SEROPREVALENCE OF HIV INFECTION IN PATIENTS WITH POSITIVE SYPHILIS SEROLOGY

SIFILIZ SEROLOJISI POZITIF HASTALARDA 'HIV' SEROPREVALANSI

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ABSTRACT
Objective: The aim of the study was to investigate Human Immunodeficiency Virus (HIV) seroprevalence in patients with positive syphilis serology.

Materials and methods: 105 (8.4%) samples, which were found positive with the rapid plasma reagin (RPR) and/or the Treponema pallidum hemaggulination assay (TPHA) tests, were also tested with the anti-HIV-1/2 quick test (INSTI HIV1/HIV2 Antibody Test, Bartel Inc. USA) for the detection of HIV, any sample that gave positive result, was submitted to enzyme linked immuno-sorbent assay (ELISA) (Behring Diagnostics, Marburg), and then western blot (WB) (HIV BLOT 2.2, Diagnostic Biotechnology Ltd. USA) as confirmatory test. The samples with positive results were also tested with the Serodia Treponema pallidum particle agglutination (TPPA) (Serodia-TPPA, Fujirebio Inc., Japan); the Murex Syphilis ICE (ICE), IgG+IgM (ELISA), (ICE Syphilis Detection Pack, Murex Biotech Limited, Dartford, UK); the Enzywell TP (TP), IgG+M (ELISA) (DIESSE, Sienna, Italy); the Captia Syphilis-M (CS-M) (IgM) (ELISA) (Captia™Syphilis-M, Trinity Biotech plc, Ireland) and the fluorescent treponemal antibody absorption assay (FTA-abs) tests (Mastaflour™-FTA-ABS, Mast Diagnostics, UK) as other specific treponemal tests.

Results: Two RPR positive TPHA negative patient sera were found as HIV seropositive with the ELISA and WB tests. Additionally, in these samples all other specific tests as the TPPA, ICE, TP, CS-M and the FTA-abs tests were found as negative. So, these two anti-HIV positive sera were evaluated as biologic false-positive (BFP) reaction of syphilis. Non of the sera with positive syphilis reaction was found as positive for anti-HIV reaction.

Conclusion: Because patients who have acquired a sexually transmitted disease (STD) have demonstrated their potential risk for acquiring HIV infection all patients with syphilis serology positive should be counseled concerning the risk of HIV.

Key words: Syphilis serology, HIV seroprevalence, BFP reaction.
The incidence of syphilis has increased significantly during the last decade, along with that of other sexually transmitted diseases (STDs) that include Human Immunodeficiency Virus (HIV) (8,30,40). Syphilis as well as other genital ulcer diseases may increase the risk of the acquisition and transmission of HIV, but also individuals with non-ulcerative STD are at increased risk for acquiring HIV since risk factors for acquiring STDs are similar, co-infections are common (1,13,25,28). Nontreponemal serologic tests for syphilis measure antibodies against cardiolipin-lecithin-cholesterol antigens. Biologic false-positive (BFP) reactions may occur transiently because of acute febrile illnesses, pregnancy, or immunization while persistently false-positive tests have been associated with collagen vascular diseases, injecting drug use and other hypergammoglobulinemia states (12,31). An unusually high incidence of biologic false-positive test results of syphilis in patients with HIV infection has been discussed (2,9,20,21,33). Syphilis serologic tests may not be a sensitive marker of prior syphilis infection in individuals with HIV infection, and it has been reported that syphilis shows atypical clinical and serological courses in HIV infected patients. Also loss of reactivity to treponemal tests is reported to occur in up to 38% of symptomatic HIV seropositives while none of the HIV seronegative individuals lost reactivity to a treponemal test. The molecular basis of the antibody/antigen reactions is not yet known(11,18,32,34,36).

The main aim of the study was to investigate HIV seroprevalence in patients with positive syphilis serology. It was also to have in account the possibility of false-positive result for Rapid Plasma Reagin (RPR) test in anti-HIV positive patients.

