Involvement of *Campylobacter jejuni* in septic arthritis: a case report

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**Introduction:** *Campylobacter jejuni* is the most common cause of human bacterial enteritis in developed countries and is a rare cause of extra-intestinal infections.

**Case presentation:** In this paper, we report a case of septic arthritis related to *C. jejuni* infection in an immunocompetent 53-year-old man with prosthetic devices who presented to us with enteritis. Following treatment with ciprofloxacin, loperamide hydrochloride and acetaminophen, he developed articular pain with painful swelling and redness in the region of the outer side of the left thigh. A diagnosis of a monoarticular non-migratory manifestation was postulated and vancomycin was started but was stopped 1 day later due to the development of skin erythema, and levofloxacin, teicoplanin and rifampicin treatment was started. An X-ray of the hip excluded dislocation of the prosthesis, while ultrasound showed an abscess in the soft tissue, confirmed by a triphasic bone scan. Aspiration of the joint fluid revealed the presence of moving, curved, Gram-negative bacilli 72 h after incubation, while growth on agar plates and tryptose broth remained negative after 5 days. Reactions for *Campylobacter* diagnosis were positive, and the micro-organism was identified as *C. jejuni*. Antimicrobial susceptibility tests revealed a sensitivity for ampicillin, ciprofloxacin, imipenem, tetracycline, erythromycin and gentamicin. Antimicrobial treatment was continued for a further 10 days with complete resolution of symptoms.

**Conclusion:** Clinicians should consider *Campylobacter* in infections without a history of a travel in the tropics. Antibiotic treatment must be carefully evaluated to take into account the local resistance to avoid clinical failure.

**Keywords:** *Campylobacter jejuni*; levofloxacin; rifampicin; septic arthritis; teicoplanin.

**Introduction**

*Campylobacter jejuni* is the most common cause of human bacterial enteritis in developed countries. The majority of cases of *C. jejuni* infections are self-limiting and do not require antibiotic treatment (Garg *et al.*, 2008). More rarely they cause extra-intestinal infections as a result of haematogenous diffusion (Yao *et al.*, 1993). *Campylobacter* haematogenous diffusion and its complications are most common in immunocompromised patients (Butzler, 2004). Occasionally, *Campylobacter* spp. may infect soft tissues resulting in cellulitis, septic arthritis, fasciitis, thrombophlebitis, myositis, erysipelas and erythema gangrenosum, and, when associated with disseminated intravascular coagulation, purpura fulminans (Cone *et al.*, 2003) and reactive arthritis (ReA).

ReA is a non-purulent joint inflammation. Symptoms typically start within 1–4 weeks of the initial infection with articular, tendon, mucosal, cutaneous and occasionally cardiac manifestation or systemic features (fever, malaise and weight loss) (Carter and Hudson, 2009).

Here, we report a case of septic arthritis related to *C. jejuni* infection in an immunocompetent patient.

**Abbreviations:** ReA, reactive arthritis; VAS, visual analogue scale.
Case report

A 53-year-old man was admitted to the Emergency Department of our hospital in Milan with fever (39.8°C), chills, watery diarrhoea and a malaise of the joints. His history revealed that a few days before the development of symptoms, he had returned from a trip in Sardinia, but he denied the consumption of raw or undercooked foods. No other clinical conditions or contact with household animals or farm animals were indicated. However, in September 2007, he underwent surgery to implant prosthesis for a bilateral coxarthrosis.

At admission, clinical evaluation revealed the presence of nausea, fever and abdominal pain [visual analogue scale (VAS); score 4], while laboratory blood tests were within normal ranges, with a C-reactive protein (CRP) level of 2.67 mg dl⁻¹ and white blood cell (WBC) count of 6.33 × 10⁹ l⁻¹. A diagnosis of enteritis was made and the patient was discharged on ciprofloxacin (500 mg every 12 h for 10 days), loperamide hydrochloride (4 mg as necessary) and acetaminophen (500 mg as necessary).

