COVID-19–Associated Fusobacterium nucleatum Bacteremia, Belgium

Article *in* Emerging Infectious Diseases · December 2020

DOI: 10.3201/eid2703.202284

6 authors, including:

Louis Wolff
Lausanne University Hospital
3 PUBLICATIONS **0** CITATIONS
SEE PROFILE

Delphine Martiny
Centre Hospitalier Universitaire Saint-Pierre
25 PUBLICATIONS **538** CITATIONS
SEE PROFILE

Véronique Yvette Miendje Deyi
University-Hospital Brugmann UVC
49 PUBLICATIONS **635** CITATIONS
SEE PROFILE

Philippe Clevenbergh
Hôpital Lariboisière - Fernand-Widal (Hôpitaux Universitaires Sant-Louis, Laribois…
90 PUBLICATIONS **3,175** CITATIONS
SEE PROFILE

Centers for Disease Control and Prevention

ISSN: 1080-6059

Volume 27, Number 3—March 2021

Research Letter

COVID-19–Associated *Fusobacterium nucleatum* Bacteremia, Belgium

Louis Wolff, Delphine Martiny, Véronique Yvette Miendje Deyi, Evelyne Maillart, Philippe Clevenbergh, and Nicolas Dauby
Author affiliations: Université Libre de Bruxelles, Brussels, Belgium (L. Wolff, D. Martiny, V.Y. Miendje Deyi, E. Maillart, P. Clevenbergh, N. Dauby); Saint-Pierre University Hospital Brussels, Brussels (L. Wolff, N. Dauby); Université de Mons, Mons, Belgium (D. Martiny); Laboratoire Hospitalier Universitaire de Bruxelles–Universitair Laboratorium Brussel, Brussels, (D. Martiny, V.Y. Miendje Deyi); Brugmann University Hospital, Brussels (E. Maillart, P. Clevenbergh)
Suggested citation for this article

Abstract

We report 4 cases of *Fusobacterium nucleatum* bacteremia associated with coronavirus disease (COVID-19). Three cases occurred concomitantly with COVID-19 diagnosis; 1 occurred on day 15 of intensive care. None of the patients had known risk factors for *F. nucleatum* bacteremia. *F. nucleatum* infection could represent a possible complication of COVID-19.

Fusobacterium nucleatum is a gram-negative anaerobic rod member of the oral and digestive microbiota (*1*). *F. nucleatum* is an uncommon cause of bacteremia; annual reported incidence is 0.22–0.34 cases/100,000 population (*1*,*2*). Risk factors for *F. nucleatum* bacteremia include malignancy, older age, alcohol abuse, immunosuppression, and dialysis; infection is often hospital-acquired (*1*,*2*). Mortality rates for *F. nucleatum* bacteremia can reach 10% (*1*,*2*).

In March and April 2020, 2 major hospitals in Brussels, Belgium, observed 4 cases of monomicrobial *F. nucleatum* bacteremia, all associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among patients with coronavirus disease (COVID-19). In contrast, the same hospitals reported a total of 4 *F. nucleatum* cases in 2019, 3 in 2018, 2 in 2017, 1 in

2016, and 2 in 2015. However, the hospital emergency plan initiated on March 14 during the first wave of the COVID-19 pandemic in Belgium prohibited all nonurgent medical care. Thus, the 2020 *F. nucleatum* incidence cannot be extrapolated and compared with previous years because of modifications of patient characteristics.

F. nucleatum was cultured from patients' blood specimens by using a BD BACTEC FX blood culture system (Becton Dickinson, https://www.bd.com) and pure isolates were successfully identified by using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, https://www.bruker.com). Cross-contamination was formally excluded because blood cultures became positive on different days and bacterial identifications were performed on separate sets of experiments (Table 1).

Using nasopharyngeal swab samples, 3 patients tested positive for SARS-CoV-2 by reverse transcription PCR (RT-PCR) by the RealStar SARS-CoV-2 RT-PCR kit (Altona Diagnostics, https://www.altona-diagnostics.com) and 1 by COVID-19 Ag Respi-Strip rapid antigen test (Coris Bioconcept, https://www.corisbio.com). All 4 patients had concomitant pneumonia compatible with COVID-19 on chest computed tomography (CT) scans. The patients were 34, 51, 52, and 70 years of age (median 51.5 years); the median age was lower than in previously reported *F. nucleatum* bacteremia (*1*,*2*), but the sample size is too small for statistical analysis. None of the patients had any classical risk factors for *F. nucleatum* bacteriemia. The youngest patient had no underlying conditions. Three patients had abdominal symptoms and 2 underwent abdominal CT with contrast, but both had unremarkable results. Three patients had symptoms of bacteremia at the time of COVID-19 diagnosis; bacteremia was diagnosed in the other patient after 15 days in the hospital intensive care unit (ICU). The ICU patient received a single 800-mg intravenous dose of tocilizumab (TCZ) to treat COVID-19–associated hyperinflammatory syndrome. Increased risk for severe infection, including bacteremia, has been associated with long-term TCZ treatment when administered for non-COVID-19 indications (*3*). To our knowledge, no previous *F. nucleatum* infection has been reported with TCZ use in general. The patient died of COVID-19–related severe respiratory failure on day 21 in the ICU, but the other 3 patients were discharged to home without complications.

Although SARS-CoV-2 infection initially was described as an agent of severe pneumonia, other organ involvements are now well described. Other studies among hospitalized COVID-19 patients have shown that 18%–48% had digestive complaints ranging from anorexia to diarrhea and abdominal pain (*4*,*5*). RT-PCR detected the virus in the feces of 48%–53% of patients with abdominal complaints and feces remained positive in 20%–33% of patients even after respiratory samples converted from RT-PCR–positive to negative (*4*,*6*). The propensity of SARS-CoV-2 to infect digestive organs might be explained by the fact that angiotensin converting enzyme 2, a known receptor used by the virus to enter human cells, has been found to be highly expressed in enterocytes (*4*,*7*).