MATERIALS and METHODS
Serum collection: 1246 sera from patients attended Department of Microbiology and Clinical Microbiology, Istanbul Faculty of Medicine, during the period 1997-1998 (April) have been screened. All sera were tested by the Rapid Plasma Reagin (RPR) (RPR carbon, Reactivos spinreact, Gerona) and the Treponema pallidum Hemagglutination Assay (TPHA) (Microspyth™-TP 200, Shield diagnostics, U.K.) for serodiagnosis of syphilis. All samples which have positive result with the RPR and/or TPHA tests were stored at −70∞C.

Tests: The RPR test was performed qualitatively. Typically, a quantitative TPHA is performed at a unique serum dilution of 1: 80. All reactive samples were subsequently tested to determine the end dilution titers by the 1: 10240. Additionally, all 105 serum samples which were positive with the RPR and/or TPHA tests were tested with anti-HIV-1/2 quick test (INSTI HIV1/HIV2 Antibody Test, Bartel Inc. USA), single use rapid assay for the detection of antibodies to Human Immunodeficiency Virus Type I and II (HIV-1/2). Any positive results were submitted to enzyme-linked immunosorbent assay (ELISA) (Behring Diagnostics, Marburg). The positive result of one sample was confirmed with Western Blot (WB) confirmatory test (HIV BLOT 2.2, Diagnostic Biotechnology Ltd. USA). It has been also tested further by the Serodia Treponema pallidum Particle Agglutination (TPPA) (Serodia-TPPA, Fujirebio Inc., Japan); the Murex Syphilis ICE (ICE), IgG+IgM enzyme immunosorbsent assay (ELISA) (ICE Syphilis Detection Pack, Murex Biotech Limited, Dartford, UK); the Enzywell TP (TP), IgG+M (ELISA) (Diese, Sienna, Italy); the Captia Syphilis-M (CS-M) (IgM) (ELISA) (Captia’Syphilis-M, Trinity Biotech plc, Ireland), and the Fluorescent Treponemal Antibody absorption (FTA-abs) assay (Mastaflour%–FTA-ABS, Mast Diagnostics, UK) which detects both IgG and IgM for the presence of antibodies reacting with specific Treponema pallidum antigens. All tests were performed and evaluated according to the manufacturer’s instructions. Additionally, just after the period, another patient serum with anti HIV (+) by ELISA and WB was also tested with the RPR, TPHA, TPPA, ICE, TP, CS-M, and FTA-abs tests for serodiagnosis of syphilis.

RESULTS
During the study period, 105 (8.4%) sera out of 1246 have been found positive with the RPR and/or TPHA tests. Thirty eight (36 %) of them were obtained from women, 67 (64 %) were from men. All these 105 sera were tested with Anti-HIV-1/2 quick test screening for serodiagnosis of acquired immunodeficiency syndrome (AIDS). Only one patient’s serum (0.95%) with the RPR test positive and the TPHA test negative was found as HIV seropositive with the ELISA and then with the WB tests. When this serum was investigated in detail, with the TPPA, ICE, TP, CS-M, FTA-abs tests for serodiagnosis of syphilis, it was found that all tests were negative. So RPR test result was concluded as biological false-positive (BFP) reaction (40). Just after this evaluation, another patient’s serum with anti HIV (+) by ELISA and WB tests was evaluated as BFP reaction, because of positive RPR but negative TPHA, TPPA, ICE, TP, CS-M, FTA-abs tests results. All together, two anti-HIV positive sera were found as BFP. These two patients were heterosexual man and had clinical manifestation of AIDS who were on treatment.

