



Review

Cervical osteomyelitis potentially caused by *Campylobacter fetus*Bassem Awada^{a,1}, Joya-Rita Hindy^{a,1}, Maria Chalfoun^b, Souha S. Kanj^{a,*}^a Division of Infectious Diseases, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon^b Medical School, American University of Beirut, Beirut, Lebanon

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ABSTRACT

Campylobacter fetus is a rare pathogen in humans. It mainly causes invasive infections in immunosuppressed patients. Herein, we report the first case of cervical vertebral osteomyelitis in a previously healthy man with a history of daily alcohol consumption. Treatment was given for six weeks with excellent clinical recovery and normalization of laboratory markers.

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Introduction

Campylobacter fetus is a Gram-negative micro-aerophilic spiral shaped bacterium which grows in a temperature between 25°C and 37 °C. It is a catalase, oxidase and nitrate positive bacteria. It was formerly known as *Vibrio fetus* and was first recognized in a 1909 English study about zoonotic abortion in domestic animals [1]. Ward et al. reported the first case of *Vibrio fetus* infection in a laboratory worker who presented with a facial pustule [2]. Véron and Chatelain introduced it as a new genus naming it *Campylobacter* [3]. It comprises three subspecies: *C. fetus subspecies fetus*, *C. fetus subspecies venerealis* and *C. fetus subspecies testudinum*. *C. fetus subspecies fetus* is the main subspecies that infects humans. It is mainly found as a colonizer in the gastrointestinal (GI) tract in the cattle and sheep which act as a reservoir. *C. fetus* sp. *venerealis* is associ-

ated with abortion and infertility in ruminants [4]. *C. fetus* is a rare human pathogen associated mainly with bacteraemia and a variety of other systemic complications. In contrast to *Campylobacter jejuni* and *Campylobacter coli*, it rarely causes gastroenteritis. Its virulence is related to the inoculum load, the level of immunosuppression and the cell structure characteristics.

Herein, we report a case of a healthy adult man with no underlying medical problems presenting with cervical vertebral osteomyelitis. Blood cultures grew *C. fetus* sensitive to all tested antibiotics. He was treated initially with a combination of ceftriaxone and ciprofloxacin then ciprofloxacin alone for 6 weeks as per the IDSA guidelines [5]. He had a good clinical response and his inflammatory markers normalized.

Case report

A 70-year-old man with a history of hypertension presented to the emergency department for a severe lower neck pain of two days duration refractory to pain killers. His history goes back to three days prior to his presentation when he started complaining of

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Fig. 1. Sagittal cervical MRI T2-weighted image showing osteomyelitis with phlegmon formation in prevertebral and epidural space at C5–C6.

fever, chills, and night sweats for two days after which he developed upper back and lower neck pain. He stated that two weeks prior to his presentation, he ate raw beef liver and had transient diarrhoea lasting for one day. However, no stool cultures were taken.

His physical examination showed tenderness at the level of the vertebra C5–C6. His laboratory results showed elevated white blood cells $12,900/\text{mm}^3$ with 72% neutrophils and 16% lymphocytes. His CRP was 128 mg/L and his ESR 78 mm/h. A cervical MRI with gadolinium showed cervical vertebral osteomyelitis at C5–C6 with phlegmon formation in the prevertebral and epidural space (Fig. 1). *Brucella* serology, and PPD were negative.

He underwent a computed tomography (CT)-guided biopsy by an anterior approach. Only a small specimen was obtained as it was a challenging procedure. The bone cultures and stains as well as TB PCR, and 16s ribosomal RNA on the bone tissue were negative. He was initially started on empirical antibiotic therapy with cefepime and vancomycin intravenously (IV). Two sets of blood cultures grew *C. fetus* after 45 and 52 h detected using Matrix-Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF).

