Letters to the Editor

Infection related arthritis induced by tonsillar *Chlamydia trachomatis* and *Streptococcal* infection

Sir,

Several studies on *C. trachomatis* induced tonsillitis or pharyngitis have been reported (1-4). However, reactive arthritis (ReA) or infection related arthritis (IRA) (5) in relation to *C. trachomatis* infection of tonsils has not been reported. We describe two patients with IRA in which their tonsils were concomitantly infected with *C. trachomatis* and *Streptococcus.*

A 29-year old female had sore throat, pyrexia of 39°C and arthritis from November 1991. Physical examination revealed swelling of elbows and knee joints. Laboratory examinations revealed WBC of 9,800/mm^3, CRP 4.3 mg/dl, ESR 47 mm/hour, anti-streptolysin O (ASO) 416 U (normal range < 240) and antistreptokinase (ASK) 1280 U (normal range in adult < 1280). *Group C Streptococcus* was isolated from throat swabs. Rheumatoid factor (RF) was negative and antinuclear antibody (ANA) was 1:160 . Antibodies against *C. trachomatis* were positive; IgG 3.45 (index: < 0.9) and IgA 1.83 (< 0.9). Sore throat, pyrexia and arthritis did not subsided in spite of administration of piperacillin 2 g/day for 7 days. Therefore, tonsillectomy was performed.

Microabscesses were demonstrated in the resected tonsils and *C. trachomatis* but no other bacteria was isolated from the abscess. RNA for *C. trachomatis* was demonstrated. Chlamydial DNA was not demonstrated from the cervical swab. No recurrence of tonsillitis and arthritis was noted thereafter.

A 56-year old housewife admitted to our hospital in 1998 for sore throat, pyrexia of 38.5°C and arthritis of both knees and right wrist joints. Her right wrist and right 1st and 2nd metaphalangeal joints were markedly inflamed and swollen. Tonsils were inflamed with two ulcers. Laboratory examination revealed WBC of 11,100 /mm^3, CRP 23.2 mg/dl and ESR 131 mm/hour. RF and ANA were negative. ASO was revealed to be 320 U and ASK was 1:640. Antibodies against were *C. trachomatis* IgG 3.47 and IgA 1.43. No other bacteria except *alpha-* and *beta-Streptococcus* were isolated from the tonsillar swab. DNA for *C. trachomatis* was demonstrated from the tonsillar swab but not from the cervical swab. Results for *mycoplasm*, Ebstein-Barr virus, syphilis, hepatitis B and C virus, cytomegalovirus, HIV, *C. pneumoniae*, mycobacterium and *Legionella pneumophlila* were negative. Infective endocarditis was not demonstrated with blood culture and echocardiogram. She was treated with panipenem/betamipron 2 g/day; however, improvement of pyrexia was not noted. Therefore, minocycline of 200 mg/day was administrated. Pyrexia subsided within 5 days and arthritis subsided within two weeks after the administration of minocycline. No recurrence of tonsillitis and arthritis was noted thereafter.

Several studies on pharyngeal *C. trachomatis* infection have shown a recent increase in the prevalence rate in the USA of 3.7% among patients from the genitourinary medicine clinic and recent reports in Japan have revealed coinciding increase in the prevalence rate (1,6). We previously reported a case of IRA induced by *Pseudomonas aeruginosa* isolated from a tonsillar abscess (7, 8). Therefore, it is evident that *Streptococcus* is not the sole bacteria that induces IRA following tonsillitis. Our patients did not have spondyloarthropathy nor HLA-B27. Since our patients did not consent to synovial biopsy, the role of *C. trachomatis* and *Streptococci* in IRA is obscure (9,10). We supposed that both bacteria were causative agents for IRA. The route of transmission of *C. trachomatis* infection is also unclear. Although oro-genital sexual contact was suspected, both patients denied this fact. The pharyngeal mucosa is not suitable for colonization by *C. trachomatis* (1, 3); however, once *C. trachomatis* colonizes in the tonsillar crypts, it is apparently more difficult to eradicate than urethral *C. trachomatis*, and prolonged or repeated administrations of antibiotics are necessary (3, 4). In conclusion, much attention should be focused on the detection of *C. trachomatis*, especially in the tonsillar microabscess, which may result in the inducement of IRA or ReA.

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Reactive arthritis induced by *Gardnerella vaginalis*

Sirs,

Reactive spondyloarthropathies are conditions in which arthritis occurs after urogenital or gastrointestinal infections.The spectrum of the arthritogenous agents is large and the list is growing continously. We describe a patient with *Gardnerella vaginalis*-induced reactive arthritis and dermatitis.

A 38-year-old woman was admitted for fever, skin rash and polyarthritis of new onset. Two weeks before she has suffered from dysuria, a pussy vaginal discharge and lower abdominal pain, together with fever up to 39° and chills. One week later, acute arthritis of the wrists appeared only to be shortly followed by additive inflammation of the small joints of the hands, elbows, knees and ankles and by the appearance of an itchy skin rash on both upper and lower extremities.

