Tropical Medicine and International Health

VOLUME 10 NO 1 PP 58–64 JANUARY 2005

Evaluation of syphilis in patients with HIV infection in Nigeria

E. N. Nnoruka[1] and A. C. J. Ezeoke[2]

1 *Department of Dermatology, University of Nigeria Teaching Hospital, Enugu, Nigeria*
2 *Department of Chemical Pathology, University of Nigeria Teaching Hospital, Enugu, Nigeria*

Summary

OBJECTIVE To document the manifestations of syphilis among patients with concurrent HIV infection over a 12-month period.

METHOD Descriptive, cross-sectional, hospital-based study of all adult patients with syphilis and HIV infection who attended the skin clinic of the University of Nigeria, Teaching Hospital, Enugu, between July 2000 and June 2001. A standardized questionnaire was used to record age, sex, marital status, occupation and risk factor for HIV infection; initial site of onset of rash/ulcers, duration of the illness, any concomitant affection of mucosa, hair and nails as well as treatments received by each patient prior to presentation. Morphological distribution of lesions, mucosal surface (conjuctival, vulval and rectal) examinations and documentation of concomitant disorders with HIV were noted by the examining dermatologist. Lesional biopsy and dark-field microscopy were undertaken to confirm diagnosis where serologic (non-treponemal and treponemal specific) tests for syphilis were inconsistent with clinical suspicion. Each patient had a routine chest x-ray, mantoux and purified protein derivative (PPD) status taken.

RESULTS Thirty-one patients (21 males) with concurrent syphilis and HIV were seen during the study period. Primary syphilis was diagnosed in nine (29%), secondary syphilis in 20 (64.5%) and latent syphilis in two (6.5%). Neurosyphilis was not observed. Prevalence of syphilis for these patients with concurrent HIV was 2.1%. Mean duration of syphilis was 3.9 months ± 1.4 and lesions of greatest concern occurred mainly on the genitalia. The glans penis was affected in 10 (32.3%) cases, the penile shaft in seven (22.6%), the oral cavity in five (16.1%), the rectum in six (19.4%) and the vulva in three (0.9%) cases. Nine (29.1%) patients had a history of primary syphilitic chancre, 19 (61.3%) had a past history of sexually transmitted disease (STD) – particularly genital ulcers – while three (9.7%) could not recall any past history of STD. Eighteen (59.3%) had a history of unprotected sex, 16 (51.7%) had multiple sexual partners, four (13.3%) had had oral sex, and one anal sex (3.3%); none admitted to being bisexual. Other relevant risk factors for HIV transmission were blood transfusion within 5 years for three (9.7%) and intravenous drug use in two (6.5%). Some patients had more than one condition as a potential source of exposure. Serological tests were weakly reactive in 17 (48.4%), strongly reactive in nine (29%) and non-reactive in five (16.1%) patients. Three patients exhibited prozone phenomenon. Treatment comprised the syndromic approach, which currently is advocated for use in primary healthcare centres without facilities for aetiological diagnosis of sexually transmitted infections.

CONCLUSION Our cases with concurrent syphilis and HIV/AIDS had unusual manifestations, responded to treatment more slowly and died sooner than cases described in Western literature due to generally lower levels of health.

keywords HIV/AIDS, syphilis associations, serology, syndromic management, West Africa

Introduction

Syphilis is a bacterial infection caused by the spirochaete *Treponema palladium*, usually sexually transmitted. The disease can infect any organ and if untreated progresses through three stages. The primary chancre of syphilis and the secondary stage with its widespread skin and mucous membrane manifestations provide the greatest likelihood for contagion. The risk of acquiring syphilis from an infected partner ranges from 30% to 51% (Wasserheit 1992; Centers for Disease Control and Prevention 1998) while the number of exposures, type of sexual activity, and morphology and distribution of the infectious partner's lesions are responsible for the variability in infectivity of syphilis (Centers for Disease Control and Prevention 1998).

Syphilis is often the presenting infection of patients with concurrent HIV infection and numerous epidemiologic and

biologic studies have shown that ulcerative and non-ulcerative sexually transmitted diseases (STDs) enhance HIV transmission (Wasserheit 1992; Clottey & Dallabetta 1993). When syphilis occurs in an HIV-infected individual, the clinical course, laboratory diagnosis and response to therapy may be altered. Cases of syphilis with concurrent HIV gained widespread attention after a 1987 case series described HIV-infected patients whose syphilis infection was either refractory to appropriate therapies or displayed a rapid progression from primary syphilis to neurosyphilis (Johns *et al.* 1987; Wasserheit 1992). Unusual manifestations of syphilis in HIV cases have been reported ever since then.

