CASE REPORT

Clostridium hastiforme bacteraemia secondary to pyometra in a 64-year-old woman

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SUMMARY

The Gram-negative, rod-shaped, anaerobe bacteria *Tissierella praeacuta* was first described in 1908 by Tissier. However, during the past decade, *Clostridium hastiforme* has been recognised as a later synonym of *T. praeacuta*. *C. hastiforme*/*T. praeacuta* has only rarely been described in previous literature as a cause of human infection. We present here a case report of *C. hastiforme*/*T. praeacuta* bacteraemia secondary to pyometra in a 64-year-old woman with a history of multiple sclerosis and an intrauterine device inserted three decades earlier. *C. hastiforme*/*T. praeacuta* was isolated from blood as well as pus from the site of infection. The patient was cured with a combination of drainage and antibiotic therapy.

BACKGROUND

Pyometra is an uncommon gynaecological condition defined as accumulation of pus inside the uterine cavity.¹ Risk factors include the presence of an intrauterine device (IUD) and postmenopausal age, resulting in hormonal and structural changes of the uterus lining.^{1–2} The most common microorganism isolated from pus discharge from the uterus is *Escherichia coli*, but anaerobe microorganisms also account for a great part, with *Bacteroides fragilis* being the most common anaerobe bacteria.³

The Gram-negative, rod-shaped *Tissierella praeacuta* was first described in 1908 by Tissier after isolation from infant faeces.⁴ In 1995, Farrow *et al*⁵ showed that the 16S rRNA sequences of the type strains of *T. praeacuta* and *Clostridium hastiforme* displayed 99.9% similarity, suggesting that they are either the same species or very close related species. Nearly a decade later, Bae *et al*⁶ managed to show that *T. praeacuta* and *C. hastiforme* had identical biochemical profiles, both stained Gram-positive and showed 96.5% relatedness by DNA–DNA hybridisation, concluding that *C. hastiforme* is a later synonym of *T. praeacuta*. We report here the first case of bacteraemia with *C. hastiforme* secondary to pyometra in a 64-year-old woman.

CASE PRESENTATION

A 64-year-old woman with a medical history of multiple sclerosis for 30 years was referred by her general practitioner to a gynaecologist in an outpatient clinic due to persistent lower back pain and a slightly elevated cancer antigen 125 of 38 U/mL. A transvaginal ultrasound showed fluid in a slightly enlarged uterus, and the following gynaecological examination revealed an occluding non-adherent process in the vagina, which was removed and

thereby revealed a line from an IUD. The IUD was removed and purulent discharge from the uterine cavity appeared. According to the patient, the IUD was implanted 33 years previously. By means of exploratory laparoscopy, ~15 mL of purulent fluid was drained and tissue from the uterus sampled for cytological and histological examination. Prior to the gynaecological examination, the patient underwent a CT scan of the thorax and abdomen which showed an IUD in fundus uteri and accumulation of fluid near the tip of the IUD, indicating an infective state.

The patient went home, but developed fever and vomiting within a few hours and was admitted to the Department of Gynaecology at the North Denmark Regional Hospital. On examination, she presented with fever (39.3°C) and tachycardia (113 bpm), indicating a septic state. A laboratory test showed an elevated C reactive protein (CRP) of 80 mg/L and white cell count (WCC) count of $15.8 \times 10^9/L$. Pyometra was suspected as the source of infection and pus from the now open uterine pyometra as well as blood samples was sent to the clinical microbiological laboratory for examination. Thereafter, antimicrobial therapy was initiated with intravenous cefuroxime 1500 mg and metronidazole 500 mg, both three times a day. Owing to persistence of fluid in the uterus visualised by transvaginal ultrasound, the patient underwent a second transvaginal drainage on day 3 by means of a female catheter. Purulent discharge was once again drained and sent for microbiological examination. Hereafter, she quickly improved and after 6 days of admission, she was discharged with oral pivampicillin 700 mg three times a day and metronidazole 500 mg, twice a day, for an additional 7 days.

At follow-up 3 weeks after admission, CRP and WCC were normalised and the patient had no signs of pyometra. A transvaginal ultrasound showed a small uterus but again, a small amount of fluid in the uterine cavity appeared. Owing to her good clinical condition, it was decided to await further drainage. At the four month visit, the patient still had no signs of pyometra, but a tiny bit of fluid remained in the uterine cavity. A dilation of the cervical canal was performed and 1.5 mL of clear fluid was drained, and a second biopsy from the uterus was performed to rule out any underlying diseases.

INVESTIGATIONS

From the blood culture system (BACTEC FX, Becton, Dickinson and Company, Franklin Lakes, USA), the Bactec LYTIC/10 Anaerobic/F bottle yielded growth after 48 hours. The initial

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microscopy showed Gram-negative rods. Subcultures were performed on 5% horse blood agar and chocolate agar (SSI Diagnostica, Hillerød, Denmark) incubated at 37°C in ambient air and 5% CO₂, and on chocolate agar supplemented with vitamin K and cysteine incubated in an anaerobic atmosphere at 37°C for 48 hours. Bacterial growth was observed on the anaerobic plate only, whereas agar plates incubated in ambient air and in 5% CO₂ were culture negative. A second Gram-staining was performed, and microscopy now revealed Gram-positive rods with terminal spores. The colonies had a butyric acid odour and were catalase-negative. Final identification was made by matrix-assisted laser desorption-ionisation time of flight mass spectrometry (MALDI-TOF-MS) on a Microflex instrument (MALDI Biotyper RTC 3.1, database version DB-5989; Bruker Daltonics, GmbH, Bremen, Germany) with *T. praeacuta* (log-score: 2.216) and *C. hastiforme* (log-score: 2.139) as best matches, as well as partial sequencing of the 16S rRNA gene. Similar to MALDI-TOF-MS, BLAST analysis indicated 99% homology with the 16S rRNA gene sequence of *C. hastiforme* strain DSM 5675 (GenBank accession X80841) and *T. praeacuta* strain ATCC 25539 (GenBank accession NR_117376).