Examination revealed acute synovitis of the mentioned joints and an urticarial rash over the arms and calves. The temperature was 38.6º, blood pressure was 110/70 and the pulse was 90 per minute. Gynecological examination showed vaginal inflammation and discharge. The rest of the physical examination was not contributory. The erythrocyte sedimentation rate was 80 mm Hg

in the first hour (Westergren), Hb was 12 gr%, WBC 12,500 with 11% bands; the rest of the blood count, routine serum biochemistry, protein electrophoresis and a general analysis of the urine were normal.
Rheumatoid factor, ANA, anti DNA, anticardiolipin,antiRNP and ANCA were negative. Serum complement levels were normal. Serological tests for hepatitis B and C, Parvovirus, Shigella, Salmonella, Chlamydia and HIV were negative and repeated blood and urine cultures were sterile. Skin biopsy was denied by the patient. Cultures from vaginal swabs grew Gardnerella vaginalis.
The diagnosis of *Gardnerella vaginalis*–induced reactive arthritis and dermatitis was posed. Treatment with small doses of corticosteroids (10 mg prednisone a day) and Flagyl (500 mg a day) was followed by a gradual reduction of the arthritis, dermatitis and and vaginal discharge. Ten days later the temperature was normal, the pathological dermal and musculoskeletal signs have disappeared and the patient resumed her previous activities. Later, she was lost to follow up, therefore a planned examination of HLA B27 antigen was not performed.
Bacterial vaginosis is a very common clinically definable condition in which a shift occurs from a predominance of lactobacilli-dominated flora to a vaginal anaerobic environment, constituted by gardnerella, micrococci, streptococci and staphylococci.The bacterial components of this condition were reported to be implicated in pelvic infections and pelvic inflammatory disease. About half of the patient are symptomatic, a malodorous discharge being the main clinical sign. Topical or oral metronidazole is the treatment of choice (1-3). Gardnerella vaginalis is a common anaerobic bacteria which may cause bacterial vaginosis and sexually transmitted disease. Its presence can be demonstrated *in vivo* by morphological bacteriological and serological methods and *in vivo* by a polymerase chain reaction (4). Gardnerella may infect the male partners and cases of Gardnerella-induced male urethritis have been reported (5).To our knowledge, only three cases of reactive arthritis, alias Reiter's syndrome related to Gardnerella were described (6-8). Two of the patients were males and in one case the organism was isolated also from a vaginal specimen taken from the patient's wife. The clinical features varied from oligoarthritis to polyarthritis and tendinitis of the lower extremities. In one patient asymptomatic sacroiliitis was disclosed by computed tomography. The extraarticular features included vulvovaginitis and urethritis, dermatitis, fever, conjunctivitis and vesicles of fingers. The HLA phenotype was B27 in two cases. Nonsteroidal antiinflammatory drug and antibiotic treatment (metronidazole or minocycline) resulted in resolution of the symptoms, however in one case, recurrence of arthritis was reported after a few months. The triggering agents for reactive arthritis are identified in only two-thirds of the cases. We propose to include Gardnerella infection among the causative factors of reactive arthritis and Reiter's syndrome.

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Treatment of recurrent oral aphthous ulcers with etanercept

Sirs,
Thalidomide was banned worldwide in 1962 after its teratogenic effects had been demonstrated. However, more recently thalidomide has received increased attention due to its anti-inflammatory and immunomodulatory properties mediated primarily by tumor necrosis factor-alpha (TNF-alpha) inhibition. Thalidomide is currently being used for treatment of graft host disease, clinical manifestations of erythema nodosum leprosum, systemic lupus erythematosus, Behçet's syndrome, multiple myeloma spontaneous and secondary aphthous ulcers. Thalidomide has gained orphan drug status for several specific indications, including treatment of recurrent aphthous stomatitis in AIDS patients (1,2).
Thalidomide is associated with several adverse effects besides teratogenicity. Peripheral neuropathy, often associated with paresthesias muscle weakness and drowsiness has been described frequently in patients receiving thalidomide. In the past five years several patients attending our Clinic have shown prompt response to the use of 100 to 200 mg of thalidomide for the treatment of recurrent aphtous stomatitis. Two patients, one with probable and the other with classical Behçet's syndrome had the medication discontinued, one due to severe drowsiness and the development of neuropathy, and the other due to severe muscle weakness and mood changes.
The exact mechanism of action of thalidomide is not known. It affects TNF-alpha function by selectively affecting TNF-alpha mRNA without directly affecting other cytokines (3,4). On the two patients mentioned above the cessation of thalidomide was followed by recurrence of aphthous lesions two and three months after discontinuation of the medication. We offered the patients the possibility of receiving etanercept, an expensive form of TNF inhibition currently in use for patients with severe forms of rheumatoid arthritis (5,6). Both patients started to receive etanercept 25 mg subcutaneously twice a week. The lesions disappeared on both patients, one after three weeks and the other after five weeks, after a six-month period we discontinued the injections and in both patients the ulcers again developed five and seven weeks after, respectively. Etanercept was reintroduced with quick clinical response similar to the first period of treatment (1).
Etanercept was first introduced in clinical practice as a medication able to reduce signs and symptoms and inhibit the progression of rheumatoid arthritis. Additional indications are now being explored including psoriasis, psoriatic arthritis and vasculitides. Our findings appears to be the first report of the potential beneficial use of etanercept in patients with severe recurrent aphthous ulcers, and confirms observations reported by Robertson et al., showing that infliximab, another anti-TNF drug, is useful in the treatment of recalcitrant orogenital ulceration of Behçet's syndrome where other forms of therapy are not available or contraindicated (7).

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