Central Nervous System Toxoplasmosis in HIV-1 Infected Patients with Persistently Normal CD4+ Cell Counts

The seroprevalence of *Toxoplasma gondii* is high in Europe and consequently also the percentage of patients with AIDS who develop central nervous system (CNS) toxoplasmosis.

In a retrospective study (supported by grants of the National Institute of Health, Project No. 8205–08) carried out on 772 patients with AIDS followed-up at our clinic from January 1985 to October 1992, we diagnosed 132 cases of CNS toxoplasmosis according to CDC guidelines (1). At the time of diagnosis, 118 patients had CD4+ cell counts lower than 200/μl, 14 had counts between 200 and 350 cells/μl, and 4 had counts higher than 600 cells/μl. These four patients, two men and two women, all former i.v. drug abusers, had attended our clinic for at least 24 months before developing CNS toxoplasmosis, and all were otherwise asymptomatic. The early neurological symptoms included seizures in two patients and progressive headache and photophobia in the other two.

In all patients brain CT scan showed hypodense lesions with peripheral annular enhancement in the temporal (case 1), occipital (case 2 and 4) and parietal (case 3) regions and in the hippocampus (case 4). Lesions were multiple except in one patient.

These four individuals had detectable levels of IgG antibodies to *Toxoplasma gondii* in sera. In one patient an IgM response was also present. Chest x-rays and blood cultures showed no pathological findings in any of the patients.

The acute episode in all patients was treated with a pyrimethamine/sulfadiazine combination. A loading dose of 50–75 mg of pyrimethamine was administered together with sulfadiazine at a daily dose of 100 mg/kg. After six weeks of treatment, CT scan demonstrated that the CNS lesions had completely disappeared in all patients. Since then, all four patients have been on long-term maintenance treatment with pyrimethamine (25 mg per day) and sulfadiazine (2 g per day). Their general condition to date is good, and their CD4+ cell counts remain higher than 600 cells/μl.

Central nervous system (CNS) toxoplasmosis in patients with AIDS has been reported to occur when CD4+ cell counts drop to 125/μl or lower (2, 3). Encephalitis caused by *Toxoplasma gondii* has also been recognized to occur in patients undergoing intensive immunodepressive therapy (4–6), but its occurrence in normal adults is rare (7). We suggest that CNS toxoplasmosis should be considered when neurological symptoms occur in HIV-infected patients, even when they are otherwise healthy and have high CD4+ cell counts.

C. Gervasoni*, T. Bini, F. Franzetti, A.L. Ridolfo, A. d'Arminio Monforte

Clinic of Infectious Diseases, University of Milan, Via G.B. Grassi 74, 20157 Milan, Italy.

References

1. **Centers for Disease Control:** Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. Morbidity and Mortality Weekly Report 1987, 36: 3S–15S.
2. **Beaman MH, Luft BJ, Remington J:** Prophylaxis for toxoplasmosis in AIDS. Annals of Internal Medicine 1992, 117: 163–164.
3. **Crowe SM, Carlin JB, Stewart KI, Lucas R, Hoy JF:** Predictive value of CD4+ lymphocyte numbers for the development of opportunistic infections and malignancies in HIV-infected persons. Journal of Acquired Immune Deficiency Syndromes 1991, 4: 770–776.
4. **Towesend JJ, Wolinsky JS, Baringer JR, Johnson PC:** Acquired toxoplasmosis: a neglected cause of treatable nervous system disease. Archives of Neurology 1975, 32: 335–343.
5. **Ruskin J, Remington JS:** Toxoplasmosis in the compromised host. Annals of Internal Medicine 1976, 84: 193–199.
6. **Frenkel JK, Nelson BM, Arias Stella J:** Toxoplasmic encephalitis. Human Pathology 1975, 6: 97–111.
7. **Krick JA, Remington JS:** Toxoplasmosis in the adult: an overview. New England Journal of Medicine 1978, 32: 335–343.

Atypical Bilateral Symmetric Erosive Chronic Polyarthritis in the Course of Lyme Disease

Lyme disease was first described in 1977 as an epidemic of oligo-arthritis in children who appeared to be suffering from chronic juvenile arthritis (1). Osteo-articular lesions may occur to a varying extent. They are generally characterized by brief but recurring asymmetric oligo-articular attacks of arthritis in the large joints or by migratory polyarthritis in both the large and small joints. Although infrequent, a symmetric sero-

negative polyarthritis similar to that of rheumatoid arthritis may be present in some cases (2). Overt arthritis appears in 60 % of untreated patients, and chronic arthritis develops in 10 % of these patients (2, 3), usually after at least a year of intermittent attacks (2). Even in these cases, the attacks are generally self-limited. Chronic forms of the disease may lead to erosions (3, 4) and, less frequently, to permanent disability (3). We report an atypical case of chronic arthritis that developed in the course of Lyme disease.