Two days later, the patient was readmitted for the persistence of symptoms and the development of articular pain (VAS: 6), and a new laboratory blood test revealed an increase in both CRP (37.27 mg dl⁻¹) and a new laboratory blood test revealed an increase in both CRP (37.27 mg dl⁻¹) and a new laboratory blood test revealed an increase in both CRP (37.27 mg dl⁻¹) and a new laboratory blood test revealed an increase in both CRP (37.27 mg dl⁻¹). Therefore, a diagnosis of ReA was postulated without any change in drug treatment. About 3 days later, his gastrointestinal symptoms improved but signs of inflammation appeared with painful swelling (VAS: 8) and redness in the region of the outer side of the left thigh. A new clinical evaluation excluded the ReA and a new diagnosis of a monoarticular non-migratory manifestation was postulated.

An X-ray of the hip excluded dislocation of the prosthesis, while an ultrasound scan showed an abscess in the soft tissue, confirmed by a triphasic bone scan.

The aspiration of the joint fluid revealed a purulent fluid (WBC count 200 × 10⁹ l⁻¹ with 96 % neutrophils), which was sent for Gram staining and culture evaluation to our laboratory. Ciprofloxacin treatment was interrupted and vancomycin (1 g every 12 h) was started. One day later, the patient developed a diffuse skin erythema, probably related to the vancomycin (Naranjo score: 6), which was therefore stopped, and empirical treatment with levo-floxacin [500 mg day⁻¹, intravenously (i.v.)], teicoplanin (200 mg every 8 h, i.v.) and rifampicin (600 mg day⁻¹, per os) was started.

For microbiological evaluation, joint fluid was inoculated onto chocolate agar, 5 % sheep blood agar, mannitol salt agar, MacConkey agar and Sabouraud agar plates, and inoculated in tryptose broth and sheep blood culture broth (Bactec Plus; BD), with the addition of FOS (nicotinamide adenine dinucleotide, haemin and bovine serum; Fastidious Organism Supplement, BD). An anaerobic bottle was positive for moving, curved, Gram-negative bacilli 72 h after incubation, while the agar plates and tryptose broth remained negative 5 days later.

The anaerobic bottle was subcultured onto 5 % sheep agar, MacConkey agar and chocolate agar, and the plates were incubated in an anaerobic atmosphere at 42 and 25–35°C in a microaerophilic environment (5 % O₂). Reactions for catalase, oxidase, nitrate reduction and rapid latex agglutination (Microgen) were positive, and a zone of growth inhibition was present around the nalidixic acid disk but not around the cephalotin disk. Therefore, a diagnosis of Campylobacter infection was made, and the positivity of the hippurate hydrolysis reaction prompted the identification of C. jejuni. Antimicrobial susceptibility tests revealed a sensitivity for ampicillin, ciprofloxacin, imipenem, tetracycline, erythromycin and gentamicin.

Antimicrobial treatment was continued for a further 10 days with complete improvement of symptoms and the patient was transferred to the department of orthopaedics for prosthesis removal.

Discussion

Previous studies have shown that bacteraemia is most common during C. fetus infection compared with C. jejuni infection, with incidences of 63 and 0.4 %, respectively (Peterson, 1994). Moreover, bacteraemia is common in both immunocompromised (e.g. hypogammaglobulinaemia, corticosteroid therapy, human immunodeficiency virus infections, hepatitis virus infections and malignant neoplasms) and elderly patients.

To date, there have been 16 reported cases of septic arthritis caused by C. jejuni, mostly involving immunocompromised patients, related to C. fetus (Joly et al., 1986; Ichiyama et al., 1998; Briedis et al., 2002) and two related to C. jejuni (Pasticci et al., 1992; Peterson et al., 1993). Here, we reported the development of septic arthritis in an immunocompetent patient caused by C. jejuni infection.

Previously, Simon and Markusse (1995) reported the development of infectious arthritis induced by C. jejuni, which developed after C. jejuni enteritis in a patient with rheumatoid arthritis, nephrotic syndrome, amyloidosis and hypogammaglobulinaemia.

