

Reactive Arthritis Following an Outbreak of *Campylobacter jejuni* Infection

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ABSTRACT. Objective. To study the occurrence and the clinical picture of musculoskeletal (MSK) complications including reactive arthritis (ReA) following an outbreak of *Campylobacter jejuni*.

Methods. An outbreak of *C. jejuni* infection occurred in 2000 in Asikkala, Finland, during which 350 exposed subjects contacted the Municipal Health Centre (MHC). All primary care physicians in the MHC were advised to refer patients with acute MSK complications to the Rheumatism Foundation Hospital (RFH) for a specialist clinical examination, which was performed ≤ 3 months after the onset of the outbreak.

Results. Fifteen subjects with acute MSK complaints (11 women, 4 men; mean age 58 yrs) were examined in the RFH, where the following MSK diagnoses were assessed: ReA (9 patients), reactive arthralgia (2), exacerbation of previous rheumatoid arthritis (3), and previous fibromyalgia (1). In the patients with ReA, all adults, the arthritis was oligoarticular in 6 patients and polyarticular in 3; one patient had monoarthritis. The most frequently affected joints were knees and ankles. Besides peripheral arthritis, one patient had clinical sacroiliitis. Of the ReA patients, the antigen HLA-B27 was positive in 33%, including the patient with sacroiliitis. At the clinical examination, 6 ReA patients had subsiding signs of synovitis, 2 had only arthralgia, and one was symptom-free.

Conclusion. The frequency of ReA following an outbreak of *C. jejuni* was low: 2.6% (9 of 350). In the ReA patients, the clinical picture was mild, the primary outcome good, and the association with HLA-B27 not high. (J Rheumatol 2004;31:528–30)

Key Indexing Terms:

REACTIVE ARTHRITIS *CAMPYLOBACTER JEJUNI* OUTBREAK EPIDEMIOLOGY

Reactive arthritis (ReA) is a sterile joint inflammation that can be triggered by infections in the gut or in the urogenital tract. At present, *Campylobacter jejuni* and *coli* are the most common bacterial enteropathogens in the developed countries^{1,2}.

To date, the literature includes reports of only 2 *Campylobacter* outbreaks followed by a rheumatological survey, with occurrences of ReA between 0.7% and 1.8%^{3,4}.

We recently had the opportunity to study an outbreak caused by *C. jejuni*. We assessed the occurrence and the clinical picture of *Campylobacter*-associated musculoskeletal (MSK) complications including ReA.

MATERIALS AND METHODS

An outbreak of acute gastrointestinal infection caused by *C. jejuni* occurred in Asikkala (population 8600), Finland, in 2000. On August 3, 2000, the first subjects of the outbreak presented at the Municipal Health Centre

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(MHC), from which the population gets public health care services. A case of campylobacteriosis was defined as a resident of Asikkala who had onset of illness between July 31 and August 20, and who had diarrhea or at least 2 of the following symptoms: fever, abdominal pain/cramps, or vomiting. This case definition was met by 350 subjects. Samples from the municipal water supply were positive for *C. jejuni*, and the strains from water were indistinguishable from strains isolated from subjects by pulsed-field gel electrophoresis.

Subjects with MSK symptoms. During the outbreak, residents of Asikkala were informed about it by leaflets, the local radio channel, and newspapers. To collect information on subjects with acute MSK complications, including ReA, that were associated with the outbreak, all primary care physicians in the MHC were advised to refer patients with such complaints to the Rheumatism Foundation Hospital (RFH) for specialist diagnostics and treatment.

Diagnostic criteria. ReA was defined as the development of synovitis (both swelling and pain) in a previously asymptomatic joint within the first 2 months after the outbreak; there could also be signs or symptoms of inflammatory low back pain (pain worse by night), tendinitis, enthesopathy, or bursitis⁵. Any other forms of joint or back pain during or after the outbreak were also recorded.

Clinical examination. All subjects with suspected ReA or other MSK manifestations referred to RFH were invited to attend a clinical examination performed by a rheumatologist. Clinical examinations were performed ≤ 3 months after the onset of the outbreak. At this examination, blood was collected for erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor (RF), and HLA-B27 analysis. Additionally, *Campylobacter* antibodies were studied by enzyme immunoassay⁶.

RESULTS

General features. Eighteen subjects were referred to the

RFH. As one subject was not in Asikkala when the outbreak took place and 2 subjects did not meet the case definition of campylobacteriosis, they were excluded. Thus, the study population comprised 15 subjects (11 women, 4 men) with a mean age of 58 years (range 18–80).

MSK symptoms and signs at the MHC. Of these 15 subjects, general practitioners had diagnosed synovitis in 8 and local joint pain or generalized arthralgia in 7 subjects. In all these subjects, the onset of new joint complaints or the exacerbation of a preexisting MSK disease arose within 2 months after the outbreak. Of all 15 subjects, 9 had some preexisting MSK disease confirmed by a physician (Table 1).

MSK symptoms and signs at the clinical examination in RFH. For all 15 subjects, a final MSK diagnosis was assessed at the RFH (Table 1). It was ReA in 9 patients. Based on the number of *Campylobacter* cases during the outbreak (n = 350), the frequency of ReA was 2.6% (9 of 350).

