1). The percentage of males with clostridial bacteremia ranges from 27,3-88,2% [3-6,8,10-20]. Other risk factors for acquiring clostridial bacteremia include diabetes mellitus, older age, immunosuppression, haemodialysis, renal insufficiency, digestive surgery, chemotherapy, liver disease and Crohn’s disease [1-4,6,8,10,12,14, 16,18-19]. Yang et al. reviewed 93 cases of *Clostridium* bacteremia and found that 25.8% of patients had hypertension [10], while Benjamin et al. reviewed 80 cases and found that 12% of patients with clostridial bacteremia had alcohol use disorder [19]. The mean age of patients with clostridial bacteremia ranges from 46-76 years, with leukemia patients being younger [3-6,8,10-21].

Regarding the association between *C. perfringens* bacteremia and SARS-CoV-2, the literature revealed one case of COVID-19 infection associated with quadruple bacterial infection including *C. perfringens* bacteremia [22]. The present case is the second in the medical literature linking those two pathogens and emphasizes the fact that SARS-CoV-2 impacts the human immunity and promotes co-infections with unusual pathogens like *C. perfringens*.

**Table 1:** Review of Clostridial bacteremia.

Author	No cases of clostridium spp. bacteraemia/ Study period	Clostridium perfringens (%)	Most common comorbidities (%)	Mortality (%)	Males (%)	Mean age
Suzaki et al. 2022 [11]	60/2000-2014	100	NR	100 MIH 24.1 non-MIH	58.1	66.5 MIH 77 non-MIH
Sarasoja et al. 2022 [12]	386/2014-2019	40.4	Malignancy (47%) Immunosuppression (25%)	26	56	76
Liu et al. 2021 [13]	17/1985-2020	100	Leukemia	58.8	88.2	46
Yamamoto et al. 2020 [5]	40/2004-2018	60	Malignancy	42.5	50.2	67.5
Stabler et al. 2020 [4]	81/2010-2018	64.3	Cancer (45.7%) Recent digestive surgery (24.7%) Chemotherapy (23.5%) Diabetes mellitus (22.2%) Renal insufficiency (22.2%)	31.4	54.3	61.4
Lopez-Fabal et al. 2018 [14]	28/2005-2015	100	Cancer (39.2%) Diabetes mellitus (25%) Immunosuppressants (21.4%) Recent surgery (17.8%) Liver disease (14.2%) Cholecystitis/cholelithiasis (14.2%)	32.1	67.8	71.4
Burgos et al. 2018 [15]	18/2005-2016	38	Cancer	16	67	62.5
Millard et al. 2016 [8]	11	100	Older age $\geq 65$ (64%) Diabetes mellitus (45%) Malignancy (18%)	27	27.3	65.8
Kim et al. 2015 [3]	114/2002-2012	35.6	Neoplasm (76.3%) Gastrointestinal symptoms (73.7%) Diabetes mellitus (14.9%) Haemodialysis (5.3%)	26.3	68.4	58
Shindo et al. 2015 [16]	33/2001-2013	100	Cancer Immunocompromised patients	15.2	57.6	75.6
Yang et al. 2013 [10]	93/2002-2011	100	Renal insufficiency (49.5%) Malignancy (41.9%) Hypertension (25.8%)	26.9	58.1	70.7
van Bunderen et al. 2010 [6]	40/1990-2010	100	Haematological disorder (22.5%) Pancreatic/gastric cancer (12.5%) Diabetes mellitus (30%)	80	55	65
Fujita et al. 2010 [17]	18/2001-2009	100	Hepatobiliary tract diseases (gallbladder stones, hepatic carcinoma)	27	72.2	75
Shah et al. 2009 [18]	25/1995-2003	60	Genitourinary/gastrointestinal malignancies Diabetes mellitus	48	44	64
Leal et al. 2008 [2]	138/2000-2006	42	Older age Hemodialysis Malignancy Crohn's disease	30	NR	NR
Benjamin et al. 2006 [19]	80/1997-2000	71	Neoplastic disease (31%) Diabetes mellitus (19%) Alcoholism (12%)	28	59	70
Rechner et al. 2001 [1]	46/1990-1997	21.7	Older age $\geq 65$ (67.4%) Diabetes mellitus (28.3%) Malignancy (47.8%)	46	NR	NR
Bodey et al. 1991 [20]	135/1972-1983	32	Malignancy	58	52	52
Ellner and O'Donnell, 1969 [21]	50/1964-1969	100	NR	90 <sup>1</sup>	NR	64

NR: Not reported, MIH: Massive intravascular haemolysis; Recovery rate.