Syphilis and HIV infection are both sexually acquired. HIV alters the natural history of syphilis as it does for some STDs (Clottey & Dallabetta 1993; Fleming & Waserheit 1999) and other diseases caused by HIV associated immune deficiency. Past syphilitic infection has also been reported as being more prevalent among patients who are homosexual, bisexual or intravenous drug users with AIDS than in the general populace (Quinn *et al.* 1988).

Ultimately, infection with one STD is a primary risk factor for a second one because in most cases similar behavioural risk factors are involved. Sexual surveys conducted over a 10-year period in Nigeria, using antenatal clinic attendees as proxy for the general population, revealed an ever increasing prevalence of HIV since 1986 when the first case was reported in Nigeria (Federal Ministry of Health, Nigeria 2001; MoHW 2001). The prevalence of HIV as of 2001 is 5.8% while the median prevalence of HIV among STI patients is 11.5% (Federal Ministry of Health, Nigeria 2001). In developing countries, reliable incidence figures on sexually transmitted infections (STIs) are scarce, although there are numerous prevalence surveys from different settings in Nigeria. These are mainly clinic-based and give a current syphilis prevalence of 2.3% (Federal Ministry of Health, Nigeria 2001; MoHW 2001). Our skin clinic, as all other healthcare institutions in Nigeria, is currently faced with an increased prevalence of HIV/AIDS as well as concomitant syphilis and other STIs. This study focuses on the manifestations of syphilis in patients with concurrent HIV.

Materials and methods

Thirty-one adult patients with syphilis and concurrent HIV who attended the skin clinic of the University of Nigeria, Teaching Hospital, Enugu, between July 2000 and June 2001 were involved in this cross-sectional hospital-based study. All patients gave informed consent before recruitment into the study. For data collection a standardized questionnaire was used and serological examinations for syphilis and HIV were conducted. We recorded age, sex, marital status, occupation and risk factor for HIV infection; initial site of onset of rash/ulcers, duration of the illness, any concomitant affection of mucosa, hair and nails as well as treatments received by each patient prior to presentation. The morphology, distribution of lesions and concomitant disorders associated with HIV were also noted by the examining dermatologist.

Manifestations of syphilis

Patients with syphilis and HIV infection have a number of unusual features apart from the classical presentation. In primary syphilis, which can be genital or extragenital, the presence of papulo-ulcerative lesions (chancre) at the site of infection associated with regional lymphadenopathy, is typical. Clinical presentations were regarded as atypical for primary syphilis if the chancres were multiple, painful or ragged.

Secondary syphilis presents as a rash or mucocutaneous lesions, usually papulosquamous, and associated with lymphadenopathy. Although classical secondary syphilis can occur in the HIV-infected, patients can progress from primary to tertiary stage in a matter of weeks (Gonzalez & Rhodes 1987). We suspected atypical secondary syphilis if the rashes were bullous, widespread or showed associated epidermal changes such as scaliness. Criteria for a diagnosis of tertiary syphilis included the involvement of cardiac, neurologic, ophthalmic, auditory or gummatous lesions.

Determination of severity of manifestation

Severe manifestations in our patients included the presence of either classical or atypically occurring lesions that were exaggerated or widespread; rarely painful or widespread bullous lesions, particularly for secondary syphilis. Lesions were plotted out on a body diagram and results were recorded as severe if there was ≥50% surface area involvement and as erythrodermic when more than 90% of the body surface area was affected in addition to an underlying erythema.

Laboratory investigations

Laboratory studies included syphilis screening by Venereal Disease Research Laboratory (VDRL) test, Rapid Plasma Reagin test (RPR), *Treponema pallidium* haemaglutination assay (TPHA); enzyme-linked immunosorbent assay (ELISA), Western blot and $CD4^+$ count for HIV. When serologic tests for syphilis were inconsistent with clinical findings, additional investigations were carried out to help

confirm the diagnosis, such as lesional biopsy and dark-field microscopy. Seronegativity may be an artefact in some instances, such as the prozone phenomenon (Taniguchi *et al.* 1995). In others, no antibody is present or it could be late recurrence, such as new onset or recurrent neuro-syphilis or recrudescent cutaneous secondary syphilis after standard regimens of antibiotic therapy. Hence tissue examination in diagnosing syphilis in patients with HIV infection is essential. Lumbar puncture was mandatory in cases of rapidly accelerated course of syphilis, with progression to tertiary syphilis within a few weeks or months of the initial infection. All patients had a chest X-ray, mantoux and PPD status taken.

