Acute anterior uveitis after yersinia infection

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SUMMARY Twenty-eight cases of acute anterior uveitis in which raised antibody titres indicated yersinia infection as a possible causative factor in the disease were studied retrospectively. In most cases the antibodies belonged to the IgA class; in only 6 cases did the presence of IgM class antibodies indicate recent infection. In half the cases also antibody titres against Chlamydia were raised. The clinical features and course of the disease did not differ from those of acute anterior uveitis due to other causes.

Acute anterior uveitis (AAU) is a common disease usually affecting young or middle-aged patients. It frequently occurs in connection with other disorders such as Reiter's disease, ankylosing spondylitis, juvenile rheumatoid arthritis, psoriatic arthritis, and sarcoidosis. It may also follow certain infections—for example, by Chlamydia trachomatis, salmonella, or yersinia—as a late complication. It is noteworthy that AAU and several of the other disorders mentioned above are correlated with the presence of HLA B27. This has also been demonstrated for the reactive arthritis that develops after acute enteritis caused by yersinia.

AAU related to yersinia infection has not been earlier studied as a separate entity. For instance, it is not known how frequently yersinia infection is the cause of AAU and whether these cases are characterised by special clinical and immunological features. The purpose of the present work was to elucidate these questions by analysing retrospectively 28 cases of AAU in which elevated antibody titres indicated yersinia infection as a possible causative factor in the disease. We have studied the ocular pathology, the rate of recurrence, and the overall prognosis of these cases, and paid special attention to the presence of certain clinical features, such as diarrhoea and arthritis.

Patients and methods

The subjects of the study were 15 women and 13 men with AAU who had significant amounts of antiyersinia antibodies in their sera. They were examined at the outpatient department of the Clinic for Ophthalmology at Turku University from March 1979 to September 1980. Patients who had AAU due to ocular trauma were excluded from the study.

The diagnosis of AAU was in all cases confirmed by biomicroscopic examination. The following laboratory tests were carried out on each patient: erythrocyte sedimentation rate (ESR), peripheral blood leucocyte count, the latex and Waaler-Rose test for rheumatoid factor, antistreptolysin O, antistaphylocysin, anti-yersinia-antibody, and anti-chlamydia antibody determinations, and x-ray examination of the chest, sinuses, and lumbosacral spine. The hospital records were reviewed with attention to the severity of the AAU and its course as well as possible recurrences and associated diseases.

The ELISA method (enzyme-linked immunosorbent assay) for IgM, IgG, and IgA class yersinia antibodies has been described in detail previously. In brief, the assay was a double antibody utilising immunoglobulin class-specific rabbit antihuman sera and swine antirabbit IgG alkaline phosphatase conjugate. The antigen preparations used were formalised whole Y. enterocolitica 0:3 and Y. pseudotuberculosis 1A bacteria and heat-treated (100°C for 1 h) Y. enterocolitica 0:9 bacteria. The results were evaluated by means of a standard curve constructed from measurements on 6 different dilutions of serum with a high concentration of the corresponding antibody to yersinia. The results are presented as percentage values of the standard serum.

Results

Of the 28 patients included in the study 15 (54%) were women and 13 (46%) were men; AAU is known
to affect both sexes equally. The patients represent primarily young and middle-aged people, the mean age being 38. The youngest patient was 17 and the oldest 65 years old. The mean age of the women was 36 years (range 23–64) and of men 43 years (range 17–65 years).

The AAU was bilateral in 6 patients. In 9 cases (32%) there had previously been AAU. The ocular pathology and the duration of the symptoms in patients who had raised anti-yersinia antibodies did not differ from the other cases of AAU treated at the same time in the Clinic for Ophthalmology. In no case was a relapse observed during the relatively short follow-up period. In only one patient was the disease so severe that systemic steroid treatment was given. All others were treated by topical mydriatics and corticosteroids. Three patients received tetracycline because of fresh arthritis and/or diarrhoea. The one patient who had systemic corticosteroid therapy received tetracycline.

The results of the laboratory tests are presented in Table 1. It is remarkable that none of the patients had a positive latex test for rheumatoid factor and only one had a positive Waaler-Rose test. The ESR remained low in most patients, and only in 2 cases was it over 40 mm/h. The other laboratory tests did not reveal any significant changes typical of AAU. In 3 patients ankylosing spondylitis was also diagnosed at this time; its duration could not be established with certainty.

The clinical features of interest in the patients are summarised in Table 2. The raised yersinia antibodies belonged in most cases to the IgA class, and in only 6 patients were the IgM antibodies raised, indicating a recent infection by yersinia. In most cases the antibodies were against Y. enterocolitica 3, in 4 against Y. enterocolitica 9, and in 3 patients against Y. pseudotuberculosis 1A. Five patients (17.9%) had diarrhoea in the initial phase, and in 3 cases (10.7%) the patient had reactive arthritis. One of those 3 patients also had raised antibodies against chlamydia in a titre of 1:32.

In 7 cases high antibody titres >1:32 against chlamydia were observed; this represents 25% of the whole material (Table 1). A further 7 patients had lower anti-chlamydia antibody titres of >1:16. Taken together, 50% of the patients thus had raised antibody titres both against yersinia and chlamydia. The question therefore arose whether these 2 agents have cross-reacting or common antigens or whether the patient had 2 infections simultaneously. The 7 sera with high antibody levels against both agents were absorbed with yersinia; in 6 cases the absorption caused no drop in the anti-chlamydia titres. One serum lost its anti-chlamydia titre of 1:128 when absorbed with yersinia. This serum is being studied further to find out whether the antibody is truly cross-reactive. Anyway it is apparent that generally the appearance of antibodies against both yersinia and chlamydia indicates double infection.