The isolate was susceptible to ciprofloxacin, erythromycin, ceftriaxone and azithromycin with diffusion disk inhibition (DDI) zone 40 mm, 40 mm, 35 mm and 50 mm, respectively. He was, therefore, shifted to ceftriaxone 2 mg IV every 12 h and ciprofloxacin 400 mg every 8 h. His CRP trended down from 128 mg/L to 17 mg/L after 8 days on IV therapy. The *C. fetus* bacteraemia warranted the search for an underlying haematological malignancy and liver cirrhosis, especially that the patient admitted to daily alcohol intake for the past 20 years. A liver fibroscan, serum and urine protein electrophoresis, and HbA1c level were done, and the results were all unremarkable. The patient was discharged on oral ciprofloxacin 750 mg per os (PO) twice daily and he completed a 6-week course. He was also discharged on tramadol and solpadeine to control the cervical pain. After 6 weeks of therapy, his symptoms completely subsided, and he did not need pain killers anymore. His CRP was back to normal with a level of 1.3 mg/L.

Discussion

C. fetus is rarely reported as a human pathogen. Unlike other *Campylobacter* sp., it is mainly associated with systemic campy-

lobacteriosis rather than gastroenteritis. The risk factors for invasive campylobacteriosis are older age, liver disease, solid organ transplant, haematological malignancy, infection with human deficiency virus, especially before the availability of highly active antiretroviral therapy, tuberculosis, renal failure, systemic lupus erythematosus, agammaglobulinemia [6–8] and chronic alcoholism [9,10]. It is rarely reported to cause systemic disease in immunocompetent patients. The incidence of *C. fetus* bacteraemia is 0.08 per 100,000 admissions [11].

Wagenaar et al. [6] reported that it is mainly transmitted to humans through direct contact with animals (cattle) and faecal-oral route after eating undercooked or raw meat. It is also possible to be infected after drinking unpasteurized milk [12]. Rennie et al. and Morooko et al. reported two cases of possible human to human transmission in neonatal intensive care unit [13,14]. Xavier et al. reported a cluster of *C. fetus* infections in men having sex with men (MSM) with no clear food source. It was suggested that sexual transmission, especially in MSM and those with high risk sexual activity, could occur and lead to *C. fetus* transmission. This mode of transmission is similar to the previously reported cases of sexually transmitted *Salmonella typhi* and *Shigella* infections [15]. In our case, the patient had recent intake of raw meat (liver) after which he had diarrhoea and then fever. However, no stool cultures were taken to document a gastrointestinal source.

Invasive *C. fetus* has been reported to cause relapsing bacteraemia [16], endocarditis [17], pericarditis [18], septic thrombophlebitis [9], meningitis [19], septic arthritis [10], vertebral osteomyelitis, cellulitis [20], pneumonia with empyema [21], infected aneurysm [22] and a thyroid abscess [23]. There are only 12 reported cases of *C. fetus* vertebral osteomyelitis (Table 1). Three of the cases were previously healthy whereas others had underlying comorbidities such as diabetes mellitus type 2, hypertension, chronic alcoholism and asthma. The majority had a full recovery. Our patient is the first case involving the cervical vertebrae as all the other reported cases involved the lumbar vertebrae. In the case we reported, the organism did not grow from the CT guided aspiration. This was likely due to a sampling error as a very tiny piece was sent to the microbiology laboratory because of technical difficulties. The absence of other organisms growing from the blood and from the aspirate, the sequence of events with the preceding diarrhoea, and the rapid response to therapy suggest that this was the cause of the vertebral osteomyelitis. This highlights the importance of always requesting blood cultures when managing patients with vertebral osteomyelitis [5].