## Conclusion

*Clostridium perfringens* bacteremia, although relatively uncommon, is associated with high mortality due to advanced age and multiple comorbidities. The early recognition of this critical infection and early initiation of appropriate treatment are key factors of a positive outcome. SARS-CoV-2 impacts human immunity and co-infections with unusual bacteria like *C. perfringens* should be considered in patients with COVID-19 infection.

## Declarations

**Sources of funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Declaration of competing interest:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**Data availability:** No data was used for the research described in this article.

## References

1. Rechner PM, Agger WA, Mruz K, Cogbill TH. Clinical features of clostridial bacteremia: a review from a rural area. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2001; 33(3): 349-353.
2. Leal J, Gregson DB, Ross T, Church DL, Laupland KB. Epidemiology of *Clostridium* species bacteremia in Calgary, Canada, 2000-2006. *The Journal of infection*. 2008 ; 57(3): 198-203. <https://doi.org/10.1016/j.jinf.2008.06.018>
3. Kim, Yeongbin & Yun, Jae & Chun, Sejong & Huh, Hee & Lee, Nam. Eleven-Year Experience of Clostridial Bacteremia at a Tertiary Care Hospital in South Korea. *Annals of Clinical Microbiology*. 2020 ; 18 : 126.
4. Stabler S, Titécat M, Duployez C, Wallet F, Loiez C, et al. Clinical relevance of *Clostridium* bacteremia: An 8-year retrospective study. *Anaerobe*. 2020 ; 63: 102202.
5. Yamamoto Y, Itoh N, Sugiyama T, Kurai H. Clinical features of *Clostridium* bacteremia in cancer patients: A case series review. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*. 2020 ; 26(1): 92-94.
6. Van Bunderen CC, Bomers MK, Wesdorp E, Peerbooms P, Veenstra J. *Clostridium perfringens* septicaemia with massive intravascular haemolysis: a case report and review of the literature. *The Netherlands journal of medicine*. 2010 ; 68(9): 343-346.
7. Shin DH, Park JH, Yoon KW, Shin JH, Kim SJ. (2003). *Clostridium perfringens* septicemia with thrombophlebitis of the portal vein. *J Infect*. 2003; 46: 253-5.
8. Millard MA, McManus KA, Wispelwey B. Severe Sepsis due to *Clostridium perfringens* Bacteremia of Urinary Origin: A Case Report and Systematic Review. *Case reports in infectious diseases*. 2016; 2981729.
9. Ingram CW, Cooper JN. Clostridial bloodstream infections. *Southern Medical Journal*. 1989; 82(1): 29-31.
10. Yang CC, Hsu PC, Chang HJ, Cheng CW, Lee MH. Clinical significance and outcomes of *Clostridium perfringens* bacteremia--a 10-year experience at a tertiary care hospital. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases*. 2013; 17(11): e955-e960.
11. Suzaki A, Komine-Aizawa S, Nishiyama H, Hayakawa S. Massive intravascular hemolysis is an important factor in *Clostridium perfringens*-induced bacteremia. *Internal and emergency medicine*, 2022; 17(7): 1959-1967.