The subject was a 15-year-old female who complained of fever, malaise and pain in her joints, which showed no signs of inflammation. According to the patient, a tick had bitten her on the right knee one month before. Investigations done at the onset of the illness showed no significant abnormality and the patient was prescribed treatment with 100 mg doxycycline twice daily for ten days and 3 g aspirin per day. Approximately 15 days after the skin lesion had appeared, the patient was hospitalized with migratory polyarthritis affecting her wrists, fingers, knees, ankles and feet. Test results were normal for normachromic normocytic anemia, thrombocytosis, total and differential leucocyte counts; the erythrocyte sedimentation rate was 100 mm. Additional tests showed normal hepatic and renal function and normal electrolyte levels; the C-reactive protein level was 12 mg/dl. There was leucocyturia and urine cultures were positive for *Proteus mirabilis*. Tests for rheumatoid factor and anti-nuclear antibodies were negative; tests for HLA antigens were positive for A1, B8, CW2, DR5 and DQW2. Serological tests were negative for *Rickettsia conorii*, *Borrelia burgdorferi*, *Salmonella typhi*, *Salmonella paratyphi A* and *Salmonella paratyphi B*, *Coxiella burnetii*, *Treponema pallidum*, *Leptospira* spp., *Yersinia enterocolitica* 0:3 and 0:9, and *Yersinia pseudotuberculosis* T1. The ECG and thoracic and skeletal x-rays were normal. Treatment was begun with 600,000 U i.m. penicillin G every 24 h for ten days, 60 mg prednisone daily with a gradually decreasing dose until discontinuation, and 3 g aspirin daily. At the end of this treatment clinical examination showed complete recovery.

Over the following three months, however, the patient suffered a progressive decline in her condition and was again hospitalized, this time with bilateral symmetric polyarthritis of the large and small joints with radiologic evidence of erosive symmetric polyarticular disease of the synovial joints (periarticular osteoporosis, marginal osseous erosions and cysts, and diffuse loss of the interosseous space). The test results were similar to those obtained on the previous occasion with the exception that an enzyme immunoassay (Platelia Lyme, Diagnostic Pasteur, France) showed elevated IgM and IgG levels for *Borrelia burgdorferi*. This was confirmed by Western blot (MarDx Diagnostics, USA), which revealed the presence of specific IgG and IgM (Table 1). In the case of IgM tests the serum was previously treated with Absorbent RF (Behring Institute, Germany). Tests for detection of non-treponemal antibodies (Rapid Plasma Reagin, Beckton-Dickinson, USA), antibodies against leptospira (Institute Pasteur, France) and *Treponema pallidum* hemagglutination (Cellognost, Behring Institute) were negative. The patient was treated with ceftriaxone 1 g i. m. twice daily for 21 days, deflazacort 15 mg daily and naproxen, 250 mg three times a day, and showed considerable improvement. At present, eight months after finishing treatment, her articular disease is stable.

Table 1: Evolution of the antibody response to *Borrelia burgdorferi* in a patient with atypical polyarthritis.

Test	No. of days after tick bite			
	30	45	90	240
EIA	negative	negative	positive	positive
Western blot, IgG	negative	negative	positive	positive
Western blot, IgM	negative	negative	positive	negative

This case of arthritis associated with Lyme disease is of particular interest for two reasons. Firstly, the illness took the form of bilateral symmetric chronic polyarthritis with osteo-articular erosions identical to those associated with rheumatoid arthritis. Secondly, there was complete absence of neurologic or cardiac complications, which is unusual in European cases of Lyme disease. The diagnosis was based on the history of a tick bite, the serological findings and an excellent response to appropriate antibiotics. In confirmed cases of Lyme disease there appears to be a direct correlation between the patient's age at the time of the initial infection and the total duration of arthritis, which tends to be shorter in younger patients (5), as in our patient. The presence of chronic arthritis with erosion of the bones and joints (2–4) may be linked with immunogenetic factors, as suggested by the association found with HLA DR4 and DR2 (5, 6). DR4 has been associated with a lack of response to antibiotic treatment, whereas DRw52 may be associated with arthritic conditions of

short duration (7). Thus, in genetically predisposed individuals, the interaction of *Borrelia burgdorferi*, HLA type II and certain T-cell receptors could be of critical importance for the type of immune response (6). This, however, was not the case in our patient.

