Late complications after a *Yersinia enterocolitica* epidemic: a follow up study

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Abstract

Ninety four Finnish conscripts were affected by a *Yersinia enterocolitica* epidemic in 1973. Thirteen years later 75 men completed a questionnaire about their present health. One half had no health problems, and the most common complaints in the other subjects were musculoskeletal disorders. Sixteen men wanted to be re-examined. In three cases a chronic connective tissue disease was diagnosed. Two men had ankylosing spondylitis. The most notable results of this study were (a) the fairly low number of late complications, (b) the close correlation between complications and the HLA-B27 antigen, and (c) the correlation between raised yersinia antibody titres and the late complications. The nature of the primary causative agent may affect the development of late complications.

Yersinia enterocolitica are common bacteria, which cause mainly gastrointestinal infections in humans. These infections are connected with some reactive diseases, especially arthritis,¹⁻³ but the mode of transmission is somewhat unclear. These bacteria have been isolated in animals,⁴ contaminated foodstuffs,⁵ and water,⁶ and person to person transmission has been suggested in some hospital epidemics.⁷

The main symptoms of the primary infection are diarrhoea, fever, and abdominal pain.² Acute reactive arthritis develops usually in a few weeks and lasts for between one month and a year.⁸ Connective tissue disease or another chronic complication may develop in the first years after the primary infection.^{8,9} Late complications do not correlate well with the clinical features of the primary infection,¹⁰ but are strongly associated with the HLA-B27 antigen.^{8,11-14} Acute infections may be treated with tetracyclines, sulpha-trimethoprim, or chloramphenicol, but the role of antibiotics is unclear.

We report a 13 year follow up study of a *Y. enterocolitica* epidemic among Finnish conscripts, which aimed at detecting possible chronic complications.

Description of the epidemic

At the end of October 1973 an epidemic occurred in Upinniemi garrison, located in southern Finland. The main symptoms were fever, gastric pain, diarrhoea, headache, cough, and malaise; increases in the sedimentation rate were only moderate. In most cases the gastroenteritis lasted for between five and seven days. One hundred and seventeen patients were

affected, of whom 94 were conscripts. Twenty two patients were admitted to the local military hospital, where they received tetracycline treatment. No reactive disorders developed.

Faecal and blood samples of the patients and asymptomatic subjects were analysed. Table 1 presents the results of these analyses. One hundred and seventeen men had marked increases in the titres against *Y. enterocolitica*. The prevalence of serotype O:9 was 60% (70/117), of serotype O:3 11% (13/117), and both types were found in 29% (34/117) of patients. In cultivation 104 fecal samples were positive—serotype O:9 was found in 64/104 (61%) fecal samples, O:3 in 8/104 (8%), and both types in 32/104 (31%) cases. Sedimentation rates were only moderately increased.

Food and water were exhaustively screened, but all analyses were negative. The patients were both naval troops and infantry with separate barracks. Two female civilian food handlers had positive cultures in their fecal samples, but their role in the transmission of the disease was unclear.

Follow up study

In 1986, 13 years after the epidemic, a follow up study was undertaken. Non-military personnel were excluded to obtain a uniform group. Eighty five of the 94 former conscripts were traced, of whom 75 responded. Table 2 presents the results of a questionnaire.

A voluntary physical re-examination was arranged in the Central Military Hospital. Thirty eight (51%) had no problems with their health and did not want to be re-examined. Of the remaining 37 with some kind of disorder, 16 (21%) wanted to be re-examined and 21 (28%) did not. In most of the latter cases the diagnoses, which included for example hypertension, kidney stones, and accidental injuries, had been verified recently in civilian hospitals and could not be connected with the epidemic. Table 3 presents the results of the thorough physical examination, radiological study, and laboratory tests.

Seven of the 16 patients had back problems—two with clinical and radiological findings of

Table 1 Results of serological analyses and cultures during the primary infection. Numbers (percentages) of cases are shown

Bacteria	Positive serology	Positive cultures
<i>Yersinia enterocolitica</i> type O:9	70 (60)	64 (61)
<i>Y. enterocolitica</i> type O:3	13 (11)	8 (8)
Both types	34 (29)	32 (31)
Total number	117	104

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Table 2 Results of the questionnaire answered by 75 conscripts in the follow up study

Problems*	Number of cases (%)
None	38 (51)
Symptoms of the musculoskeletal system	
Back pain	22 (29)
Arthralgias	17 (23)
Muscular pains	16 (21)
Rigidity of the joints	14 (19)
Swollen joints	7 (9)
Tendinitis	6 (8)
Symptoms of the gastrointestinal tract	10 (13)
Chronic gastritis	
Haemorrhoids	
Symptoms of the skin	15 (20)
Psoriasis	
Atopic or allergic eczema	
Dermatitis herpetiformis	
Symptoms of the eyes	3 (4)
Allergic conjunctivitis	
Traumatic changes	
Symptoms of the cardiovascular system	2 (3)
Hypertension	
Arrhythmias	
Symptoms of the kidneys or urinary tract	2 (3)
Kidney stones	
Prostatitis	
Hyperthyroidism (toxic)	2 (3)
Alcoholic hepatitis	1 (1)
Peripheral neuropathy	1 (1)

*Some patients had more than one problem.

ankylosing spondylitis. In one case Scheuermann's disease was diagnosed. Two men had prominent scoliosis. Results of all the radiological and laboratory tests were normal in two patients, and a weak musculature was the only finding.

