Letter to the Editor

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Prosthetic hip joint infection caused by *Campylobacter fetus*: A case report and literature review

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Article history
Received: 8 March 2017; Revision Requested: 4 September 2017; Revision Received: 5 September December 2017; Accepted: 6 September 2017

Sir,

Campylobacter spp usually causes gastrointestinal illness and occasionally severe systemic infections. Most cases of intestinal campylobacteriosis are caused by *Campylobacter jejuni* or *Campylobacter coli* [1] but *Campylobacter fetus* is the most commonly detected pathogen causing *Campylobacter* bacteraemia [2,3]. Septic arthritis caused by this microorganism have been reported previously and are likely to become more common given the increased numbers of devices implanted and widespread use of immunosuppressive therapy.

These microorganisms are fastidious and require microaerobic growth conditions and appropriate culture methods. It is a microaerophilic, Gram-negative, spiral-shaped bacterium that grows between 25ºC and 37ºC. The incubation temperature of 42ºC, which is often routinely used to isolate *Campylobacter* spp, precludes the recovery of at least 20% of *C. fetus* isolates that do not grow at this temperature. On the other hand, use of cephalothin containing media, for the selective isolation of *C. jejuni* and *C. coli*, inhibits growth of *C. fetus*. It is also remarkable that microorganisms associated with prosthetic joint infections (PJI) are found in biofilms; thus, methods such as implant vortexing and sonication, which sample the prosthesis surface, provide improved sensitivity for PJI diagnosis compared to conventional periprosthetic tissue cultures [4].

Moreover, it is described the use of extraintestinal samples as blood or cerebrospinal fluid, which have less contaminating organisms and allow detection without the use of selective media [5]. Once a suspected *C. fetus* isolate is obtained, phenotypic or molecular methods can be used to confirm the species. In many cases, phenotypic methods have limitations and genotypic identification of the species has been recommended. Subspecies differentiation has no direct clinical relevance but might support a better understanding of de epidemiology.

Infections mainly affect persons at higher risk, including elderly and immunocompromised individuals [5]. Septicaemia, with fever but without apparent localized infection, is reported in most of cases [3,6]. Other manifestations may be the result of neurological infections, osteomyelitis, lung abscesses, arthritis, perinatal infections and vascular pathology [7,8,9]. Predisposing factors for *C. fetus* infection include conditions that result in immunosuppression, cardiovascular disease with valve abnormalities, liver disease, diabetes mellitus and medical device implants. Elderly people and pregnant women, without any underlying disease are also at risk [3,7]. In healthy young are rarely reported and such infections, are generally associated with occupational contact with animals [5]. In relation to the pathogenesis, the isolation or detection of DNA of *C. fetus* from stools of healthy people indicates that intestinal colonization may also occur without diarrhoea [10]. The limited ability of these microorganisms to breach the host defenses in otherwise healthy individuals may explain why dissemination of infections is mainly observed in immunocompromised individuals [6,11]. It has been demonstrated for this pathogen the preference for endovascular surfaces and a genomic variation that contributes to differences in the clinical infections and virulence [12].

We report a case of *C. fetus* infection involving a prosthetic hip joint. We considered immunocompromised patients to be those receiving chemotherapy, radiotherapy, or immunosupressors. Blood cultures were processed using the BD BACTEC FX (Becton Dickinson, Sparks, MD) and microbiological cultures were realized by standard procedures. Identification and determination of antibiotic susceptibility were performed using Phoenix Automated Microbiology System (BD Diagnostic Systems) and Epsilon Test (BioMérieux, France). EUCAST breakpoints were applied (EUCAST 2014). We reviewed the literature regarding *Campylobacter* PJI .

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The case was a 60-year-old male with severe pain in left hip joint. Nonspecific febrile was the main symptom. He had undergone a left total hip replacement 10 years earlier. Associated risk factors were: elderly, diabetes mellitus, immunosuppressive disease, vascular pathology and prosthetic hip joint. Clinical signs were lumbar and thoracic pain, anorexia, nausea, crampy lower abdominal pain, pleural effusion, chronic obstructive pulmonary disease and heart failure.