Adequate response to treatment

Benzathine penicillin 2.4 million units intramuscularly, as two injections at separate sites was given, and repeated for two more doses, at weekly intervals. Patients were followed up clinically and serologically using the non-treponemal and TPHA tests every 3 months for a year. For cases with chancre, treatment was combined with the syndromic approach for the treatment of genital ulcer diseases, which includes treatment with drugs against other possible common causes of genital ulcers in our environment (in accordance with the Federal MOH for Nigeria recommendations, 2001).

Treatment was regarded as adequate when post-treatment values of VDRL/RPR and TPHA had dropped fourfold within 6–12 months and clinical signs or symptoms of active syphilis had cleared. Frequent post-treatment examinations with serologic testing were conducted to assure declining titres by 3 months, non-reactivity by 6–12 months, and re-treatment where titres failed to decline (Centers for Disease Control 1993).

Statistical analysis

All analysis was performed using the Statistical Programme for Social Sciences (SPSS) package, with a 95% confidence level. The prevalence of clinical and laboratory characteristics in patients were reported as percentages.

Results

A total of 31 patients with concurrent syphilis and HIV were seen during the study period. Twenty-one (67.7%) were males (Table 1). The age group 15–47 years was the most affected. They accounted for 61.3% of patients with syphilis and HIV in this study. All HIV infections were HIV type-1. The prevalence of syphilis amongst our patients with concurrent HIV was 2.1% and the mean duration of syphilis infection was 3.9 months. Lesions of greatest concern to the patients occurred mainly on the genitalia.

Table 1 Sex distribution of 31 patients with syphilis and HIV

	Male	Female
Syphilis and HIV/AIDS	21 (67.7%)	10 (32.3%)
Mean age (years)	29 ± 3	23 ± 7
$CD4^+$ count/mm^3	103	88

Types of manifestations

Primary syphilis was diagnosed in nine (29.0%) cases, secondary syphilis in 20 (64.5%) cases while two (6.5%) had latent syphilis. The glans penis was affected in 10 (32.3%) cases, the penile shaft in seven (22.6%), the oral cavity in five (16.1%), the rectum in six (19.4%) and the vulva in three (0.9%) cases. There was a significant difference by gender, the prevalence being higher in males than females ($P > 0.001$).

Nine patients (29.1%) had a history of primary syphilitic chancre, 19 (61.3%) had a history of STD, particularly genital ulcers, and three (9.7%) could not recall any past STD. Risk factors included unprotected sex in 18 (59.3%), multiple sexual partners in 16 (51.7%), oral sex in four (13.3%), anal sex in one (3.3%) case; none admitted to being bisexual. Other relevant risk factors for HIV transmission were blood transfusion within the past 5 years in three cases (9.7%) and intravenous drug use in two cases (6.5%). Some patients had more than one condition as a potential source of exposure.

Table 2 shows the clinico-epidemiologic features of syphilis of our patients. The disease affected the glabrous skin in 17 (54.8%), mucosa in eight (25.8%), while 13 (41.9%) had several sites affected simultaneously.

Severity of manifestations

Eleven patients (35.5%) presented with lesions that were no different from those of syphilis mono-infection cases amongst the general populace; 16 (51.6%) patients presented with florid and unusual lesions that affected more than 50% of their body; and four (12.6%) had extensive bullous lesions. Papulo-ulcerative chancres were seen at the various sites of inoculation in nine (29%) patients with primary syphilis, who also had associated regional lymphadenopathy. These chancres were atypical in appearance, multiple in seven (22.6%) and painful and ragged in two (6.5%) patients.