**Discussion**

Our observations indicate that AAU after yersinia infection does not clinically differ from that caused by other aetiological factors. Only 5 patients had had diarrhoea that suggested the possibility of yersinia as primary cause of the disease. This is in concordance with the clinical observation that, in patients who later develop arthritis, diarrhoea is not a prominent initial symptom. The general symptoms were mostly mild. The ESR was low, and only 2 patients had a
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value higher than 40 mm/h, whereas in yersinia arthritis the ESR value is usually high.\(^\text{13,14}\) Only one of the patients (case 10) had severe general disease. She had originally a yersinia enteritis with diarrhoea, followed by severe arthritis. At this time she was bedridden for several weeks with synovitis in many joints and extensive muscular atrophies. She recovered well, however, and had a successful pregnancy after this. Throughout this time the antibody titres of the IgA class remained high. Stool cultures did not yield yersinia. After the delivery she developed AAU but recovered well from this also. Then, suddenly and surprisingly, the antibodies disappeared, and at present she is clinically quite healthy.

Only in 3 cases did the patient also have arthritis. This suggests that these 2 complications of yersinia infection can hardly have a common pathogenic pathway. Only in 6 patients was the AAU bilateral. Interestingly, relapsing AAU is not restricted to the same eye but may affect one or the other. It seems therefore that some unknown factor is needed to trigger the inflammatory process in the eye.

In 26 of the 28 cases the IgA class antibodies against yersinia were raised and only in 12 cases were high levels of IgG class antibodies observed. Of these, 2 had the IgG antibodies as the only class present in their sera. In 6 patients high IgM class antibodies indicated that the yersinia infection had been recent. The observation is in accordance with the findings that in yersinia arthritis the IgA class antibodies are high and remain elevated for prolonged periods even after the acute joint symptoms have disappeared.\(^\text{9,15-16}\) The reason for this phenomenon remains unclear, and persistence of the antigen in the organism, for example, has not been demonstrated. In any case it is obvious that high IgA anti-yersinia antibodies are correlated with the occurrence of post-infectious complications, although their role remains obscure.

The present material indicates that yersinia infection as a cause ofpostinfectious AAU is far less common than chlamydia infection. In the present series as many as 14 (50%) patients had anti-chlamydia antibodies, 7 (25%) of these at a high level. The same high incidence of anti-chlamydia antibodies has been observed also in another follow-up study in our clinic,\(^\text{1}\) whereas out of 121 consecutive cases of AAU only 13 (10-7%) could be considered as caused by yersinia. Moreover, 3 patients in our material had as an underlying disease ankylosing spondylitis, to which AAU is known to be correlated. The absorption studies of the sera show that at least in 6 out of the 7 cases studied the patient had both chlamydia and yersinia infection simultaneously. It is not possible to conclude whether one of the 2 or both infections together caused the AAU.

A practical problem related both to the arthritis and AAU after yersinia infection is the possible need of antibiotic treatment. It seems that in both diseases\(^\text{13,14,17}\) the bacteria disappear quickly from the stools and the diagnosis has to be based on the demonstration of antibodies; in our material stool cultures were not carried out. The same holds true also for chlamydia, which can rarely be isolated at the time of diagnosis of AAU.\(^\text{1}\) In the present study 4 patients received tetracyclines and the others were treated only with topical mydriatics and steroids. All recovered well. It seems reasonable to apply antibiotic therapy only in the cases where high levels of IgM antibodies indicate recent infection, when yersinia can be cultured from the stool, or when diarrhoea and abdominal pains are still present or closely connected with the illness.

In conclusion, AAU may be frequently related to yersinia infection. The clinical disease does not differ from that caused by other aetiological factors, such as chlamydia, and is not connected with the occurrence of other late complications of yersinia infection such as erythema nodosum or reactive arthritis. Although immunological mechanisms are a major factor in the pathogenesis of the different postinfectious complications, their actual role and character still remain obscure. Apparently some local factors are necessary to trigger the final inflammatory process in the eye.

References

Notes

Contact lens fitting
The Rudolph Ellender Medical Foundation Inc. will hold the 22nd annual instructional course in contact lens fitting on 1-4 April 1982 at New Orleans, Louisiana, USA. Details from Jos. A. Baldone, MD, President, 136 South Roman Street, New Orleans, LA, USA.

Centenary of Sydney Eye Hospital: International Scientific Meeting
An international scientific meeting celebrating the centenary of Sydney Eye Hospital will be held on 3-7 April 1982. The venue is the Sydney Hilton Hotel, Level 9, 259 Pitt Street, Sydney 2001, Australia, to which registrants are advised to make their bookings direct, indicating that they are part of the conference. The theme of the meeting is 'Current concepts in ophthalmology' and emphasises management. Keynote lectures will be given in plenary sessions at the beginning of each morning and afternoon. These will be followed by a choice of symposia chaired by the overseas visitors who will give position papers allowing time for discussion. Inquiries about registration to Miss A. Fitzgerald, c/o The University of Sydney, Department of Clinical Ophthalmology, Sydney Eye Hospital, Sir John Young Crescent, Woolloomooloo, New South Wales 2011, Australia.

Clinical vision research
A course on 'Clinical vision research: epidemiologic and biostatistical approaches' will be held 29 April to 1 May 1982 in Sarasota, Florida (immediately before the 1982 ARVO meetings). The course is an introduction to contemporary methods and principles of clinical vision research, and is sponsored by the National Eye Institute and Epistat Associates. Further information from Catherine M. Beinhauer, Epistat Associates, PO Box 214, Norwich, Vermont 05055, USA.