Until today, there are no clear guidelines for the treatment of invasive campylobacter diseases. Several reports noted fatal outcome with the usage of 3rd generation cephalosporins as an empiric monotherapy for patients with *Campylobacter* bacteraemia. This was attributed to the antimicrobial resistance caused by beta-lactamase production. However, Pacanowski et al. noted in a retrospective study that *C. fetus* was different than the other species since it was susceptible to cephalosporin and penicillin [24]. In addition, Trembley et al. reported a cluster of 59 *C. fetus* isolates being susceptible to penicillin, gentamicin and imipenem and none of them were beta lactamases-producers [25]. Many experts advocate the use of gentamicin as an empiric therapy for invasive campylobacteriosis because of low MIC and rarely reported gentamicin resistance. Carbapenems including imipenem is a good empiric choice as it is well reported to be sensitive with good favourable outcomes [24]. Fluoroquinolones should not be used empirically as monotherapy in invasive campylobacteriosis due to the increase of reported resistance worldwide [24]. However, it is a good choice after susceptibility results are out as it has a good tissue penetration with high oral bioavailability. Duration of treatment of *C. fetus* vertebral osteomyelitis should be guided by clinical response and normalization of the inflammatory markers.

Table 1
Published case reports of *Campylobacter fetus* vertebral osteomyelitis.

Date – First Author	Age – sex	Comorbidities	Vertebral osteomyelitis level	Positive culture	Antibiotic treatment	Outcome
2018 – Olaiya D et al. [26]	72 – F	Previous <i>S. aureus</i> endocarditis s/p AVR and CABG	S5/L1	Tissue culture with identification through MALDI-TOF	Amoxicillin 2 mg IV every 4 h plus oral doxycycline 100 mg twice daily for 2 weeks then shifted to amoxicillin 2 mg every 8 h PO for 8 weeks	Recovered
1985 – Francioli P et al. [20]	78 – M	COPD Asthma DM type 1 Uveitis Chronic alcoholic consumption	Lumbar	Blood and Tissue culture	A failed course of erythromycin 1 mg IV every 6 h for 21 days then shifted to IV ampicillin 2 g 4 times a day for 6 weeks then de-escalated to oral amoxicillin 750 mg 4 times a day for 24 weeks Doxycycline (dose N/A) and erythromycin (dose N/A) for 3 months	Recovered
1991 – Mathieu E et al. [27]	36 – F	Previously healthy	L5/S1	Bone culture	Meropenem 2 mg IV every 8 h for 26 h then de-escalated to ampicillin 12 g per day completed for 85 days	Recovered
1992 – Bachmeyer C et al. [29]	62 – M	N/A	N/A	Not noted	Not noted	Death
1999 – Yamashita K et al. [30]	66 – M	L4-L5 disc herniation s/p L4 hemi-laminectomy BPH s/p TURP	L5/S1	Epidural fluid culture	Fosfomycin 2 mg twice daily IV for two weeks followed by clindamycin 0.6 g twice daily for two weeks then started on alternating doxycycline 100 mg per day for two weeks and erythromycin 800 mg per day for two weeks for a period of 5 months	Recovered
2002 – Ozeki T et al. [31]	49 – M	N/A	L4/L5	Blood and CSF culture	N/A	Recovered
2010 – Chaillon A et al. [32]	91 – F	N/A	L2/L3 and L3/L4	Bone culture with positive 16 S ribosome	Started empirically on ofloxacin 400 mg twice daily and rifampin 100 mg twice daily then shifted to amoxicillin (dose N/A) for 5 weeks	Recovered
2012 – Tanaka A et al. [33]	37 – M	Previously healthy	L2/L3 and L3/L4	Bone and blood culture	Cefotaxime, ciprofloxacin, and minocycline (doses N/A) IV for 13 weeks then shifted to one or two drugs of the following antibiotics: ciprofloxacin, minocycline and erythromycin (doses N/A) for 11 months	Recovered
2016 – Choi HS et al. [34]	81 – M	ESRD	L3/L4	Blood cultures and 16S rRNA sequencing	Azithromycin (dose N/A) PO for 6 weeks	Recovered
1. 2018 – Laenens D et al. [35]	53 – M	HTN DM type 2 HIV on HAART	L4/L5	Bone culture	Ceftriaxone 2 mg IV daily then switched to ciprofloxacin 500 mg twice daily for 6 weeks	Recovered