Skin rashes observed amongst those with secondary syphilis were mainly exaggerated papulosquamous

Table 2 Clinico-epidemiological features of syphilis in the study group ($n = 31$)

Pattern of syphilis	No. of patients (%)	Site at onset	Clinical category
Cutaneous			
Glaborous skin	19 (61.3)	Trunk 9	HIV
		Upper limbs 10	HIV symptom
Hair loss	3 (9.7)	Trunk 2	HIV
		Upper limbs 1	AIDS
Palms and soles of feet	15 (48.4)	Extremities 11, trunk 4	AIDS
Mucosal			
Oral (lips)	9 (29)	Extremities 3, lips 3	HIV
		+Trunk 3	HIV symptom
Buccal (mouth)	7 (22.6)	Roof of the palate 3, extremities + trunk 4	HIV
Anal (condylomata lata)	5 (16.1)	Extremities + trunk 1, anal verge 4	HIV symptom
Genitalia*	13 (41.9)	Glans penis 9 or shaft of penis 4	HIV
Multiple combined sites	27 (87.1)	Trunk ± extremities	HIV
		±Anus 9	AIDS
Oral + genitalia	12 (38.7)	Genitalia 7 ± lips 5	HIV
Cutaneous + mucosal + genitalia	17 (54.8)	Trunk 7 ± genitalia 5, Extremities 5	HIV symptom
Others	3 (9.7)	Generalized 3	Full blown AIDS

* Patients had more than one site affected and also had more than one lesion.

eruptions found on the trunk and extremities, affecting the palms and soles of the feet as well in 16 (51.6%) patients and bullous/vesicular in four (12.9%). These lesions usually covered more than 50% of the body. As new lesions continued to erupt, central necrosis developed on the older ones. However five (16.1%) patients had associated epidermal changes ranging from slight scaling to crusting minimally sparing the palms, soles and mucosa with associated regional lymphadenopathy. Two (6.5%) patients had nodules with central necrosis and impetiginization on the chest wall and trunk. Lesions on the palms and soles of the feet of these patients on presentation were annular erythematous and hyperpigmented. A punched out ulcer was also observed on the left side of the soft palate. The coexistence of this muco-cutaneous gummatous lesion on the soft palate (characteristic of tertiary syphilis) with lesions of early and advanced secondary syphilis suggests rapid progression of syphilitic disease in this patient.

Serological investigations revealed 17 (48.4%) weakly reactive (titre of 1:2) cases, nine (29%) strongly reactive (titre of 1:16 and above), five (16.1%) non-reactive patients. These five were those with clinical features of syphilis that failed to test positive to both VDRL and RPR, while TPHA was repeatedly non-reactive in three. Serial dilution of sera of these three yielded positive results (prozone pheneomenon). Further testing (dark field examination and biopsy) also confirmed the diagnosis of all.

Antibodies for HIV were positive by both ELISA and Western blot analysis and all patients were HIV-1 positive. Dark field examination of exudates from skin lesions/ulcers showed spirochetes in 29 (93.5%) patients and biopsies from non-necrotic skin lesions of all patients confirmed secondary syphilis based on the presence of superficial and deep perivascular infiltrates of macrophages, lymphocytes and plasma cells with a lichenoid pattern in some sections. Numerous granulomas were present in a few, with both giant cells and epitheliod cells within the dermis. Warthin-Starry stain for treponemas was also positive. In those three patients with features in keeping with latent syphilis, cerebrospinal fluid analysis yielded nothing of significance, protein levels were within normal range, cells were not present and VDRL was negative.

Treatment response

Treatment given to syphilitic patients with retroviral disease was benzathine penicillin 2.4 mega given intramuscularly and three times at weekly intervals. Alternative treatment given to one of the patients with penicillin allergy was doxycycline 100 mg orally twice-daily for 15 days. Patients were followed up clinically and serologically using the non-treponemal test, and TPHA were performed every 3 months. For those with chancre, treatment was combined with the syndromic approach for the

treatment of genital ulcer diseases. Only 10 patients (32.3%) were followed through to the end of the study, 11 (35.5%) cases were lost to follow-up and the remaining 10 cases (32.3%) were reported dead.

Several limitations hindered monitoring of treatment amongst our patients. Ten (32.3%) were presumed to have taken their medication, although not at the prescribed times/periods, based on lack of funds (for drugs and transportation). This may have been a major drawback for all of our patients. As drugs were not always administered during the follow-up period, some patients did not feel compelled to attend.

Of these 10 patients, five (50%) were cured as their initial VDRL and RPR were weakly reactive at 3 and 6 months and by 9 and 12 months both VDRL and RPR became non-reactive, while their TPHA titres showed a steady fourfold drop. Three (9.7%) had high unresponsive titres (VDRL, RPR and TPHA titres) throughout the study period and two (6.5%) patients were not cured at all (based on both deteriorating clinical picture and laboratory findings). In view of the small number of patients recorded during the treatment and follow-up period, we did not statistically analyse the treatment response.