During the first evaluation, laboratory tests were negative, systemic diseases were excluded and an acute ReA was the initial diagnosis. A few days later, both clinical evaluation and laboratory tests excluded acute ReA because it is a oligoarticular, asymmetrical arthritis that involves knees, ankles or wrists of immunocompetent patients (Bremell et al., 1991; Locht and Krogfelt, 2002; Brzank and Wollenhaupt, 2013) and develops about 10 days after the beginning of enteritis (Keat, 1983; Hannu et al., 2004) (Table 1). In contrast, our patient showed painful swelling and redness in the region of the outer side of the left thigh that developed about 1 day after the enteritis, and a diagnosis of septic arthritis was postulated, and empirical
treatment with vancomycin was started with the development of side effects.

As in our previous studies (Gallelli et al., 2006, 2009, 2015; Gareri et al., 2007, 2008; De Vuono et al., 2014; Mumoli et al., 2014), the Naranjo scale (Naranjo et al., 1981) was used to evaluate the association between the drug and side effects, and we documented a probable association between vancomycin and skin erythema (Naranjo score: 6); therefore, this treatment was changed to levofloxacin, teicoplanin and rifampicin.

Several authors have shown that patients with Campylobacter infection may have extra-intestinal complications such as ReA (Berden et al., 1979; Pönkä et al., 1980; Eastmond et al., 1981; Gumpel et al., 1981). In our patient, clinical evaluation documented a monoarticular involvement excluding ReA, while microbiological cultural analysis of joint fluid, using enrichment broth, after an incubation of 72 h, as well as laboratory tests (i.e., positivity to catalase, oxidase, nitrate reduction, rapid latex agglutination and hippurate hydrolysis) determined the presence of C. jejuni.

The identification of Campylobacter strains is not easy because they slow-growing organisms (Bullman et al., 2012), and some microbiology laboratories do not routinely keep primary isolation media, incubated beyond 48 h, and specimens are not routinely inoculated onto enriched medium, which allows the growth of Campylobacter spp.

In a questionnaire-based study performed on 870 consecutive patients with Campylobacter-positive stool cultures and 1440 matched controls, Hannu et al. (2002) found that 45 of the patients (7 %) had ReA, suggesting that this is common following Campylobacter infection. However, in this as well in other studies, the first focus was the identification of bacteria in stool and not in other sites, and this could have underestimated the diagnosis of septic arthritis.

In our laboratory, we do not routinely carry out culture investigations in joint liquids because they require enrichment broth, after an incubation of 72 h, as well as laboratory tests (i.e., positivity to catalase, oxidase, nitrate reduction, rapid latex agglutination and hippurate hydrolysis) determined the presence of C. jejuni.

In conclusion, clinicians should consider Campylobacter infection in the presence of an immunocompetent patient with prosthetic devices who develops articular pain after enteritis without a history of a travel in the tropics. As the isolation of bacteria in blood may be negative in the presence of antibiotic treatment, culture of synovial fluid may help in diagnosis. Antibiotic treatment must be carefully evaluated to consider the local resistance in order to avoid clinical failure.

**Table 1. Clinical differences between ReA and septic arthritis**

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<thead>
<tr>
<th>Characteristic</th>
<th>ReA</th>
<th>Septic arthritis</th>
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<tbody>
<tr>
<td>Immune system</td>
<td>Immunocompetent</td>
<td>Immunodepressed</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Migratory oligoarticular</td>
<td>Monoarticular</td>
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<tr>
<td>Timing after enteritis</td>
<td>10 days later</td>
<td>1 day later</td>
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Bottieau et al. (2011) reported that C. jejuni represents the leading pathogen following travel to southern Asia, and is associated with a high rate of resistance to fluoroquinolones (53 %) and with clinical failure (33 %). Recently, Iovine (2013) showed that C. jejuni is naturally transformable, and the acquisition of additional genes imparting antibiotic resistance is likely.

A previous study found that, as erythromycin, ciprofloxacin and tetracycline are the recommended antibiotics, in Italy, the prevalence of antibiotic resistance is very high, particularly for ciprofloxacin (42.9 % during 2004–2005) and tetracycline (50.0 % during 2004–2005) (Crotti and D’Annibale, 2008). In contrast, our patient had not travelled to Asia but had been to Sardinia (Italy), and antimicrobial susceptibility tests revealed a sensitivity for ampicillin, ciprofloxacin, imipenem, tetracycline, erythromycin and gentamicin. Empirical treatment was not changed, with complete resolution of symptoms.

References


