

## Successful Treatment of *Campylobacter fetus* Hip Joint infection with the association Amoxicillin-Clindamycin

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### Abstract

Bacteria of the genus *Campylobacter* are important causes of enteritis in humans. Even though a number of extraintestinal infections caused by *Campylobacter fetus* have been reported to date, surgical site infections with *C. fetus* are a rare entity and their therapeutic care is not consensual. We present a case of femoral infection with *Campylobacter fetus* successfully treated with the association amoxicillin-clindamycin despite the extended resistance phenotype of the strain.

**Keywords:** *Campylobacter*, *Campylobacter fetus*, Surgical site infection, SSI

### Case Report

Our patient was a 71-year-old woman reporting excessive consumption of alcohol and tobacco; she had undergone a right osteosynthesis using the Proximal Femoral Nail Antirotation System (PFNA) (Depuy Synthes, CA, USA) 18 months before. She was well until 3 days prior to admission, when she presented a non-inflammatory subcutaneous collection next to the surgical scar. She had no local lymphadenopathy, no lymphangitis; she had no systemic or gastrointestinal symptoms. Her initial C-reactive protein level was 21 mg/l (normal < 5 mg/l), and her white cell count was 21 G/l (normal: 2-8 G/l) (80% neutrophils). Radiological investigations showed bone consolidation but a deep abscess was highlighted by the material. Surgical management of the patient consisted of removing the nail and washing off the affected joint. Five intraoperative samples including aspirated purulent material and tissue were collected. Gram staining of cultures at the laboratory was reported as negative. Intravenous empiric antibiotic therapy combining piperacillin-tazobactam (4 g\*3/d), vancomycin (1 g/d) and gentamicin (160 mg/d) was administered. Three days after the surgery, the five samples collected were positive for *Campylobacter fetus*. The Antimicrobial susceptibility to ampicillin, amoxicillin-clavulanate, gentamicin, erythromycin and tetracycline were tested by disk diffusion on MHF medium (BioMérieux, Marcy l'Etoile, France) with the 0.5 McFarland standard, after 48 h of microaerophilic incubation at 37°C, as recommended [1]. Ertapenem and ciprofloxacin were tested using the E-test method on MHF medium (BioMérieux). Then we decided to test other antibiotics to achieve a synergistic combination therapy. We tested piperacillin-tazobactam, cefotaxime, clindamycin and sulfamethoxazole-trimethoprim using the E-test method. Complexity of the case was discussed at a multidisciplinary meeting; an intravenous antibiotic regimen was decided in accordance with the resistance phenotype of the strain, combining amoxicillin (2 g\*4/d) and clindamycin (600 mg\*3/d) for an initial period of 3 weeks, completed with a course of oral amoxicillin associated with clindamycin. Two weeks after initiating the antibiotic therapy, the C-reactive protein level was below 5 mg/l,

but the peripheral leukocyte count remained elevated, unchanged since admission. This white cell count normalized after 3 weeks of treatment, allowing the oral course of antibiotic therapy. The antibiotic regimen was continued for a total of 8 weeks. The patient recovered well and no recurrence was reported 12 months after the end of the treatment.

### Discussion

*Campylobacter* species are Gram-negative bacilli causing acute gastroenteritis with diarrhea, abdominal pain, fever, and nausea. *Campylobacter* infections are endemic worldwide and hyperendemic in developing countries. Production animals and wild animals are the main reservoirs for these organisms. Infections are associated with contaminated animal foodstuffs or water. Infants and young adults are most often infected [2]. Most patients with acute and prolonged infections caused by *C. fetus* present severe and underlying disease including a deficiency in humoral immunity, cirrhosis of the liver, malignancy or diabetes [3]. A hematological dissemination arising from an intestinal focus followed by a secondary localization (aneurysm, arthritis, prosthetic infections) is usually considered [4,5] as consistent with the tropism and properties of *C. fetus*. Our patient did not completely demonstrate the typical features of patients with *Campylobacter* prosthesis infection: she was relatively old but showed no underlying pathology; she did not report recent fever or digestive disorders. The hypothesis of an intraoperative infection by contiguity from the scar in a patient with impaired general condition is preferred.

The certainty diagnosis is done through the microbiology laboratory [6]. The samples were cultured, as is our laboratory routine, on chocolate agar plates and on sheep-blood agar plates incubated in 5% CO<sub>2</sub> and anaerobically at 37°C [7,8]; small discrete translucent colonies were present 72 h later on both the chocolate agar plate and the sheep-blood agar plate incubated in CO<sub>2</sub>. Microscopic examination revealed spiral-shaped bacilli with darting motility, Gram-negative stained, highly suggestive of *Campylobacter* genus. The strain was perfectly identified as *C. fetus* using the MALDI-TOF MS (Matrix-Assisted Laser Desorption-

Ionization time-of-flight Mass Spectrometry) system (Bruker Daltonik®, Bremen, Germany) after an extraction procedure (score of 2.2). This result was confirmed by the use of the *Neisseria-Haemophilus* NH card on a Vitek2® automated system (BioMérieux).

## Conclusion

Concerning antimicrobial therapy of osteoarticular infections with *C. fetus*, there is no established consensus for the treatment of such entities. Despite the absence of randomized clinical trials and the low number of reported cases, a synergistic combination between two antimicrobial agents should be administered [9]. The third-generation cephalosporins (3GC) are frequently administered empirically in the context of deep infections in immunocompromised patients; however, various studies on the susceptibility profiles of *C. fetus* to 3GC have reported significant proportion of resistant strains of the order of 13% in Quebec, more in France [10]. On E-test, the MIC (Minimum Inhibitory Concentration) to cefotaxime of our strain was 4 mg/l, therefore resistant according to the recommendations of the EUCAST, 2015. More generally, the strains are frequently resistant to penicillins by secretion of a  $\beta$ -lactamase inhibited by clavulanic acid but not by the sulbactam or tazobactam; this is why *C. fetus* is resistant to piperacillin-tazobactam, administered immediately after surgical excision in our case. Carbapenems, despite the lack of published studies, would be the drugs of choice for the treatment surgical site infections with *C. Fetus* [11]. The MICs to amoxicillin and ertapenem were 0.5 mg/l and 0.047 mg/l respectively, corresponding to the sensitivity of the strain to these antibiotics. Fluoroquinolones, generally used in first-line treatment in *Campylobacter* enteritis are associated with a high rate of treatment failure when administered as monotherapy in empirical treatment of infection with *C. Fetus* [12]. Furthermore, the literature provides a common resistance of *C. fetus* to fluoroquinolones [13]. Our strain showed a susceptibility to ciprofloxacin; however, given the numerous failures published, we preferred to avoid this molecule. Among the aminoglycosides, gentamicin is most often administered in this type of infection, due to low MICs obtained, the absence of reported resistance and rapid bactericidal effect [10]. Given the toxic effects of aminoglycosides on kidney for prolonged treatments, we did not use gentamicin. Finally, there is very little data on the sensitivity of *C. fetus* to the family of macrolides and lincosamides-synergistines, unlike *C. Jejuni* [14]. Clindamycin, belonging to lincosamides, which is recommended in some cases of bone and joint infections with *Staphylococcus*, appeared interesting taking into account its pharmacokinetics, and pharmacodynamic properties, and tolerance as well. The strain in our case was susceptible to clindamycin. The combination therapy finally administered was amoxicillin (2 g\*4/d) and clindamycin (600 mg\*3/d). This treatment was successful on *C. fetus*.

This successful treatment of *C. fetus* hip joint infection with the association amoxicillin-clindamycin should be useful for further cases.

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