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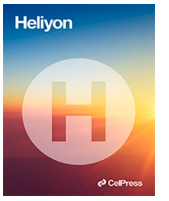

Case report

Campylobacter coli enteritis associated with *Campylobacter fetus* bacteremia, spondylodiscitis, and late CIED-related endocarditis, a case report

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ABSTRACT

Campylobacter sp. is widely considered a leading causative agent of bacterial food-borne gastrointestinal illness. Discitis and endocarditis caused by *Campylobacter* spp. are extremely rare. We describe the case of a 94-year-old man who was admitted for recent lumbar pain, diarrhea, and fever. *C. fetus* and *C. coli* were identified by MALDI-TOF from blood and stool samples respectively. MRI of the spine showed L5–S1 discitis. Patient was treated with 6 weeks of amoxicillin with clinical and microbiological response until cardiac implantable electronic device (CIED) related endocarditis occurred four weeks after the end of the antibiotic treatment. He was treated with another 6 weeks amoxicillin regimen, with a favorable outcome after a 6-month follow-up. Enteric infection with *Campylobacter* spp. in a debilitated patient should raise the possibility of a co-infection with another more invasive species such as *C. fetus*, leading to systemic invasion. In case of *Campylobacter fetus* bacteremia, a search for endocarditis and spondylodiscitis is recommended even in the absence of specific clinical signs.

1. Introduction

Campylobacter spp. are typical enteritis bacteria of which *C. jejuni* and *C. coli* are most often involved [1]. Transmission to humans occurs mainly through the consumption of contaminated food, *Campylobacter* being a common commensal of the gastrointestinal tract of poultry (*C. jejuni*), cattle and sheep (*C. fetus*) or pigs (*C. coli*) [1]. *C. fetus* rarely causes diarrhea but can lead to blood dissemination and invasive infections, more likely in immunocompromised elderly patients. *C. fetus* virulence is attributable to a surface layer protein capsule which impairs complement activation by a lack of C3b binding [1]. Co infection with multiple *Campylobacter* species is rarely described in humans. Here, we report an unusual case of *C. coli* enteritis associated to a *C. fetus* bacteremia complicated by discitis and cardiac implantable electronic device (CIED)-related endocarditis.

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2. Case report

A 94-year-old caucasian man presented to the emergency department for recent falls, lower back pain and acute febrile diarrhea. Comorbidities were relevant for ischemic heart disease and chronic renal failure. His body temperature was 37,2 °C. Abdomen was soft and painless. Systemic examination was within normal limits otherwise. The ECG was in regular sinus rhythm with no obvious conduction disorder. Laboratory analysis revealed white blood cell count 18 G/L, C-reactive protein 109 mg/L. *Campylobacter* spp. was detected in a stool sample using the Seegene Allplex™ GI-Bacteria (I) assay and smooth colonies grew after 48h of incubation at 35 °C under microaerophilic condition on Karmali selective plates. MALDI-TOF (Bruker Daltonics, Wissembourg, France) enabled the identification of *C. coli* with a high confidence score. Antibiotic susceptibility testing performed by disk diffusion method on Mueller-Hinton plates supplemented with blood (Biorad®) found susceptibility to amoxicillin and azithromycin and resistance to ciprofloxacin and tetracycline. Blood culture taken in the emergency room was positive after 96h of incubation in the BacT/ALERT® VIRTUO™ detection system. Subculture of the blood culture revealed the presence of *C. fetus* identified by MALDI-TOF. Antibiogram by disk diffusion was completed by accurate MICs determined by E-test gradient strips. *C. fetus* was susceptible to amoxicillin (MIC 0.75 mg/L),