Abbreviations: AVR: aortic valve replacement, BPH: benign prostatic hyperplasia, CABG: coronary aortic bypass grafting, COPD: chronic obstructive pulmonary disease, CSF: cerebrospinal fluid, DM: diabetes mellitus, ESRD: end-stage renal disease, F: female, GI: gastrointestinal, HAART: highly active antiretroviral therapy, HIV: human immunodeficiency virus, HTN: hypertension, IV: intravenous, MALDI-TOF: Matrix-Assisted Laser Desorption/Ionization-Time Of Flight, M: male, MRI: magnetic resonance imaging, N/A: not available, PO: per os, rRNA: ribosomal ribonucleic acid, TURP: transurethral resection of prostate.

Conclusion

This reported case highlights the importance of *C. fetus* as a possible pathogen causing vertebral osteomyelitis, even in otherwise immunocompetent patients. It also emphasizes on the importance of requesting blood cultures in such cases as the CT guided aspirate can be non-diagnostic because of sampling errors.

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Competing interests

None declared.

Ethical approval

Not required.

References

- [1] Reay DJM. Baron 11th, 1839-. Report of the Departmental Committee appointed by the Board of Agriculture and Fisheries to inquire into and report upon the subject of agricultural education in England and Wales. Printed for H.M.S.O., by McCorquodale & Co., Ltd.; 1908.

