

Case report

***Campylobacter fetus* bacteraemia related to venous access device. Case report and literature review.**

Abstract:

Campylobacter fetus is a gram negative, microaerophilic bacterium which can cause bacteraemia and invasive infection in humans. Its cause is considered to be close contact with animals and/or consumption of contaminated food of sheep or bovine origin and, therefore, the primary infection site is usually the intestine. Here we report an unusual case of an adult male with catheter-related bloodstream infection caused by *C. fetus*, and we review other published cases.

Keywords:

Campylobacter, *Campylobacter fetus*, bacteraemia, catheter, case report

Introduction

Campylobacter fetus is a gram negative, microaerophilic bacterium that grows between 25 and 37°C. Unlike other species of the same genus, many of the *C. fetus* strains do not grow at 42°C[1]. Three subspecies are included in the species: *C. fetus* subs. *fetus*, *C. fetus* subs. *venerealis*[2] y *C. fetus* subs. *testudinum*[3], being the first one responsible of most of human infections.

Common in the cattle herd, it is a rare microorganism in clinical practice whose manifestations range from acute diarrhea to systemic infections[4]. Recent studies estimated that this microorganism causes about 3% of gastroenteritis and approximately 20% of *Campylobacter* bacteremias[5,6]. The mortality rate of *Campylobacter* invasive infections has been established at around 14%[7]. The most common route of infection is considered to be close contact with animals and/or consumption of contaminated food of sheep or bovine origin[1].

Due to its relatively low prevalence, the clinical and microbiological management of bacteremia caused by *C. fetus* is poorly outlined. For this reason, we report the case of an adult male with catheter-related bloodstream infection caused by *C. fetus*, and we review other published cases.

Case description

A 77-year-old male, diagnosed with colorectal adenocarcinoma with pulmonary progression, came to the emergency room of the University Hospital Virgen del Rocío (Seville, Spain) after an episode of chilling and myalgia. The patient has been carrying a *Port-a-Cath*® reservoir for a year which is no longer in use after completion of FUFA

(folinic acid and fluorouracil) therapy. He reported that symptoms began few minutes after the *Port-a-Cath* cleaning by flushing with sodium heparine. The device point of insertion did not show local signs of infection but given the proximity between the device maintenance and the appearance of symptoms, differential blood cultures were taken and sent to the microbiology laboratory. After clinical exploration and considering the patient's general condition, with no symptoms other than fever, he was discharged home with the diagnosis of transient bacteremia by manipulation of the *Port-a-Cath*, awaiting microbiological confirmation.

Two series of blood cultures were received in the laboratory: one extracted through the *Port-a-Cath* and the other obtained by venipuncture and were incubated in both aerobic and anaerobic conditions in an automatic *BACTEC Fx*® system (Becton Dickinson). After 29 hours of incubation, the system alerted that the cultures were positive. Gram stain revealed small, very thin, clustered Gram-negative rods. Direct identification from the blood culture pellet by mass spectrometry without pretreatment (*Microflex LT*® (Bruker Daltonics)[8] did not show conclusive results. The blood culture was inoculated in plates where bacterial growth was observed after 48 hours of incubation at 35°C in 5% CO₂ atmosphere on blood agar and brucella agar, with no growth on MacConkey agar. The oxidase reaction was positive and the hydrolysis of hippurate negative. Analysis by mass spectrometry with formic acid pretreatment, identified *Campylobacter fetus* with a score of 2.47.

The antibiotic sensitivity study was carried out on Mueller-Hinton agar supplemented with 5% horse blood and 20 mg/L of β-NAD, in a microaerophilic atmosphere at 35°C using MIC gradient strips (*Liofilchem*®, Italy) of amoxicillin/clavulanate, ciprofloxacin, and imipenem. The interpretation was based on the recommendations of the Antibiogram Committee of the French Society of Microbiology (CA-SFM)[9] with the following results: sensitive to amoxicillin-clavulanate (MIC 0.75) and imipenem (MIC 0.25); and intermediate to ciprofloxacin (MIC 0.50)

The patient was contacted by telephone and asked to come to the hospital in order to remove the device, as it was not in use for the administration of treatments. Treatment with amoxicillin-clavulanic acid 500/125 mg every 8 hours for 15 days was prescribed. The patient was re-interrogated, and he reported an episode of mild but persistent diarrhea 3 months earlier. In subsequent check-ups, the patient remained asymptomatic and the control blood cultures were negative .