12. Sarasoja M, Nilson B, Wide D, Lindberg Å, Torisson G, Holm K. Epidemiology, aetiology and clinical characteristics of clostridial bacteraemia: a 6-year population-based observational study of 386 patients. *European Journal of Clinical Microbiology and Infectious Diseases*. 2022; 41(11): 1305-1314.
13. Liu F, Xue S, Zhang Y, Yang J, Hu J, et al. Clostridium perfringens sepsis in three patients with acute leukemia and review of the literature. *International journal of hematology*. 2021; 113(4): 508-517.
14. Lopez-Fabal, M.F, Sanz, N, Ruiz-Bastian, M, Barros, C, Gomez-Garces JL. Clostridium perfringens bacteraemia, an analysis of 28 cases over 10 years in a university hospital of Madrid. *Enfermedades infecciosas y microbiologia clinica (English ed.)*. 2018; 36(4): 225-228.
15. Burgos, Paula & Nanjappa, Sowmya & Snyder, Matthew & Bitetzakis, Christopher & Greene, John. (2018). Evaluation of Clostridium Bacteremia in the Cancer Population: A Case Series. *Infectious Diseases in Clinical Practice*. 26. 1. 10.1097/IPC.0000000000000655.
16. Shindo Y, Dobashi Y, Sakai T, Monma C, Miyatani H, Yoshida Y. Epidemiological and pathobiological profiles of Clostridium perfringens infections: review of consecutive series of 33 cases over a 13-year period. *International journal of clinical and experimental pathology*. 2015; 8(1): 569-577.
17. Fujita H, Nishimura S, Kurosawa S, Akiya I, Nakamura-Uchiyama F, Ohnishi K. Clinical and epidemiological features of Clostridium perfringens bacteremia: a review of 18 cases over 8 year-period in a tertiary care center in metropolitan Tokyo area in Japan. *Internal medicine (Tokyo, Japan)*. 2010; 49(22): 2433-2437.
18. Shah M, Bishburg E, Baran DA, Chan T. Epidemiology and outcomes of clostridial bacteremia at a tertiary-care institution. *TheScientificWorldJournal*. 2009; 9: 144-148.
19. Benjamin B, Kan M, Schwartz D, Siegman-Igra Y. The possible significance of Clostridium spp. in blood cultures. *Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases*. 2006; 12(10): 1006-1012.
20. Bodey GP, Rodriguez S, Fainstein V, Elting LS. Clostridial bacteremia in cancer patients. A 12-year experience. *Cancer*. 1991 ; 67: 1928-1942.
21. Ellner PD, O'Donnell ED. Non-Fatal Clostridium Perfringens Bacteremia. *Journal of the American Geriatrics Society*. 1969; 17: 644-647.
22. Jimenez KP, Kaur KS, Chang AY, Chang E. A Case of Sars-Cov-2 Associated With Quadruple Bacterial Coinfection. *Chest*. 2022; 162(4): A604.
23. Adams, B. N, Lekovic, J. P, & Robinson, S. Clostridium perfringens sepsis following a molar pregnancy. *American journal of obstetrics and gynecology*. 2014; 210(1): e13-e14.
24. Chinen K. Sudden death caused by Clostridium perfringens sepsis presenting as massive intravascular hemolysis. *Autopsy & case reports*. 2020; 10(3): e2020185.

**Manuscript Information:** Received: September 08, 2023; Accepted: October 10, 2023; Published: October 12, 2023

**Authors Information:** Siasios Panagiotis<sup>1\*</sup>; Zaires Aristidis<sup>1</sup>; Karapiperis Dimitrios<sup>2</sup>; Antoniou Dimitra<sup>1</sup>; Kachrimanidou Melina<sup>3</sup>

<sup>1</sup>Microbiology Department, 424 General Military Hospital, Thessaloniki, Greece.

<sup>2</sup>Clinic of Infectious Diseases, 424 General Military Hospital, Thessaloniki, Greece.

<sup>3</sup>First Department of Microbiology, Aristotle University of Thessaloniki, Medical School, Thessaloniki, Greece.

**Citation:** Panagiotis S, Aristidis Z, Dimitrios K, Dimitra A, Melina K. *Clostridium perfringens* bacteremia in an 89-year-old man with COVID-19 infection: Case report and brief literature review. Open J Clin Med Case Rep. 2023; 2134.

**Copy right statement:** Content published in the journal follows Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>). © **Panagiotis S (2023)**

**About the Journal:** Open Journal of Clinical and Medical Case Reports is an international, open access, peer reviewed Journal focusing exclusively on case reports covering all areas of clinical & medical sciences.

Visit the journal website at [www.jclinmedcasereports.com](http://www.jclinmedcasereports.com)

For reprints and other information, contact [info@jclinmedcasereports.com](mailto:info@jclinmedcasereports.com)