- [2] Ward BQ. The apparent involvement of *Vibrio fetus* in an infection of man. *J Bacteriol* 1948;55:113–4.
- [3] Véron M, Chatelain R. Taxonomic study of the genus *Campylobacter* Sebald and Véron and designation of the neotype strain for the type species, *Campylobacter fetus* (Smith and Taylor) Sebald and Véron. *Int J Syst Evol Microbiol* 1973;23:122–34, <http://dx.doi.org/10.1099/00207713-23-2-122>.
- [4] Mshelia GD, Amin JD, Woldehiwet Z, Murray RD, Egwu GO. Epidemiology of bovine venereal campylobacteriosis: geographic distribution and recent advances in molecular diagnostic techniques. *Reprod Domest Anim Zucht* 2010;45:e221–230, <http://dx.doi.org/10.1111/j.1439-0531.2009.01546.x>.
- [5] Barbari EF, Kanj SS, Kowalski TJ, Darouiche RO, Widmer AF, Schmitt SK, et al. 2015 Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. *Clin Infect Dis* 2015;61:e26–46, <http://dx.doi.org/10.1093/cid/civ482>.
- [6] Wagenaar JA, van Bergen MAP, Blaser MJ, Tauxe RV, Newell DG, van Putten JPM. *Campylobacter fetus* infections in humans: exposure and disease. *Clin Infect Dis* 2014;58:1579–86, <http://dx.doi.org/10.1093/cid/ciu085>.
- [7] Fernández-Cruz A, Muñoz P, Mohedano R, Valerio M, Marín M, Alcalá L, et al. *Campylobacter* bacteremia: clinical characteristics, incidence, and outcome over 23 years. *Medicine (Baltimore)* 2010;89:319–30, <http://dx.doi.org/10.1097/MD.0b013e3181f2638d>.
- [8] Ledina D, Ivić I, Karanović J, Karanović N, Kuzmičić N, Ledina D, et al. *Campylobacter fetus* infection presenting with bacteremia and cellulitis in a 72-year-old man with an implanted pacemaker: a case report. *J Med Case Rep* 2012;6:414, <http://dx.doi.org/10.1186/1752-1947-6-414>.
- [9] Vesely D, MacIntyre S, Ratzan KR. Bilateral deep brachial vein thrombophlebitis due to *vibrio fetus*. *Arch Intern Med* 1975;135:994–5.
- [10] Kilo C, Hagemann PO, Marzi J. Septic arthritis and bacteremia due to *vibrio fetus*: report of an unusual case and review of the literature. *Am J Med* 1965;38:962–71, [http://dx.doi.org/10.1016/0002-9343\(65\)90017-3](http://dx.doi.org/10.1016/0002-9343(65)90017-3).
- [11] Gazaigne L, Legrand P, Renaud B, Bourra B, Taillandier E, Brun-Buisson C, et al. *Campylobacter fetus* bloodstream infection: risk factors and clinical features. *Eur J Clin Microbiol Infect Dis* 2008;27:185–9, <http://dx.doi.org/10.1007/s10096-007-0415-0>.
- [12] Klein BS, Vergeront JM, Blaser MJ, Edmonds P, Brenner DJ, Janssen D, et al. *Campylobacter* infection associated with raw milk. An outbreak of gastroenteritis due to *Campylobacter jejuni* and thermotolerant *Campylobacter fetus* subsp. *fetus*. *JAMA* 1986;255:361–4, <http://dx.doi.org/10.1001/jama.255.3.361>.
- [13] Morooka T, Umeda A, Fujita M, Matano H, Fujimoto S, Yukitake K, et al. Epidemiologic application of pulsed-field gel electrophoresis to an outbreak of *Campylobacter fetus* meningitis in a neonatal intensive care unit. *Scand J Infect Dis* 1996;28:269–70, <http://dx.doi.org/10.3109/00365549609027170>.
- [14] Rennie RP, Strong D, Taylor DE, Salama SM, Davidson C, Tabor H. *Campylobacter fetus* diarrhea in a Hutterite colony: epidemiological observations and typing of the causative organism. *J Clin Microbiol* 1994;32:721–4, <http://dx.doi.org/10.1128/JCM.32.3.721-724.1994>.
- [15] Marchand-Sénécal X, Bekal S, Pilon PA, Sylvestre J-L, Gaudreau C. *Campylobacter fetus* cluster among men who have sex with men, Montreal, Quebec, Canada, 2014–2016. *Clin Infect Dis* 2017;65:1751–3, <http://dx.doi.org/10.1093/cid/cix610>.
- [16] Righter J, Wells WA, Hart GD, McNeely DJ. Relapsing septicemia caused by *Campylobacter fetus* subsp. *fetus*. *Can Med Assoc J* 1983;128:686–9.
- [17] Loeb H, Bettag JL, Yung NK, King S, Bronsky D. *Vibrio fetus* endocarditis: report of 2 cases. *Am Heart J* 1966;71:381–6, [http://dx.doi.org/10.1016/0002-8703\(66\)90479-0](http://dx.doi.org/10.1016/0002-8703(66)90479-0).