DISCUSSION
Treponema pallidum and HIV are both sexually transmitted agents of infectious diseases with epidemiological similarities, and therefore co-infect the same host (26). The presence of genital ulcerative disease is also an important risk for the acquisition of HIV infection because of providing a possible portal of entry or exit for HIV (27,35). For women with genital ulcers, a 3.3-fold increase in the risk of acquiring HIV has been shown.
in Kenya (19). In a study about correlation between syphilis and HIV infection, it is reported that whether the prevalence of lower genital tract infections among HIV-seropositive women’s was higher than among high-risk HIV-seronegative women, and syphilis was more prevalent among HIV-seronegative women (8% vs. 6%) (4). The elevated risk of HIV-1 infection among patients with syphilis supports the hypothesis that syphilis enhances the sexual transmission of HIV-1 (24,29). In another study, in the summary of the experience with baseline STDs among high-risk youth with and without HIV infection from US, they screened for syphilis and found totally 28/334 (8.3%) HIV infected and 6/157 (5%) HIV uninfected adolescents (aged 12-19 years) by RPR or by history, as a result syphilis was more common among HIV infected than HIV uninfected (38). In another study in which 8932 cornea donors were screened, 103 (1.15%) had reactive screening for syphilis serology and 35 (0.39%) were HIV-1 seropositive. No donor with positive syphilis serology by the Venerial Disease Research Laboratory (VDRL) or RPR and FTA-abs or microhemagglutination-Treponema pallidum was also HIV-1 seropositive (10). Additionally, it is reported that, HIV-positive donors had an increased risk for being positive for syphilis antibodies (28). According to our results, poor correlation between positive syphilis serology and HIV seroprevalence has been found. HIV infection may modify the clinical presentation (15), or course of syphilis (23). The relationship between HIV clinical disease stage and syphilis serology is unclear. The situation is further complicated by high VDRL titers in HIV patients leading to the prozone phenomenon (16). A study performed among 4863 patients, confirmed that BFP reactions are more common in HIV-positive patients, 4% versus 0.8% of HIV-uninfected patients (31). HIV infection may affect the serological response to syphilis, which may be either enhanced or decreased (5,42). In a study, 5% of the samples gave false positive and high titer results with VDRL in HIV (+) males (7). In another study, it is reported that nonspecific screening methods, and perhaps even the specific treponemal tests, are not enough to exclude syphilis in HIV-infected individuals because of false-reactions, and suggest that to apply Western-blot to investigate the inconsistencies for syphilis (14). In another study, it is reported that in 7 cases both HIV and RPR were positive, but 5 of them were negative by FTA-abs, so 5(1.4%) were evaluated as BFP reaction (6). Additionally, it is reported that serological findings (both RPR and TPHA) may be altered in the presence of HIV infection (9). It is concluded that the Capita Syphilis G enzyme immuno assay (ELA) were of similar specificity and sensitivity in HIV-positive patients as a marker of past syphilis in HIV infected patients (41). In our phenomenon, in two sera with HIV-positive RPR test was reactive, but TPHA and other treponemal tests done were non-reactive. This might account for nonspecific immunoglobulins that could react with the RPR test, or might diminished response of antibodies to various treponemal antigens. It is reported that non-specific screening methods, and perhaps even the specific treponemal tests are not enough to exclude syphilis in HIV-infected individuals (9). On the other hand, it is reported that, HIV-positive donors had an increased risk for being positive for syphilis antibodies (28). In a study, about correlation between syphilis and HIV infections of 8932 cornea donors screened, 103 (1.15%) had reactive screening for syphilis serology and 35 (0.39%) were HIV-1 seropositive. No donor with positive syphilis serology by VDRL or RPR and FTA-abs or microhemagglutination-Treponema pallidum was also HIV-1 seropositive (10). According to our results, poor correlation between positive syphilis serology and HIV seroprevalence had been found. The main reason of this is that HIV seroprevalence was low in Turkey especially at that period when the study samples were collected. It is reported that anti-HIV seroprevalence was 0.001% in 1,773,943 donors between 1987 and 2003 (17). Another reason may be that sera with positive syphilis serology were not collected from high-risky individuals for HIV, such as males who have engaged in homosexual activity and intravenous drug users. For example, there is a reported rate of 6% for anti-HIV1/2 in intravenous narcotic addicts (39). In summary, all syphilis patients should be counseled concerning the risk of HIV because patients who have acquired an STD have demonstrated their potential risk for acquiring HIV infection. For that reason, it is recommended that all patients with syphilis positive sera have to be investigated for HIV and all patients who have HIV positive sera have to be investigated for syphilis (3,4,22,37).

REFERENCES


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