Antimicrobial susceptibility testing was performed by the use of McFarland standard 1.0 on brucella sheep blood agar with Etest (BioMérieux, Marcy l'Etoile, France) with the following results: penicillin G MIC: 0.016 mg/L, meropenem MIC: <0.002 mg/L, clindamycin MIC: 4 mg/L and metronidazole MIC: 0.125 mg/L. *Tissierella praeacuta/C. hastiforme* was susceptible to all antimicrobial agents tested following the EUCAST Clinical Breakpoints, V. 6.0.

Gram-staining of the pus from the uterine cavity initially showed Gram-negative rods. However, anaerobic cultures after 48 hours grew Gram-positive *C. hastiforme* with terminal spores, as well as *B. fragilis*. *Clostridium hastiforme* from pus also was susceptible to all antimicrobial agents, tested as mentioned above. Biopsies from the endometrium were sent to the Department of Pathology. Cytological and histological examinations of the material sampled before admission showed severe acute and chronic inflammation and focal bacterial colonies without signs of malignancy. Biopsies sampled at the 4 month visit appeared normal without inflammatory changes or suspicion of malignancy.

DISCUSSION

To the best of our knowledge, this is the first report of *C. hastiforme* (or *T. praeacuta*) bacteraemia secondary to pyometra. We were able to isolate the bacteria from blood and pus from the site of the primary infection. The patient had a history of multiple sclerosis and the same IUD implanted for more than three decades, which may have triggered the uterine infection. It is plausible that *C. hastiforme* as well as *B. fragilis* had migrated from the vagina into the uterus and were able to grow in an anaerobic environment with dissemination of *C. hastiforme* to the bloodstream.

The genus *Clostridium* comprises >200 species with the majority being obligate anaerobic, Gram-positive, spore-forming rods.⁷ However, the number of clinically significant clostridia from human infection is limited and Clostridial bacteraemia is mainly due to *C. septicum*, *C. tertium* and *C. perfringens*, with more than half of these patients having gastrointestinal anomalies or underlying malignancies, such as carcinoma of the colon.⁷ *Tissierella praeacuta/C. hastiforme* is a rare cause of human infection. A review of the literature only reveals a few case reports with highly variable infection sites, including brain abscess,⁸ eyelid gas gangrene,⁹ pseudarthrosis,¹⁰ blood^{10–12} and

colonisation in a 4-year-old boy with combined immune deficiency.¹³

Whether *T. praeacuta/C. hastiforme* is an extremely rare cause of infection remains unknown. With increased usage of MALDI-TOF-MS, the term 'first case' may have a potential limitation since there may be a possibility of previous cases of bacteraemia with *T. praeacuta/C. hastiforme* reported with only the simple identification as *Clostridium* species. Vegetative cells of *Clostridium* species are pleomorphic, and Gram-staining usually shows Gram-positive rods, although some species such as *C. clostridioforme*, *C. hathewayi*, *C. innocuum* and *C. ramosum* may appear Gram-negative, while *C. tetani* also appears Gram-negative when spores have formed.⁷ Our initial microscopy also showed Gram-negative rods, and only after anaerobic subcultivation did the isolate turn out Gram-positive. We did not perform a parallel KOH test, but it is possible that the false-negative Gram-staining may have been caused by protracted incubation, as discussed by Bae *et al.*⁶

Treatment of pyometra usually involves drainage of the uterine cavity, as well as empiric antibiotics that include coverage for anaerobe bacteria.³ The traditional antibiotics against *Clostridium* species (except *C. difficile* and *C. tertium*) include penicillin, piperacillin-tazobactam, imipenem or meropenem, metronidazole and vancomycin.⁷ Similar to previous reports, our isolate of *T. praeacuta/C. hastiforme* was highly susceptible to β-lactam antibiotics and metronidazole. The patient was cured with drainage supplemented with intravenous β-lactam antibiotic and metronidazole for 6 days, followed by 7 days of oral pivampicillin and metronidazole.

In conclusion, this report illustrates the importance of considering anaerobe culture when treating patients with abscesses or infections such as pyometra in a naturally existing anatomical cavity. *Clostridium hastiforme* has only rarely been described as a human pathogen and never as a cause of pyometra. With better diagnostics, such as MALDI-TOF-MS, more bacteria are easily identified and presently, it is therefore unknown whether *C. hastiforme* is a true rare cause of infection or not. Finally, this case highly illustrates that IUDs should be removed in postmenopausal women in order to avoid complications.

Learning points

- ▶ Physicians and clinical microbiologists should be aware of complicating anaerobe pathogens in the diagnostics and treatment of patients, especially when focus involves abscesses.
- ▶ It is important for clinical microbiologists and treating physicians to know that Gram-staining is not always clear and further examinations are needed to make a final diagnosis.
- ▶ Intrauterine devices should be removed according to the manufacturer's product information to minimise the risk of complications.

Contributors HLN and DF-D performed the bacteriological investigations and initiated the case study. MØ was the primary contributor to the manuscript and handled the treatment and follow-up in close collaboration with clinicians. All authors contributed to the preparation of the final manuscript.

Competing interests None declared.

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