Discussion

Syphilis is often the presenting infection of patients with concurrent HIV infection. However, it is not considered as an opportunistic infection, nor is it included among the diseases diagnostic of HIV infection (Centers for Disease Control 1987; Tremont 1987). In HIV patients, syphilis appears to progress more rapidly through its clinical stages, often having an atypical clinical presentation. Only few of our HIV co-infected cases had clinical presentations typical of individuals with syphilis mono-infection. Most of our cases' manifestations were florid and unusual, particularly amongst those patients with advanced HIV infection. Extensive or multiple chancres were seen in seven of the nine cases with primary syphilis. These chancres/ulcers could have been altered as well by coexistence of herpes simplex, particularly for those with painful punched out ulcers on their genitalia. Those with secondary syphilis had gross involvement of the entire skin with an exaggerated papulosquamous rash as well as granulomatous warty ulcers in the anal region and condyloma lata scattered on their perineum. One patient exhibited the coexistence of a mucocutaneous gummatous lesion on the soft palate characteristic of tertiary syphilis with lesions of early and advanced secondary syphilis suggesting a rapid progression of syphilitic disease within a very short time.

Cell-mediated and humoural immunity plays a role in the immunologic response to syphilis. HIV infection is associated with numerous immunologic abnormalities, including profound defects in macrophage function. In addition, peripheral CD4 (helper) lymphocytes from patients with AIDS have a decreased ability to assist B cells in the production of immunoglobulins (Tremont 1987; Leishman 1988). Reactivation of treponemal infection has been known to occur in the presence of HIV, despite presumed adequate treatment in the past for individuals exposed previously to syphilis. This may have applied to some of the 19 patients with a past history of STD who presented with secondary syphilis rapidly.

Routine serologic tests (VDRL, RPR) for syphilis amongst our patients gave varied responses and could not be relied upon for active disease, particularly for those that were seronegative on presentation. Further investigations such as dark field microscopy examination and histopathologic examinations were then carried out. This is very useful particularly in developing countries where facilities for the more precise tests such as flourescent treponema antibody absorption test and microhaemaglutination assay for antibodies to *Treponema pallidium* are not readily available. Some patients who were seronegative (for syphilis) and yet had syphilis (secondary syphilis) were considered to have advanced immunosuppression as reflected by their CD4 counts, which ranged between $\leq 150 \pm 11.3$ cells/mm^3. This is in keeping with other studies that have shown defects in antibody responses to infections amongst HIV-infected patients (Bowen *et al.* 1985) particularly amongst HIV-infected men with Kaposi's sarcoma and secondary syphilis (Hicks *et al.* 1987). Most of these men were found to be highly infectious for syphilis and simultaeneously seronegative and immunodeficient. A similar picture of seronegativity could be obtained in early primary syphilis.

Three of the five patients had non-treponemal non-reactive tests, their undiluted serum samples with high antibody titres failed to react initially because of the antibody excess (prozone effect). These also failed to show titre drops even after repeated treatment. This could also have been because of advanced immunosuppression, with B-cell dysregulation accounting for the delayed serologic titre response after syphilis treatment. Usually, the normal biologic response should be a fourfold drop after treatment within 3 months.

Most patients could not be followed up. Some may have defaulted after confirmation of their diagnosis/illness for fear of being discriminated against. Others (11, 35.5%) failed to keep their appointments 5–7 months (mean 6.1 ± 3 months) after treatment because of poverty and abandonment by family members due to the stigma associated with HIV/AIDS in Nigeria.

Neurosyphilis was not observed in this study, probably because our patients died faster than those reported in Western literature (Leishman 1988; Gregory *et al.* 1990) because of generally poorer levels of health. Ten cases (32.3%) were reported dead.

In poor tropical areas and developing countries in Africa, the best treatments of STDs are standardized and syndromic. The syndromic approach is excellent for urethral discharge and genital ulcers. However, it is clear that the specificity of this approach is debated in vaginal discharge (Over & Piot 1993). The syndromic approach recommends standard treatment schemes according to the clinical symptoms of genital discharge, genital ulcerations, and vaginal discharge in regard to each locality/country. This approach was therefore used for the majority with syphilitic chancres as well as those with secondary syphilis particularly high-risk cases because syphilitic infection and the presence of a chancre are risk factors that predispose to HIV infection. Most of our patients were unaware of the fact that they also had HIV. One patient said during his counselling session that he could not have HIV because he felt that 'HIV was the junior brother to gonorrhoea' and after all he only had a tiny ulcer on his glans. Currently, in Nigeria the syndromic approach is being integrated into primary healthcare centres as a means of treatment of STIs/ prevention of HIV/AIDS. In this era of attention to HIV infection, the 'other' STDs have escalated. Antimicrobial therapy for bacterial STDs such as syphilis is associated with cure. However, screening of sexual partners and treatment is mandatory to prevent re-infection, continued spread, or both. Hopefully, this is where the syndromic approach might prove its worth for Africa.