Biochemical and blood parameters were: haemoglobin concentration 9.7 g/dl (normal range: 13.5-17.5 g/dl), neutrophil count 13.1 x 10^9/L (normal range: 1.8-8 x 10^9/L), erythrocyte sedimentation rate 65 mm/h (normal range: 0-10 mm/h), C-reactive protein 14.45 mg/dL (positive > 1 mg/dL), glutamate pyruvate transaminase 64 U/L (normal range 7-40 U/L) and gamma-glutamyl-transpeptidase 265 U/L (normal range 10-50 U/L).

The fluid obtained from hip aspirate contained numerous white blood cells and was positive for *C. fetus* after 48 h of incubation. The same organism was grown from blood cultures and tissue taken from around the prosthesis. Interestingly, he did not have gastrointestinal or systemic symptoms and signs preceding or during the hip joint infection.

The infection required total removal of the prosthesis and the treatment in the first period of their income was imipenem associated with azithromycin for 6 weeks. In the second half, after 15 days without antibiotics new samples were microbiologically negatives. The absence of microorganisms was demonstrated and held on prosthetic replacement removing the spacer. The clinical course was favourable.

Twenty one cases (including our case) have been reported (table 1). Fourteen patients were infected with *C. fetus*, three with *C. jejuni* and one with *C. coli, C. gracilis, C. lari or C .upsaliensis*. The average age of *C. fetus* infection was 70.79 years (SD = 10.44). The antimicrobial therapy used was variable employing imipenem, gentamicin, amoxicillin, azithromycin, chloramphenicol, tetracycline, erythromycin, ceftriaxone or roxithromycin. The duration of treatment was very different, from 3 days to 3 months for patients with *C. fetus* infections.

C. fetus is a pathogen affecting almost exclusively patients with immunosuppression and chronic debilitating diseases. The patients with joint replacements are a target to consider too. Recent literature insured that yearly number of combined knee and hip arthroplasties are increasing [13]. The infection of prosthetic devices is rare but it is possible that other cases go unrecognized as *Campylobacter* spp may require prolonged incubation on media routinely used for suspected prosthetic joint infection.

This microorganism has a protein surface layer which provides resistance to opsonization, easily form an extraintestinal infectious focus [14] and can cause systemic infections and others (lung abscess, urinary infection, meningitis, subdural abscess, arthritis, peritonitis and cholecystitis). Furthermore, *C. fetus* shows a special tropism for the human vascular endothelium via bacteriasurface receptors [15,16], be an added risk factor in these complicated patients [9].

We report here one case of infection caused by *C. fetus* in a patient with vascular pathology and prosthetic hip joint. In our study we highlight various aspects. On the one hand the diagnosis in our patients was made by blood cultures, fluid obtained from hip aspirate and tissue taken from around the prosthesis. Furthermore this case occurred without diarrhoea, as the least of the cases described in the series. Finally antimicrobial therapy was carried out by azithromycin and imipenem for 6 weeks and the infection required total removal of the prosthesis. The duration of treatment in cases of table 1 with *C. fetus* infection was wery different, from 3 days with gentamicin and azithromycin to 3 months with ceftriaxone and roxitrhromycin.

Addition, we report here 20 *Campylobacter* PJIs by others authors where fourteen patients were infected with *C. fetus* (table 1) [17-28]. The predominance of *C. fetus* is in keeping with its propensity to cause bacteraemia, possibly related to its relative resistance to the bactericidal activity of serum [29]. The therapeutic regimens and the treatment duration were quite different. Most patients were elderly and immunocompromised, were elderly where its shows the difference in the mean age of infected patients, 28.6 years for *C. Jejuni /C. coli* versus 68.4 years *for C. fetus* described previously by other authors [30].

All patients had risk factors such as chronic lymphocytic leukaemia, heart failure, diabetes mellitus, immunosuppressive therapy, liver cirrhosis, lung cancer, renal transplant and rheumatoid arthritis being susceptibility to infection by this organism and others.

Our patient demonstrates the typical features of patients with campylobacter joint prosthesis infection as most are elderly, immunocompromised and nonspecific febrile illness. In contrast to most cases reported, this case was diagnosed without diarrhoea in a patient with vascular pathology, in addition to being a carrier of a prosthetic hip joint.