Five patients had problems in the knee or ankle joints—three men had an injured meniscus shown by arthroscopy of the knee, one man had primary gout confirmed by examination of a synovial sample, and one man had secondary gout due to diuretics.

Four men had musculoskeletal disorders in the shoulders—one had rheumatoid arthritis, one had a cervical syndrome, one had chronic subacromial bursitis, and in one case prominent muscular tension was the only finding.

Five men were HLA-B27 positive—two had ankylosing spondylitis, one had rheumatoid arthritis, one had scoliosis, and one had an injured meniscus of the knee.

Four men had marked increases (1/160) in the antibodies against *Y. enterocolitica* O:9, and one an increased titre against type O:3 also. The immunoglobulins were IgG class (radioimmunoassay).

The use of antibiotics during the primary infection did not correlate with the complications.

Case reports

In patient No 1 (table 3), a 31 year old man, periodic back pain and rigidity of the spine had begun two years after the military service. The first radiological changes were found at the beginning of the 1980s, but the diagnosis remained open. In this examination we found a prominent sclerosis of the sacroiliac joint and mild arthrosis of the spine. Physical examination showed slight rigidity of the spine. The patient needed no regular drugs; he was HLA-B27 positive.

Patient No 2 (table 3), also 31, developed active inflammation of the hip and sacroiliac joints about one year after the military service. Thereafter he had progressive symptoms of the spine after streptococcal tonsillitis and chlamydial urethritis. He took anti-inflammatory drugs regularly. We found clear radiological changes of spondylarthrosis in the spine, and physical examination showed prominent rigidity of the spine. He was HLA-B27 positive.

Discussion

Yersiniosis is associated with chronic arthritis,^{8 15-17} ankylosing spondylitis,^{8 9} carditis and rheumatic fever,^{2 18} uveitis,¹⁹ and nephritis.²⁰ In this study musculoskeletal disorders were predominant. In three cases chronic connective tissue disease was diagnosed.

Titres of IgA, and especially IgG, antibodies may remain raised for a long time in yersinia triggered arthritis.¹⁰ In this study the cause of the primary infection was mainly *Y. enterocolitica* type O:9, and antibodies to serotype O:9 were predominant on re-examination. Patients with chronic, clinically evident disease had raised antibodies against *Y. enterocolitica*. The presence of these complexes has been found to correlate with prolonged joint symptoms.²¹ The role of these complexes in the development of chronic disease is still uncertain. Use of antibiotics in the primary infection did not correlate with later symptoms.

Presence of the HLA-B27 antigen strongly increases the risk of reactive diseases.^{8 14} In

Table 3 Clinical findings of the follow up examinations of 16 patients

Case No	Symptoms and signs	Radiology	Antibodies to:		HLA-B27	RF*	SR*
			<i>Y. ent</i> O:3	<i>Y. ent</i> O:9			
1	Back pain, rigidity of the spine	Sacroiliitis, ankylosing spondylitis	80	160	+	—	2
2	Back pain, rigidity of the spine	Ankylosing spondylitis	80	160	+	—	10
3	Swollen joints, synovitis in hands	Rheumatoid changes	—	—	+	+	25
4	Back pain, muscular tension	—	160	160	—	—	8
5	Back pain	Spinal stenosis	80	160	—	—	1
6	Back pain	Scoliosis	40	—	+	—	3
7	Knee pain, injured meniscus in arthroscopy	—	—	—	—	—	3
8	Knee pain, injured meniscus in arthroscopy	—	80	—	+	—	8
9	Knee pain, operated knee	—	—	—	—	—	3
10	Shoulder pain	Cervical arthrosis	40	—	—	—	9
11	Ankle pain, hypertension, hyperuricaemia	—	—	80	—	+	20
12	Ankle pain, primary gout (synovial sample)	—	—	—	—	—	8
13	Back pain	Scoliosis	—	40	—	—	8
14	Back pain	—	—	—	—	—	7
15	Shoulder pain	Periarthritis	—	80	—	—	6
16	Shoulder pain	—	—	—	—	—	4

*Y ent = *Yersinia enterocolitica*; RF = rheumatoid factor; SR = sedimentation rate.

some reports 20% of subjects with HLA-B27 had indications of ankylosing spondylitis.¹² In this study two of the five positive patients had ankylosing spondylitis, one had rheumatoid arthritis, and one had clinical symptoms of ankylosing spondylitis without any radiological findings. The prevalence of ankylosing spondylitis in the Finnish population in general is 0.4–1.0%,²² whereas in this study we found a prevalence of 1.7% (2/117).

Thus, in conclusion, the major problems after the yersinia infection were musculoskeletal disorders; ankylosing spondylitis, in particular, correlated with the disease. These results also show that the HLA-B27 antigen has a prominent role in the development of late complications. The low incidence of detected late complications may be the result of the examination technique based on a questionnaire but may depend also on the nature of the primary causative agent.

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