Discussion

Unlike other *Campylobacter* species, there is a strong association between *C. fetus* bacteremia and certain underlying risk factors: an advanced age[10], neoplasms, immunosuppressive treatment[11] and the presence of intravascular devices (especially vascular reservoirs)[7]. It is widely known that long-term implantable vascular access devices, such as *Port-a-Cath*, implies a high risk of infection[12,13], which can be produced by colonization from the skin flora, by poor handling of the device by health personnel or by hematogenous seeding[14]. It has been reported that *C. fetus* can colonize

the human intestine without causing diarrhea or inducing very mild symptoms[15] and its ability to cause bacteremia with dissemination to secondary foci has been widely established[1]. Given that the patient suffered gastrointestinal symptoms three months earlier, we propose that the most likely route of colonization was hematogenous, in the context of a mild intestinal infection that leads to a previously undetected bacteremia. The recommended treatment of systemic infections caused by *C. fetus* is the use of amoxicillin-clavulanate, carbapenems, macrolides or fluoroquinolones[16]. The management of colonized intravascular devices in cancer patients is always conditioned by an assessment of the potential risk versus the benefit of keeping the device implanted[17]. In this case, as it was not in use, removal was clearly desirable.

After a review of the published literature, there are very few documented cases of catheter-related infections caused by this microorganism. As shown in **Table 1**, there are three published cases of infection from a venous access device implanted to provide oncological treatment. The chosen treatment was described only in one of them, which also included the removal of the device. On the other hand, a handful of cases of infection of ascitic fluid caused by *C. fetus* associated to peritoneal dialysis have been published. However, it is difficult to clearly establish that the source of infection in all these cases was the catheter and not an undetected abdominal focus as suggested in Kubota et al.[18]. Therefore, we only included the case in which it is confirmed that the infection origin is the peritoneal dialysis catheter[19].

We believe that all the cases collected here, together with the one we report, suggest the need to pay special attention to mild gastrointestinal and/or diarrheal symptoms in patients with long-term access devices. Despite their low severity and their spontaneous resolution, these conditions can cause a transient bacteremia or peritonitis which may be enough to set up a reservoir in those patients. The ability of different species of the genus *Campylobacter* to growth in biofilms is well known[23], and recently a case of endocarditis due to *C. fetus* on a prosthetic valve on which the microorganism had established a biofilm, has been credited[24].

From a microbiological point of view, the traditional phenotypic identification of the hippurate negative species of *Campylobacter* is usually not very satisfactory due to the complexity of their taxonomy. However, mass spectrometry achieves 100% agreement compared to molecular techniques and is currently the most recommended method for routine identification.[12]. On the other hand, susceptibility determinations has not been well resolved, since the EUCAST guide only provides cutoff points for thermophilic *Campylobacter* species, which require incubation at 42°C. That makes impossible to refer the cutoff points to *C. fetus*. Only the French guide takes these considerations into account and is the only one recommended[25].

Sex	Age	Origin	Treatment	Outcome	Reference
--	--	Port-a-Cath	--	--	[20]*
--	--	Port-a-Cath	--	--	[20]*
M	40	Port-a-Cath	- Device withdrawal	Recovery	[21]

			- Ciprofloxacin (800 mg/day) + gentamicin (200 mg/day) (3 days). - Oral ciprofloxacin (1.5 g/day) (3 weeks)		
F	68	Hemodialysis catheter	- Gentamicin i/v (1 mg/kg) + Ciprofloxacin	Recovery	[22]**
M	55	Peritoneal dialysis	- Catheter withdrawal - Meropenem i/v	Recovery	[19]

Table 1: Summary of cases of biomedical device infection found in the literature

* This work is an extensive review of *Campylobacter* bacteremias and no further information of these cases is provided.

** Identification is carried out at the genus level and the authors concluded that is *C. fetus* as the most probable species.

Conclusion.

This clinical case points out the difficulty to diagnose *Campylobacter fetus* bacteraemia, as it is a rare microorganism in human infections. Any undergoing immunosuppressing treatment makes the patient more vulnerable to any opportunistic pathogen, while the use of long-term access devices for those treatment increases the risk of colonization and infection. In this sense, this case is a wake up call to make a careful management of devices.

Ethical Approval and Consent :

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

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