- [18] Kanj SS, Araj GF, Taher A, Reller LB. *Campylobacter fetus* pericarditis in a patient with beta-thalassemia: case report and review of the literature. *Clin Microbiol Infect* 2001;7:510–3, <http://dx.doi.org/10.1046/j.1198-743x.2001.00300.x>.
- [19] Gubina M, Zajc-Satler J, Mehle J, Drinovec B, Pikelj F, Radsel-Medvescek A, et al. Septicaemia and meningitis with *Campylobacter fetus* subspecies intestinalis. *Infection* 1976;4:115–8, <http://dx.doi.org/10.1007/BF01638729>.
- [20] Francioli P, Herzstein J, Grob JP, Vallotton JJ, Mombelli G, Glauser MP. *Campylobacter fetus* subspecies *fetus* bacteremia. *Arch Intern Med* 1985;145:289–92.
- [21] Targan SR, Chow AW, Guze LB. *Campylobacter fetus* associated with pulmonary abscess and empyema. *Chest* 1977;71:105–8, <http://dx.doi.org/10.1378/chest.71.1.105>.
- [22] Lozano P, Rimbau EM, Martínez S, Ribas MA, Gómez FT. *Campylobacter fetus* infection of a previously excluded popliteal aneurysm. *Eur J Vasc Endovasc Surg* 1999;18:86–8, <http://dx.doi.org/10.1053/ejvs.1998.0755>.
- [23] El Beayni NK, Araj GF, Beydoun S, Kozah M, Tabbarah Z. *Campylobacter fetus* thyroid gland abscess in a young immunocompetent woman. *IDCases* 2020;19:e00681, <http://dx.doi.org/10.1016/j.idcr.2019.e00681>.
- [24] Pacanowski J, Lalonde V, Lacombe K, Boudraa C, Lesprit P, Legrand P, et al. *Campylobacter* bacteremia: clinical features and factors associated with fatal outcome. *Clin Infect Dis* 2008;47:790–6, <http://dx.doi.org/10.1086/591530>.
- [25] Tremblay C, Gaudreau C. Antimicrobial susceptibility testing of 59 strains of *Campylobacter fetus* subsp. *fetus*. *Antimicrob Agents Chemother* 1998;42:1847–9, <http://dx.doi.org/10.1128/AAC.42.7.1847>.
- [26] Olaiya D, Fok R, Chakrabarti P, Sharma H, Greig J. *Campylobacter fetus* spondylodiscitis: a case report and review of the literature. *IDCases* 2018;14:e00468, <http://dx.doi.org/10.1016/j.idcr.2018.e00468>.
- [27] Mathieu E, Koeger AC, Rozenberg S, Bourgeois P. *Campylobacter* spondylodiscitis and deficiency of cellular immunity. *J Rheumatol* 1991;18:1929–31.
- [28] Ikeda K, Manabe Y, Fujiwara S, Omote Y, Narai H, Abe K. *Campylobacter fetus* meningitis and pyogenic spondylodiscitis in a healthy young woman. *Case Rep Neurol* 2019;11:299–303, <http://dx.doi.org/10.1159/000503814>.
- [29] Bachmeyer C, Grateau G, Sereni D, Cremer GA. [*Campylobacter fetus* spondylodiscitis]. *Rev Rhum Mal Osteoartic* 1992;59:77–9.
- [30] Yamashita K, Aoki Y, Hiroshima K. Pyogenic vertebral osteomyelitis caused by *Campylobacter fetus* subspecies *fetus*. A case report. *Spine* 1999;24:582–4, <http://dx.doi.org/10.1097/00007632-199903150-00018>.
- [31] Ozeki T, Nokura K, Koga H, Yamamoto H. [A case of meningoencephalitis and spondylodiscitis caused by *Campylobacter fetus* subsp. *fetus* infection]. *Rinsho Shinkeigaku* 2002;42:38–41.
- [32] Chaillon A, Baty G, Lauvin MA, Besnier JM, Goudeau A, Lanotte P. *Campylobacter fetus* subspecies *fetus* spondylodiscitis. *J Med Microbiol* 2010;59:1505–8, <http://dx.doi.org/10.1099/jmm.0.023382-0>.
- [33] Tanaka A, Takahashi J, Hirabayashi H, Ogihara N, Mukaiyama K, Shimizu M, et al. A case of pyogenic spondylodiscitis caused by *Campylobacter fetus* for which early diagnosis by magnetic resonance imaging was difficult. *Asian Spine J* 2012;6:274–8, <http://dx.doi.org/10.4184/asj.2012.6.4.274>.
- [34] Choi HS, Shin SU, Bae EH, Ma SK, Kim SW. Infectious spondylitis in a patient with chronic kidney disease: identification of *Campylobacter fetus* subsp. *testudinum* by 16S ribosomal RNA sequencing. *Jpn J Infect Dis* 2016;69:517–9, <http://dx.doi.org/10.7883/yoken.JJID.2015.461>.
- [35] Laenens D, Plazier M, van der Hilst JCH, Messiaen P. *Campylobacter fetus* spondylodiscitis in a patient with HIV infection and restored CD4 count. *BMJ Case Rep* 2018;2018, <http://dx.doi.org/10.1136/bcr-2018-225272>.