In the ReA patients, who were all adults, the arthritis was oligoarticular in 6 patients and polyarticular in 3; one patient had monoarthritis. The most frequently affected joints were knees and ankles. Besides peripheral arthritis, one patient had clinical sacroiliitis. No case of Reiter's triad was diagnosed.

At the clinical examination in RFH, 6 of the 9 ReA patients still had signs of synovitis, with the clinical impression that the arthritis was subsiding, 2 patients had only arthralgia, and one was symptom-free. Of the 15 subjects, 5 (33%) were HLA-B27 positive. Of the 9 ReA patients, 3 (33%) were HLA-B27 positive, including the patient with sacroiliitis. Further, the serum of 4 patients (27%) contained *Campylobacter* antibodies; 3 of these had ReA, and one reactive arthralgia.

DISCUSSION

Nine patients following an outbreak of *C. jejuni* infection

Table 1. Characteristics of 15 patients examined at the Rheumatism Foundation Hospital (RFH) following an outbreak of *C. jejuni* infection.

Patient	Age, yrs	Sex	Preexisting MSK Diagnosis	Positive Stool Culture for <i>C. jejuni</i> at MHC	Joint Symptoms and Signs at MHC	Joint Symptoms and Signs in RFH	Laboratory Findings in RFH			Final MSK Diagnosis in RFH
							HLA-B27	ESR, mm/h	Campylobacter Antibodies	
1	54	M	OA	ND	S: (L) MTP, (L) ankle	S: (L) midtarsal P: (L) MTP	–	21	IgM+	ReA
2	18	M	JRA	ND	P: (R) ankle, (L) knee	Nil	+	11	–	JRA
3	80	F	OA	ND	S: MCP P: MTP	P: MTP	+	25	–	ReA
4	47	F	Nil	ND	P: hips, lower back	S: (R) SI P: hips	+	6	IgM+	ReA (sacroiliitis)
5	73	F	RA	ND	P: (L) midtarsal	P: (L) midtarsal	+	18	–	RA
6	80	F	OA	ND	S: (L) knee P: shoulders	Nil	–	24	–	ReA
7	49	F	Nil	–	S: knees P: ankles, wrists	P: (R) knee	+	3	–	ReA
8	38	F	FM	ND	P: lower back, GA	P: GA	–	12	–	FM
9	75	M	Nil	+	S: (R) knee P: (R) hip	S: (R) knee	–	10	–	ReA
10	65	M	Nil	ND	S: (L) knee P: (R) knee, (L) wrist, (L) MCP, lower back	S: (L) wrist P: (L) MCP	–	5	–	ReA
11	80	F	Nil	+	P: knees, MTP, IP of toes	Nil	–	23	–	ReArthr
12	35	F	Arthr	+	GA	Nil	–	11	IgM+	ReArthr
13	65	F	Arthr	ND	S: knees, ankles P: lower back	S: (R) knee	–	13	IgA+	ReA
14	42	F	Nil	–	S: (R) knee	S: (R) knee	–	9	–	ReA
15	72	F	RA	ND	GA	Nil	–	14	–	RA

A: abdominal pain; Arthr: unspecified arthralgia; D: diarrhea; ESR: erythrocyte sedimentation rate; Fe: fever; FM: fibromyalgia; GA: generalized arthralgia; IP: interphalangeal; JRA: juvenile rheumatoid arthritis; (L): left; MHC: Municipal Health Centre; MCP: metacarpophalangeal joint; MSK: musculoskeletal; MTP: metatarsophalangeal joint; ND: not done; OA: osteoarthritis; P: pain; (R): right; RA: rheumatoid arthritis; ReA: reactive arthritis; ReArthr: reactive arthralgia; S: synovitis; SI: sacroiliac joint.

were diagnosed as having acute ReA. This 2.6% frequency of ReA is compatible with findings of previous *Campylobacter* outbreak studies sharing occurrences of ReA between 0.7% and 1.8%^{2,3}. We delivered information on campylobacteriosis both to the municipality residents and to general practitioners of Asikkala, and therefore it is unlikely that any clinically relevant cases were missed. Similarly, visits of inhabitants to doctors outside the region were not probable, because financial compensation for the costs of the outbreak was organized by the local authorities.

As often in outbreak settings, stool cultures were not done for all exposed subjects. Also, only a quarter of the patients referred to the RFH had positive *Campylobacter* antibodies. The measurement of the *Campylobacter* antibodies only once at the clinical examination, however, and the interval between the onset of the outbreak and this examination, which was up to 3 months, probably contributes to our low prevalence of positive *Campylobacter* antibody levels.

The clinical picture of ReA, mainly oligoarthritis affecting predominantly the weight-bearing joints of the lower extremities, did not differ from that described previously in ReA attributable to *Campylobacter*^{7,8}. The figure for HLA-B27 positivity was 33%, while the corresponding figure is 14% in the Finnish general population⁹. In outbreak studies, a low frequency of HLA-B27 antigen has been observed also with ReA triggered by *Salmonella*^{10,11}.

The outcome for ReA cases was good: one-third of the patients had recovered from the acute ReA during the subsequent 3 months, and in two-thirds, recovery was progressing favorably. This finding is in accord with results of a recent large population based study of *Campylobacter*-triggered ReA⁵.

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