The treatment of arthritis in the third stage of Lyme disease is problematic (8). Since tetracyclines and penicillin G had been administered to our patient previously, we decided to give ceftriaxone, which yielded excellent clinical results. The antibody response to *Borrelia burgdorferi* can involve a response of both IgG and IgM. Other studies have shown that some patients never develop antibodies at a detectable level (9–13). In some patients IgM antibodies remain elevated throughout the illness, i.e. the period of arthritis, (13, 14). Specific IgG antibody, on the other hand, is generally not detectabte during the first weeks of illness, but patients become positive months later when arthritis occurs, and levels often remain high for years. Craft et al. (14) detected IgM antibody in some patients with arthritis even though IgG antibodies were clearly elevated. In our study, both IgG and IgM levels were elevated when the patient presented with articular lesions. These results suggest that the persistence of specific IgM antibodies may also be associated with more severe forms of the disease. The mechanism behind this persistent response is still unknown, but it may not necessarily require an intact spirochete (10).

The findings in this study indicate the continuing need to investigate the possibility of *Borrelia burgdorferi* infection in all cases of chronic polyarthritis, with special attention to those cases originally diagnosed as chronic juvenile arthritis.

J. Gutiérrez[1]*, M. Palermo[2], M.C. Maroto[1], M. Abellan[2]

[1] Departamento de Microbiología and [2]Servicio de Reumatología, Hospital Universitario de Granada, Granada, Spain.

References

1. **Steere AC, Malawista SE, Snydman DR, Shope RE, Andiman WA, Ross MR, Steele FM:** Lyme arthritis: an epidemic of oligoarticular arthritis in children and adults in three Connecticut communities. Arthritis and Rheumatism 1977, 20: 7–17.
2. **Steere AC, Gibotsky A, Patarroyo ME, Winchester RJ, Hardin JA, Malawista SE:** Chronic Lyme arthritis. Clinical and immunogenetic differentiation from rheumatoid arthritis. Annals of Internal Medicine 1979, 90: 896–901.
3. **Steere AC, Shoen RT, Taylor EBA:** The clinical evolution of Lyme arthritis. Annals of Internal Medicine 1987, 107: 725–731.
4. **Lawson JP, Steere AC:** Lyme arthritis: radiologic findings, Radiology 1985, 154: 37–43
5. **Szer IS, Taylor E, Steere AC:** The long-term course of Lyme arthritis in children. New England Journal of Medicine 1991, 325: 159–163.
6. **Yoshinari NH, Reinhardt BN, Steere AC:** T cell responses to polypeptide fractions of *Borrelia burgdorferi* in patients with Lyme arthritis. Arthritis and Rheumatism 1991, 34: 707–713.
7. **Steere AC, Dwyer E, Winchester RJ:** Association of chronic Lyme arthritis with HLA-DR4 and HLA-DR2 alleles. New England Journal of Medicine 1990, 323: 219–223.
8. **Dattwyler RJ, Volkman DJ, Halperin JJ, Luft BJ:** Treatment of late Lyme borreliosis – randomised comparison of ceftriaxone and penicillin. Lancet 1988, i: 1191–1194.
9. **Corpuz M, Hilton E, Lardis MP, Singer C, Zolan J:** Problems in the use of serologic tests for the diagnosis of Lyme disease. Archives of Internal Medicine 1991, 151: 1837–1840.
10. **Schwartz BS, Goldstein MD, Ribeiro JMC, Schulze TL, Shaled SI:** Antibody testing in Lyme disease. A comparison of results in four laboratories. Journal of the American Medical Association 1989, 262: 3431–34.
11. **Ma B, Christen B, Leung D, Vigo-Pelfrey C:** Serodiagnosis of Lyme borreliosis by Western immunoblot: reactivity of various significant antibodies against *Borrelia burgdorferi*. Journal of Clinical Microbiology 1992, 30: 370–376.
12. **Grodzicki RL, Steere AC:** Comparison of immunoblotting and indirect enzyme-linked immunosorbent assay using different antigen preparations for diagnosing early Lyme disease. Journal of Infectious Diseases 1988, 157: 790–797.
13. **Zöller L, Burkard S, Schafer H:** Validity of Western immunoblot band patterns in the serodiagnosis of Lyme borreliosis. Journal of Clinical Microbiology 1991, 29: 174–184.
14. **Craft JE, Grodzicki RL, Steere AC:** Antibody response in Lyme disease: evaluation of diagnostic tests. Journal of Infectious Diseases 1984, 149: 789–795.

Native Valve Endocarditis Caused by *Staphylococcus capitis*

Staphylococcus capitis, a coagulase-negative staphylococcus, is part of the normal flora of the skin of the human scalp, forehead, eyebrows, face, neck and ears (1, 2). Recently, three cases of en-