The therapeutic regimens, duration and surgical strategies (one or two stage resection arthroplasties, implant retention or debridement) of these patients were quite different. The most cases of *C. fetus* and *C. jejuni* PJI were treated with a combination of antimicrobials. Our patient was successfully treated consisting of removal of the prosthesis, surgical washout and debridement. The antimicrobial therapy was included carbapenems associated with macrolides in the first time. It is possible that the early removal and treatment contributed to the favourable outcome of case. It is not clear what the most effective antimicrobial therapy was or its duration, but from the cases reported long-term suppression appears unnecessary. The choice of antibiotics for treatment is controversial; some authors advocate the use of imipenem since *C. fetus* infections in immunocompromised patients are very serious. Ciprofloxacin and macrolides were an adequate choice for other cases described [31,32]. Antimicrobial regimens for the management of *Campylobacter* PJIs included β-lactams, aminoglycosides, macrolides, fluoroquinolones, clindamycin and tetracyclines in other cases.

Table 1 ***Campylobacter prosthetic*** **joint infections reported in the literature**

Species	Nº of cases	Age range	Male patients (%)	Prosthetic hip joint infection (Nº)	Prosthetic knee joint infection (Nº)	Underlying disease or relevant exposure
C. fetus	14	52-88	57	8	4	
David et al	a	72	Male	-	Knee	Cattle Farmer
Yao et al	b	75	Male	Hip	-	Chronic Lymphocytic Leukemia, Prednisone
Bates et al	c	68	Female	Hip	-	Rheumatoid Arthritis, Prednisolone
Chambers et al	d	72	Male	Hip	-	Alcohol Abuse, Chronic Granulocytic Leukemia, Hypertension
Joly et al	e	70	Male	Hip	-	Liver Cirrhosis, Alcohol Abuse
Meyer et al	f	71	Female	-	Knee	Diabetes Mellitus Chronic Obstructive Pulmonary Disease Rheumatoid Arthritis,
	g	53	Male	*	*	Diabetes Mellitus Hypertensive Cardiomyopathy Rheumatoid Arthritis
	h	80	Female	**	**	Diabetes Mellitus Hypertensive Cardiomyopathy Rheumatoid Arthritis
Prendki et al	i	88	Male	Hip	-	Lung Cancer
	j	70	Female	-	Knee	Liver Cirrhosis
	k	85	Female	Hip	-	Liver Cirrhosis
	l	52	Female	-	Knee	-
	m	75	Male	Hip	-	Renal Transplant
Current	n	60	Male	Hip	-	Diabetes Mellitus Immunosuppressive Disease, Vascular Pathology
C. jejuni	3	60-77	100	1	2	
Peterson et al	a	60	Male	Hip	-	AIDS, B Cell Lymphoma, Haemophilia
Shawn et al	b	75	Male	-	Knee	Cattle farmer
Prendki et al	c	77	Male	-	Knee	Immunosuppressive Disease
C. coli	1	60	100	1	0	
Sharp et al	a	60	Male	Hip	-	Obesity, Hypertension Ingestion of contaminated raw oysters
C. gracilis	1	74	100	0	1	
Almeida et al	a	74	Male	-	Knee	Cattle Farmer
C. lari	1	81	100	1	0	
Werno et al	a	81	Male	Hip	-	Tibial Osteoblastic Osteosarcoma
C. upsaliensis	1	24	100	0	1	
Issartel et al	a	24	Male	-	Knee	Osteoblastic Osteosarcoma

*Cellulitis of the right leg; **Septic arthritis of the right shoulder.

C. fetus infection is rare, but can have important implications for patients with prosthetic joints. This infection should be suspected particularly in those patients with nonspecific febrile illness, acute gastroenteritis and immunosuppressive diseases, furthermore, this infection can be related to prosthetic devices in hospitalized patients being an important systemic disease. Most of cases occurring after recent gastroenteritis, consideration should be given to postponing elective arthro-

plasty surgery in patients who have had a recent episode of bacterial gastroenteritis.

Campylobacter infections of prosthetic devices are likely to become more common given the increased numbers of devices implanted and widespread use of immunosuppressive therapy.

Finally, based on our review of the literature, we concluded that it is important for clinicians should alert the clinical microbiology laboratory to the possibility of *C. fetus* infection when there is a compatible clinical syndrome, so that appropriate culture media and incubation conditions are used.

FUNDING

None to declare

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest

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