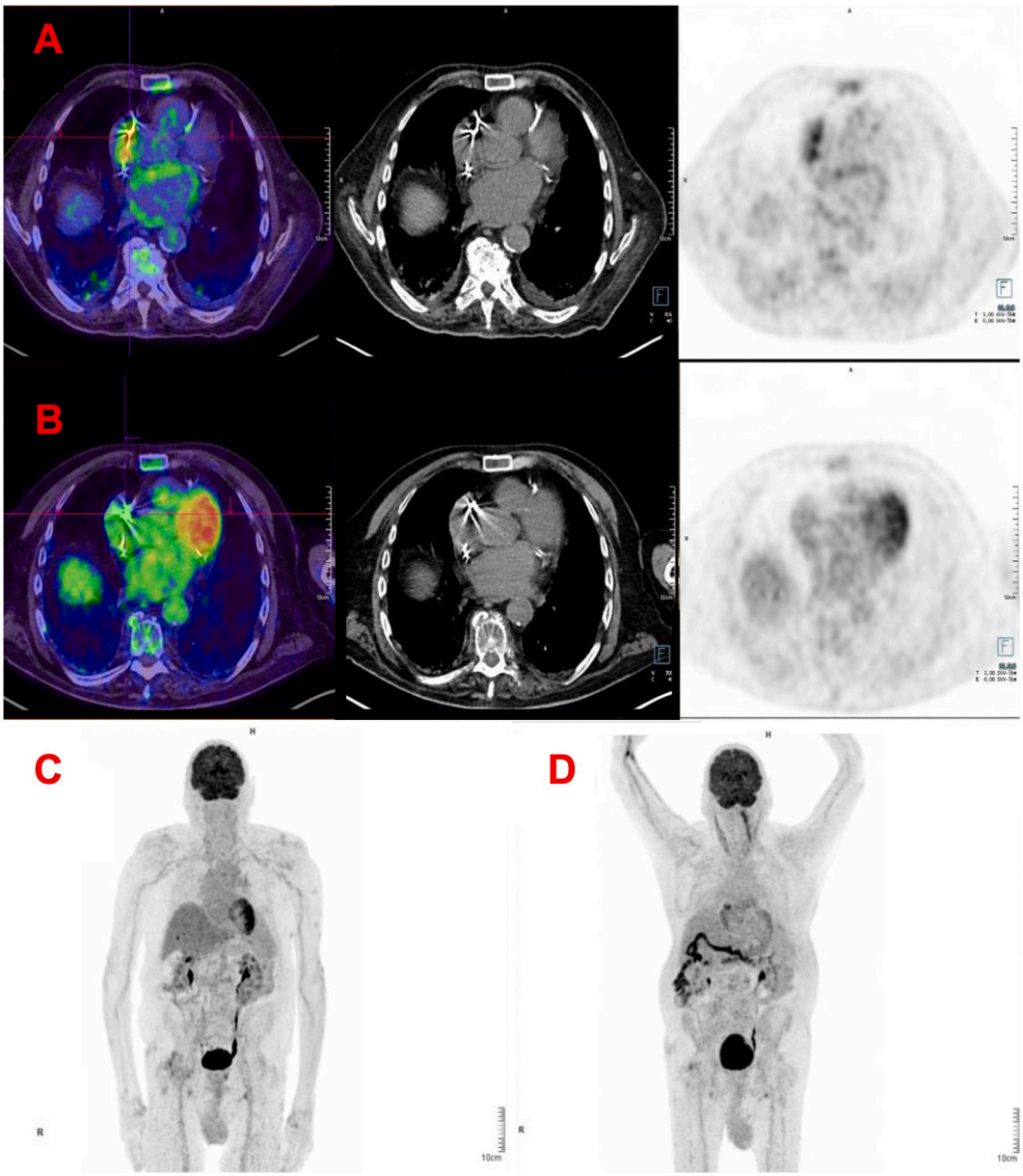

Fig. 1. 18-FDG TEP scanner hypermetabolism of the right atrial portion of the pacemaker lead (A and C). Complete regression of the hypermetabolism after 6 weeks of antibiotics (B and D).

azithromycin (MIC 0.38 mg/L), ciprofloxacin (MIC 0.5 mg/L), ertapenem (MIC 0.25 mg/L) and tetracycline.

A spinal magnetic resonance imaging revealed an hypersignal in L2-L3 disc space, and L3-L4 endplates with major infiltration of the anterior paravertebral soft tissues. A18F-FDG PET/CT confirmed lumbar disc and abscess hypermetabolism with no other abnormalities. *Trans*-thoracic echography showed no vegetation. *Trans*-esophageal echocardiography was not performed because of patient age and comorbidities.

Intravenous amoxicillin was initiated (100 mg/kg/d) for 8 weeks.

Lumbar pain disappeared as well as the inflammatory syndrome. Three blood cultures taken one week after the end of the antibiotic treatment were negative. The patient was considered cured. Two weeks later, the onset of symptomatic high-grade conductive disorders required the implantation of a right atrio-ventricular CIED. Fourteen days later, the patient developed fever up to 39 °C with chills. Skin near the insertion of the CIED was mildly inflammatory and indurated. Three days later fever was still present, and incision becomes dehiscent. CT body scanner and transthoracic echocardiography were within normal limits. Two blood cultures taken 2 days apart were positive for *C. fetus*. The antibiotic susceptibility was identical to the first *C. fetus* isolate. 18F-FDG PET/CT scan found an intense heterogeneous uptake of tracer in the right atrial portion of the CIED lead, but not in the pocket (Fig. 1). There was no spinal fixation. CIED was not removed due to the age of the patient. Intravenous amoxicillin 100 mg/kg/day was started for 6 weeks. Fever and inflammatory signs disappeared. The patient did not experience any side effects. Three months after the end of amoxicillin, 18F-FDG PET/CT scan found complete metabolic regression of the right atrial focus on contact with the CIED lead and absence of other infectious foci (Fig. 1). Six months after discharge the patient is doing well without any infection or relapse.

