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A retrospective study on HIV and syphilis

Studio retrospettivo su HIV e sifilide

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INTRODUCTION

Sexually transmitted infections (STIs) are a major global health priority also because of their inter-relationships with Human Immunodeficiency Virus (HIV) infection; syphilis is among the most common of these infections and can increase the risk of getting and transmitting HIV [1-4]. Following the introduction in the mid-1940s of penicillin, the incidence of syphilis dropped significantly worldwide to reach the lowest levels in the mid 1990's [5-7]. During last years an increase in incidence, predominantly among men who have sex with men (MSM), but also among sex workers has been identified [4-6]. This increase is even higher in people with HIV infection [8, 9]. In Italy all physicians are required to report new cases of syphilis to the national register but, according to European Center for Diseases Control (ECDC) data, less than 10% of Italian physicians respect this rule [9]. Therefore the actual number of cases may be underestimated. The aim of this study is to describe epidemiological and clinical features of syphilis cases in HIV-infected patients referring to an Infectious Diseases Department in Naples from 2002 to 2011.

METHODS

We retrospectively examined the charts of 402 consecutive HIV-infected patients referring to our clinic from January 2002 to December 2011and collect their clinical data.

Syphilis diagnosis was made according to clinical features and/or standardized laboratory testing. Criteria for infection (in absence of symptoms) were serological: new evidence of RPR positivity or a threefold increase in RPR titer and/or a positivity of IgM anti *Treponema pallidum*. Reinfection was defined as a new increase in RPR titer six months later the former recovery.

On the basis of clinical findings and serological tests, untreated syphilis was classified as follows: *primary syphilis* (ulcer or chancre at the infection site, painless regional lymphadenopathy); *secondary syphilis* (clinical findings that include, but are not limited to, disseminated maculo-papular eruption with or without rush affecting the palms and soles, oral mucosal erosions, generalized lymphadenopathy); *latent syphilis* (seroreactivity without other evidence of disease) divided in early latent if there was a documented seroconversion in the last year, late latent if seroconversion was later than one year but already known and latent of unknown duration when the date of initial infection cannot be established; and *tertiary syphilis* (cardiovascular and neurological syphilis) [20].

STATISTICAL ANALYSIS

Incidence is presented as per person year and incidences of the various years were included for comparison in a linear regression model. Data are presented as mean ± standard deviation for quantitative variables distributed in

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Gaussian fashion or median (interquartile range) for those variables distributed in non-Gaussian fashion. Qualitative variables are reported as percentage.

RESULTS

Between January 2002 to December 2011, a total of 50/402 HIV-infected patients (273 males, 129 females) were confirmed to have syphilis. Thirty-two of them (64%) presented a latent syphilis of unknown duration. In 16 patients a diagnosis of early latent syphilis was made. One patient was diagnosed as primary syphilis and another one as secondary syphilis (skin rash). Two patients had a reinfection. Table 1 shows demographic, clinical, and viro-immunological features of the patients.

Figure 1 shows an increasing trend in the rate of syphilis cases x 100 person per year (PPY) during the years of the observation. This trend is at the limit of statistical significance (P=0.07). The overall rate and the number of cases increased between 2006 and 2011, with a peak in 2007 and 2008 (2.4 and 2.7 x 100 PPY respectively). None of syphilis cases presented were reported to the Italian national register.

Among cases of latent syphilis of unknown duration, 17 were concomitant with a newly diagnosed HIV infection (about 50%). The percentage has raised over time, ranging from 33% (2002) to 44% (2011) with a peak of 77.7% in 2010 (Figure 2). Only one patient came at our observation for syphilis as the main clinical problem (the one with secondary syphilis) and discovered HIV infection at the same time. Therefore, 36% (18/50) of the all syphilis infected patients had a simultaneous diagnosis of both infections.

Homosexual contacts were the most frequent routes of infection (70%).

Syphilis was predominant among patients in categories A according to CDC staging of HIV infection (68%) but four patients received simultaneous diagnosis of syphilis and AIDS (Table 2).

No patients had a clinical involvement of CNS. Therefore, no patient underwent a lumbar puncture.

Table 1 - Demographic, virological, clinical and immunological features of the overall cases of syphilis (n=50).

Age (years)	40.9±9.5
Gender	M: 91.8% F: 8.2%
Risk behaviour	Homosexual: 69.4% Heterosexual: 26.5% i.v. drug user: 4.1%
CD4 (cells/μL)	521±341
HIV-RNA (UI/mL)	530 (40-54,775)
On-treatment	53.1%

Data are presented as mean ± standard deviation for quantitative variables distributed in Gaussian fashion or median (interquartile range) for those distributed in non-Gaussian fashion. Qualitative variables are reported as percentage.