The reservoir of *F. nucleatum* is generally considered to be the oral cavity (*8*). Only 1 of these patients had oral symptoms, but no oral lesions were observed. The 3 other patients had abdominal symptoms, suggesting that bacteremia might be the consequence of translocation from the digestive tract (*9*). *F. nucleatum* has been shown to colonize colon mucus with associated mucosal inflammation (*10*).

In conclusion, digestive tract invasion by SARS-CoV-2 and secondary inflammatory response might promote translocation of opportunistic pathogens, such as *F. nucleatum*, and further research could elucidate this interaction. Nonetheless, our observations suggest that anaerobe bacteremia should be considered as a complication of COVID-19.

Dr. Wolff is a resident in internal medicine at Saint-Pierre University Hospital Brussels, Belgium. His research interests include immunology and medical education.

Top

Acknowledgment

We thank Adrian Griffiths for English language revision.

Top

References

1. Afra K, Laupland K, Leal J, Lloyd T, Gregson D. Incidence, risk factors, and outcomes of *Fusobacterium* species bacteremia. BMC Infect Dis. 2013;13:264. DOI PubMed
2. Nohrström E, Mattila T, Pettilä V, Kuusela P, Carlson P, Kentala E, et al. Clinical spectrum of bacteraemic *Fusobacterium* infections: from septic shock to nosocomial bacteraemia. Scand J Infect Dis. 2011;43:463–70. DOI PubMed

3. Bykerk VP, Östör AJK, Alvaro-Gracia J, Pavelka K, Román Ivorra JA, Nurmohamed MT, et al. Long-term safety and effectiveness of tocilizumab in patients with rheumatoid arthritis and inadequate responses to csDMARDs and/or TNF inhibitors: an open-label study close to clinical practice. Clin Rheumatol. 2019;38:2411–21. DOI PubMed
4. Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARS-CoV-2. Gastroenterology. 2020;158:1831–1833.e3. DOI PubMed
5. Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. Am J Gastroenterol. 2020;115:766–73. DOI PubMed
6. Cheung KS, Hung IFN, Chan PPY, Lung KC, Tso E, Liu R, et al. Gastrointestinal manifestations of SARS-CoV-2 infection and virus load in fecal samples from a Hong Kong cohort: systematic review and meta-analysis. Gastroenterology. 2020;159:81–95. DOI PubMed
7. Lamers MM, Beumer J, van der Vaart J, Knoops K, Puschhof J, Breugem TI, et al. SARS-CoV-2 productively infects human gut enterocytes. Science. 2020;369:50–4. DOI PubMed
8. Abed J, Maalouf N, Manson AL, Earl AM, Parhi L, Emgård JEM, et al. Colon cancer-associated *Fusobacterium nucleatum* may originate from the oral cavity and reach colon tumors via the circulatory system. Front Cell Infect Microbiol. 2020;10:400. DOI PubMed
9. Han YW. *Fusobacterium nucleatum*: a commensal-turned pathogen. Curr Opin Microbiol. 2015;23:141–7. DOI PubMed
10. Strauss J, Kaplan GG, Beck PL, Rioux K, Panaccione R, Devinney R, et al. Invasive potential of gut mucosa-derived *Fusobacterium nucleatum* positively correlates with IBD status of the host. Inflamm Bowel Dis. 2011;17:1971–8. DOI PubMed

Top

Table

Table. Characteristics of 4 cases of *Fusobacterium nucleatum* bacteremia in patients with COVID-19, Belgium

Top

Suggested citation for this article: Wolff L, Martiny D, Miendje Deyi VY, Maillart E, Clevenbergh P, Dauby N. COVID-19–associated *Fusobacterium nucleatum* bacteremia, Belgium. Emerg Infect Dis. 2021 Mar [*date cited*]. https://doi.org/10.3201/eid2703.202284

DOI: 10.3201/eid2703.202284

Original Publication Date: December 08, 2020

URL Validation failed because the page https://doi.org/10.3201/eid2703.202284 does not exist (HTTP error 404).

The author "Véronique Yvette Miendje Deyi" has three or more given-name parts, and only one surname part. Please check the author name segmentation and manually apply character styles to fix the segmentation if necessary.

The URL https://www.bd.com has been redirected to https://www.bd.com/en-us. Please verify the URL.

No table matches the in-text citation "Table 1". Please supply the missing table or delete the citation.

The URL https://www.altona-diagnostics.com has been redirected to https://www.altona-diagnostics.com/en/. Please verify the URL.

CrossMark reports this article was originally posted as a Preprint at https://doi.org/10.1101/2020.02.17.20023721. (Ref. 4 "Xiao, Tang, Zheng, Liu, Li, Shan, 2020")

CrossMark reports this article was originally posted as a Preprint at https://doi.org/10.1101/2020.04.25.060350. (Ref. 7 "Lamers, Beumer, van der Vaart, Knoops, Puschhof, Breugem, et al., 2020")

The table "Table. " is not cited in the text. Please add an in-text citation or delete the table.

Comments

Please use the form below to submit correspondence to the authors or contact them at the following address:

Nicolas Dauby, Department of Infectious Diseases, CHU Saint-Pierre, Brussels, Belgium

Return Address

Send To

◉ Authors ○ Editors

Comments

10000 character(s) remaining.

Send

Top

Page created: December 04, 2020 8:03 PM EST
Page updated: December 08, 2020 8:25 PM EST
Page reviewed: December 08, 2020 8:25 PM EST