Conclusion

Our patients with concomitant syphilis and HIV presented similarly to those reported in Western literature, but their response to treatment was much slower and they died sooner due to the generally low levels of health, such that progression to neurosyphilis was not observed. A larger number of AIDS patients is being proposed for further studies to determine if these differences are peculiar to the West African subregion or Africa as a whole.

References

Bowen DL, Lane HC & Fauci AS (1985) Immunopathogenesis of the acquired immunodeficiency syndrome. *Annals of Internal Medicine* **103**, 704–709.

Centers for Disease Control (1987) Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. *Morbidity and Mortality Weekly Report* **36** (Suppl), 3S–9S.

Centers for Disease Control (1993) Sexually transmitted diseases treatment guidelines. *Morbidity and Mortality Weekly Report* **42**, 40–44.

Centers for Disease Control and Prevention (1998) HIV prevention through early detection and treatment of other sexually transmitted diseases – United States. *Morbidity and Mortality Weekly Report* **47** (RR-12), 1–24.

Clottey C & Dallabetta G (1993) Sexually transmitted diseases and human immunodeficiency virus, epidemiologic synergy. *Infectious Disease Clinics of North America* **7**, 753–770.

Federal Ministry of Health, Nigeria (2001) STD/HIV Technical Report 1–3.

Fleming TD & Waserheit JN (1999) From epidemiological synergy to public health policy: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sexually Transmitted Infections* **75**, 3–17.

Gonzalez E & Rhodes AR (1987) Syphilis. In: *Dermatology in General Medicine*, 3rd edn. McGraw-Hill, New York, pp. 2408–2409.

Gregory N, Sanchez M & Buchness MR (1990) Clinical and laboratory studies. The spectrum of syphilis in human immunodeficiency virus infection. *Journal of the American Academy of Dermatology* **22**, 1061–1067.

Hicks CB, Benson PM, Lupton GP *et al.* (1987) Seronegative secondary syphilis in a patient infected with the human immunodeficiency virus (HIV) with Kaposi's sarcoma: a diagnostic dilemma. *Annals of Internal Medicine* **107**, 492–495.

Johns DR, Tierney M & Felsenstein D (1987) Alteration in the natural history of neurosyphilis by concurrent infection with the human immunodeficiency virus. *New England Journal of Medicine* **316**, 1569–1572.

Leishman K (1988) AIDS and syphilis. *Atlantic Monthly* **Jan**, 17–26.

MoHW (2001) *Syndromic Management of Sexually Transmitted Infections for Nigeria: Manual for Health Workers*. Abuja, Nigeria, pp. 3–38.

Over M & Piot P (1993) HIV infection and sexually transmitted diseases. In: *Disease Control Priorities in Developing Countries* (eds DT Jamison, WH Mosely, AR Measham & JL Babadilla) Oxford University Press, New York, pp. 445–529.

Quinn TC, Glasser D, Cannon RO *et al.* (1988) Human immunodeficiency virus infection among patients attending clinics for sexually transmitted diseases. *New England Journal of Medicine* **318**, 197–203.

Taniguchi S, Osato K & Hamada T (1995) The prozone phenomenon in secondary syphilis. *Acta Dermato-Venereologica* **75**, 153–154.

Tremont EC (1987) Syphilis in the AIDS era. *New England Journal of Medicine* **316**, 1600–1601.

Wasserheit JN (1992) Epidemiology synergy: interrelationships between HIV and other STDs. *Sexually Transmitted Diseases* **19**, 61–77.

Authors
Edith N. Nnoruka, Department of Dermatology, College of Medicine, University of Nigeria Teaching Hospital, PMB 01129, Enugu, Nigeria. Tel.: +234 042 452549; E-mail: nkechi_nnoruka@yahoo.com (corresponding author)
A.C.J. Ezeoke, Department of Chemical Pathology, College of Medicine, University of Nigeria Teaching Hospital, PMB 01129, Enugu, Nigeria. E-mail: alexiusezeoke@yahoo.co.uk