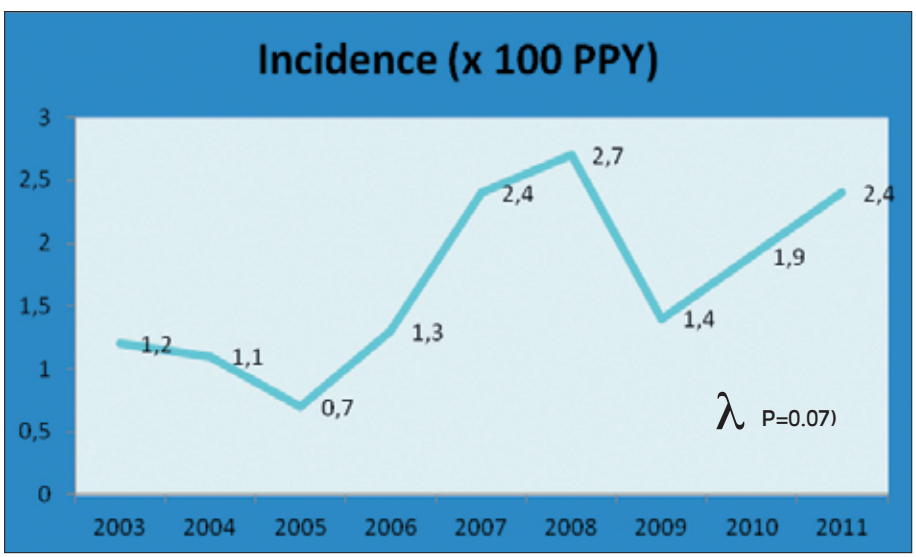

Figure 1 - Incidence of syphilis (x100 person per year) during study period.

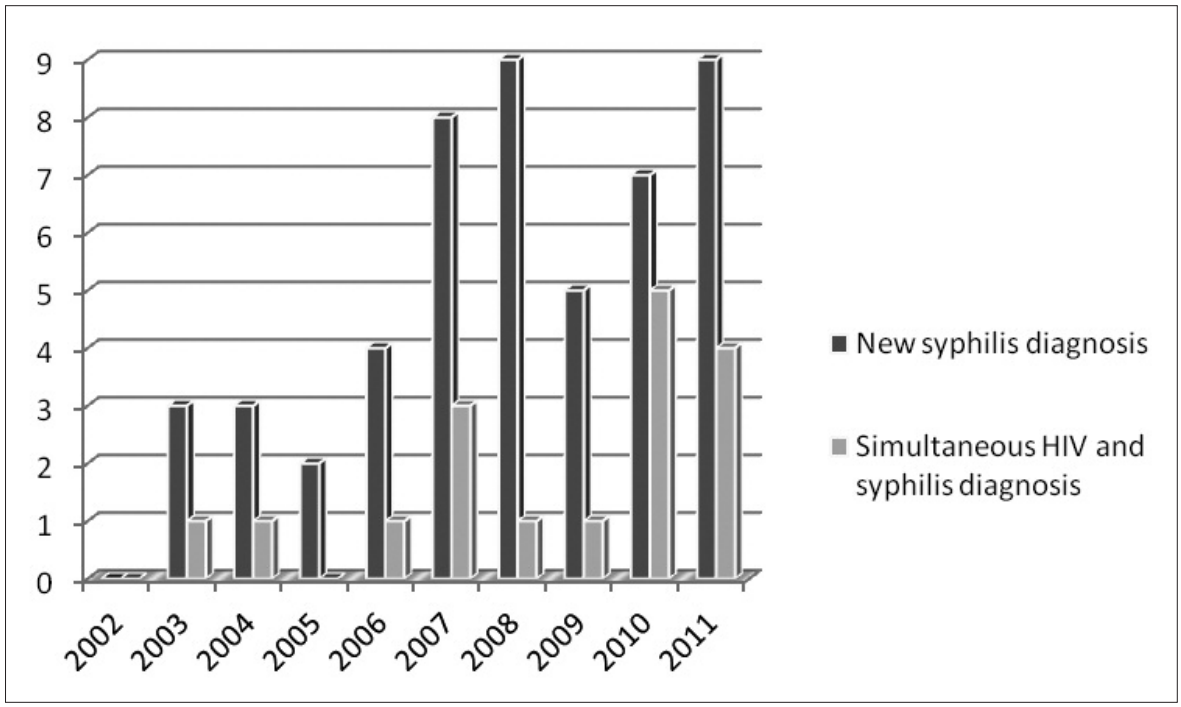

Figure 2 - HIV and syphilis simultaneous diagnosis. Dark grey bars show total number of syphilis infections; Light grey bars show number of HIV and syphilis diagnosis made at the same time.