3. Discussion

In one study conducted on 358 *Campylobacter* spp. positive poultry and meat samples obtained from retail in UK, more than one *Campylobacter* species was identified in 10.3 % of the samples, and multiple subtypes of the same species (usually *C. jejuni*) in 18.2 % [2]. Richardson et al. revealed that 7.5 % of human fecal samples from patients with acute enteritis contained multiple *C. jejuni* strains but not different species [3]. Rocca et al. reported a case of a patient with *C. jejuni* gastroenteritis and *C. fetus* meningitis [4].

C. fetus is a non-thermophilic species whose prevalence in human feces is probably underestimated by microbiology laboratories that perform culture at 42 °C [5]. In our case, *C. fetus* colonies could not be obtained from feces even though the culture was performed at 35 °C.

One hypothesis is that *C. coli* was predominant in the patient's feces and since we cannot differentiate *Campylobacter* species on Karmali plates, minority colonies of *C. fetus* went unnoticed. To the best of our knowledge, this is the first report of a *C. fetus* and *C. coli* coinfection in human.

A recent retrospective study of 592 *Campylobacter* bloodstream infections in France reported *C. fetus in* 42.6 % of cases [6]. Through the interaction with specific endothelial receptors, *C. fetus* have an affinity for the endothelium with ability to form biofilm [7]. Tinevez et al. reported endocarditis in 11 % of the 99 patients with *C. fetus* bacteremia. Among them, 69 % were on prosthetic valves or material devices. Relapse (defined by $>$ 1 new positive blood culture with *Campylobacter* spp. after clinical sign resolution and apyrexia or negative control blood culture) occurred in 8 % of cases and was associated with delayed initiation of an efficient antimicrobial therapy, diabetes, and coexistence of an osteoarticular location [8]. In our patient, relapse seems indeed to be the most likely hypothesis to explain the secondary CIED infection, although we cannot completely rule out reinfection as strain sequencing could not have been performed. According to the 2017 HRS expert consensus statement on cardiovascular implantable electronic device, our patient presented with superficial CIED site infection and CIED endocarditis [9]. According to Dukes 2023 revised criteria, the diagnosis of early certain CIED endocarditis was retained on abnormal FDG uptake on CIED leads, fever and two positive blood cultures with a microorganism that rarely cause IE. *Campylobacter* CIED infections are extremely rare. Five other cases were reported in the literature [10–14]. *C. fetus* was involved in 83 % of the cases including ours. In 50 % of cases, the infection was a simple pocket infection. Time from PM implantation to symptoms ranged from 1 week to 17 years. Combined lead extraction and appropriate antibiotic therapy is recommended in case of CIED infections [9]. Acquired resistance to fluoroquinolones is reported in 60 % of strains, *C. coli* harbors macrolides resistance in 24 % of cases and *C. jejuni* and *C. coli* are resistant to cephalosporins, with a 10 RR of death if empirically prescribed [15]. Amoxicillin-clavulanate, gentamicin and imipenem appear to be the best empirical therapies. In our case, patient age and fragility determined us to attempt cure with medical treatment alone without lead extraction and close clinical follow-up.

4. Conclusion

Although rare, *Campylobacter* spp. spondylodiscitis and endocarditis should be considered in debilitated patients with systemic infection signs associated or following *Campylobacter* enteritis. Finally, this case highlights the possibility of co-infections with different *Campylobacter* species and the risk of systemic infections.

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Consent for publication

Informed consent was obtained from the patient for the publication of all images, clinical data and other data included in the main manuscript.

Ethical approval

Not applicable.

Data availability statement

No data was used for the research described in this article and deposited into a publicly available repository.

Additional information

No additional information is available for this paper.

CRediT authorship contribution statement

Sébastien Gaultier: Writing – review & editing, Writing – original draft, Conceptualization. **Agnès B. Jousset:** Writing – review & editing, Writing – original draft. **Mary Soudani:** Validation. **Alix Durroux:** Validation. **Liliana Mihaila:** Validation. **Marie Neiss:** Validation. **Rocco Collarino:** Writing – review & editing, Validation. **Stéphane Jauréguiberry:** Validation. **Lelia Escaut:** Writing – review & editing, Writing – original draft, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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