Table 2 - Number of cases of syphilis, stratified for CDC category and simultaneous diagnosis.

Category (CDC '93)	*Cases n=50*	*Simultaneous diagnosis (n=18)*
A1	6 (12%)	3
A2	19 (38%)	10
A3	1 (2%)	0
B1	2 (4%)	0
B2	8 (16%)	1
B3	7 (14%)	0
C2	1 (2%)	0
C3	6 (12%)	4

DISCUSSION

The results of our retrospective study show a moderate increase of syphilis cases in the last five years, especially in HIV-infected persons, most of them were MSMs as reported in largest European epidemiological studies [8-9, 15].
Among patients monoinfected with syphilis, the most recent ECDC data (period 1990-2010) show that infections were more frequently discovered in MSM (55%), and three times more frequently in men than in women [9]. The overall incidence in 1990-2010 period in Europe was 4.4/100,000 people. Age distribution shows a shift towards older age of infection during the period 2000-2010. In fact, in 2000 the most represented cohort of patients was younger than 25 years, while in 2010 there was a predominance of patients older than 25 years. In contrast with our data, ECDC reports a decrease in the overall rate of new infections. However, ECDC underlines that this trend appears to be the sum of two different events: 1) a decreasing trend in four countries (Bulgaria, Romania, Latvia, Estonia) which had reported very high rates in the 1990s; 2) an increase in other countries after a decrease which had been observed until 1999. They also conclude that the increase can be due to active case detection or improved reporting, but at the same time, there is overwhelming evidence that behavioral changes, particularly among MSM, have contributed to the increasing trends in many countries [9].
The occurrence of syphilis cases in well-known HIV seropositive persons highlights the risk that the increased well-being and survival due to HAART therapy can increase at-risk sex be-

haviours which forewarn of future spread in HIV infections.
Another worrying finding of our study is the relatively high rate of simultaneous diagnosis of advanced HIV disease and syphilis that shows an unconsciousness of the risk of transmitting both infections. Our study confirms the results of an Italian survey (10). In that study 83 (56%) out of 147 HIV/syphilis coinfected patients were unaware of their HIV seropositive status. Therefore it is important to restart HIV prevention campaigns to let at-risk people more aware of persistence of sexually transmitted diseases, to reinforce the importance of early diagnosis and treatment both of syphilis and HIV infection, and to minimize the risk of transmission of these two STIs.
Finally, it is noteworthy that even our syphilis cases were not reported to the national Italian register and this confirms the underestimation reported by ECDC. Therefore physicians and even specialists in STIs must report all new cases of syphilis to have more robust data on incidence and prevalence of the disease.

Keywords: syphilis, HIV, AIDS.

SUMMARY

In the early 1990s a reduction in the rate of sexually transmitted infections (STIs) occurred, although recent years have seen an increase. The aim of this study was to examine epidemiological and clinical features of syphilis cases in patients with HIV infection. We reviewed the charts of HIV-infected patients referring to our centre in the period 2002-2011. Fifty of the 402 consecutive HIV-positive patients (12.4%) received a diagnosis of syphilis. An increasing trend in the number of syphilis cases was observed within the period of the study. Most patients with syphilis (64%) presented a latent syphilis of unknown duration. About half of these received a concomitant diagnosis of HIV infection. Men who have sex with men (MSM) were the largest group. In the years 2002-2011, the incidence of syphilis in HIV-infected patients increased in our centre, notably among MSM. There is an urgent need for campaigns aiming to prevent STIs.

RIASSUNTO

Nei primi anni 90 si è verificata una riduzione nei tassi di infezioni sessualmente trasmesse seguita da un aumento negli anni successivi. Scopo dello studio è stato quello di esaminare le caratteristiche epidemiologiche e cliniche dei casi di sifilide nei soggetti con infezione da HIV. Abbiamo esaminato retrospettivamente tutti i soggetti con infezione da HIV seguiti presso il nostro centro nel periodo 2002-2011. Cinquanta dei 402 pazienti consecutivi HIV positivi (12,4%) avevano ricevuto una diagnosi di lue; nel periodo oggetto dello studio è stato riscontrato un trend in aumento del numero dei casi. La maggior parte dei pazienti con sifilide (64%) presentava una forma latente di durata sconosciuta. Circa la metà di questi soggetti aveva ricevuto una diagnosi simultanea di infezione da HIV.
Gli omosessuali maschi erano il gruppo maggiormente rappresentato. In conclusione, negli anni 2002-2011, l'incidenza della sifilide nei soggetti anti-HIV positivi nel nostro centro è aumentata, in particolare tra gli omosessuali maschi. Vi è pertanto un bisogno urgente di campagne tese alla prevenzione delle infezioni sessualmente trasmesse.

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