Does Syphilis Impact on HIV Infection When Both Diagnoses are Concomitant?

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Abstract

Purpose: To examine if there are any epidemiological, clinical or immunovirological differences between men who have sex with men (MSM) who are simultaneously diagnosed with syphilis and HIV infection, compared with those who are only diagnosed with HIV infection.

Methods: All cases of HIV-MSM diagnosed at our centre in 2009-2015 were reviewed, excluding those with a diagnosis of syphilis previous to the HIV infection. Epidemiological, clinical, and analytical data at the time of HIV diagnosis were recorded, and patients with a simultaneous diagnosis of syphilis were compared with those without syphilis.

Results: During the study period 566 patients were diagnosed with HIV infection (446 MSM); 37 patients were excluded, so the final sample included 409 MSM. Of these, 72 (17.6%) were diagnosed with syphilis at the same time as their diagnosis of HIV infection. Syphilis was asymptomatic in 34 (47.2%) cases. The epidemiological, and clinical characteristics were similar in patients with or without syphilis, and no differences were found in basal viral load (4.67 vs 4.66 log copies/mL p=0.3) or CD4 cell count (431 vs 428 cell/μL p=0.7).

Conclusions: Syphilis does not impact on the clinical presentation or on the immunovirological parameters when the diagnoses of both syphilis and HIV are coincident. The specific weight that Treponema pallidum infection may have in HIV infected patients not on antiretroviral therapy is minimum.

INTRODUCTION

Since the early 2000s there has been a resurgence of syphilis in North America and Europe, mainly in men who have sex with men (MSM) who are coinfected with HIV [1,2]. In Spain the annual prevalence rate of syphilis has also risen in recent years, again mostly in the group of MSM with HIV [3,4]. HIV and Treponema pallidum, the causative agent of syphilis, share transmission pathways and their concomitant diagnosis is not uncommon [1]. The coexistence of both infections can result in interactions between them. Syphilis produces genital lesions that increase the risk of HIV transmission [5] and it can also impact negatively on the immuno-virological status of patients who have HIV [6,7]. Syphilis causes viral load blips in virologically suppressed patients on antiretroviral therapy (ART), as well as a reduction in the CD4 lymphocyte count [6,7]. The importance of this interaction is that co-infection increases the risk of HIV transmission [8]. The aim of this study was to examine if there are any epidemiological, clinical or immunovirological differences between men who have sex with men (MSM) who are simultaneously diagnosed with syphilis and HIV infection, compared with those who are only diagnosed with HIV infection.

METHODS

We reviewed all cases of MSM with HIV infection diagnosed at our centre between 2009 and 2015. For several years the Spanish Guidelines [9] have recommended that the initial screening of HIV infection should include serological testing for Treponema pallidum. The initial screening at our centre includes a treponemal test, IgG and IgM using an enzyme-linked immunosorbent assay (ELISA). If the test is positive, a non-treponemal test, rapid plasma reagin (RPR), is done and if this is also negative another treponemal test is done with microhaemaglutination (TPHA). The diagnostic criteria for syphilis are: treponemal and RPR both positive, except for patients with primary syphilis, who only require a positive RPR. The diagnostic criteria for syphilis are: treponemal and RPR both positive, except for patients with primary syphilis, who only require a positive RPR. Asymptomatic patients with a negative RPR and two positive treponemal tests are considered to have latent syphilis of uncertain duration. Patients were excluded from this study if they had a prior diagnosis of syphilis in order to...
avoid confounding factors in the serological tests. We examined epidemiological, clinical, immunological and virological variables of all patients at the time of HIV diagnosis. Patients with a simultaneous diagnosis of syphilis were compared with those without syphilis. The statistical analysis was done using SPSS® v18.0 and R®. Prior to the descriptive analysis of any variable its distribution was studied in the whole cohort using the mean if the variable adjusted to normality or the median if it did not. Comparison of proportions was done with the bilateral Fisher test. To evaluate the degree of association or independence between a normally distributed quantitative variable with a dichotomous category, the means of the distributions of the quantitative variable were compared in the two categories with the Student t test. For quantitative variables that did not follow a normal distribution the Wilcoxon non-parametric test was used. In all cases statistical significance was set at p< 0.05.

RESULTS

During the study period a total of 566 patients were diagnosed with HIV infection, of whom 446 were MSM. For this study we excluded 37 patients who had a clinical and/or serological history of syphilis. Thus, the final sample included 409 MSM, with a mean age of 34.5 years (Table 1). Of these, 72 (17.6%) were diagnosed with syphilis at the same time as their diagnosis of HIV infection, the syphilis being asymptomatic in 34 (47.2%) and symptomatic in 38 (52.7%) of them. There were 23 cases of secondary syphilis, 12 of chancre and 3 patients had other symptoms (two panuveitis, and one urethritis). One patient with secondary syphilis was diagnosed with neurosyphilis. Table (1) shows that the epidemiological, clinical and immuno-virological characteristics were similar in the two groups (patients with or without syphilis). No differences were found in basal viral load or CD4 cell count. Nor were there differences between the patients with symptomatic syphilis and the patients without syphilis.

DISCUSSION

In this study we found that those patients who received a diagnosis of syphilis concomitant with the diagnosis of HIV infection had similar epidemiological, clinical and immuno-virological characteristics to those who were just diagnosed with HIV alone.

A large French case-control study [7] reported that HIV-infected patients with syphilis had an almost 2-fold risk of an increased viral load than the controls without syphilis, even the patients receiving ART, as well as a moderate and transient reduction in the CD4 cell count. These results are similar to those seen by others [6,10,11]. Other studies, though, have failed to find either this effect [12,13], or a similar progression to AIDS or death [14]. The mechanism by which syphilis impacts on the immuno-virological parameters of HIV infection is likely the immune activation of the host cells, with an increase in the expression of the HIV receptors and coreceptors (CD4, CCR5 and CXCR4), facilitating the entry of HIV into the cell [15]. In addition,

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with syphilis</th>
<th>Patients without syphilis</th>
<th>p-value</th>
<th>Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nº of patients</td>
<td>72 (17.6)</td>
<td>337 (82.4)</td>
<td>0.6</td>
<td>409</td>
</tr>
<tr>
<td>Age (years)</td>
<td>35.1 (27.0-42.8)</td>
<td>34.4 (26.5-40.5)</td>
<td>0.6</td>
<td>345 (26.7-41.1)</td>
</tr>
<tr>
<td>European</td>
<td>59 (84.3)</td>
<td>286 (86.9)</td>
<td>0.5</td>
<td>345 (86.4)</td>
</tr>
<tr>
<td>Other</td>
<td>11 (15.7)</td>
<td>43 (13.1)</td>
<td></td>
<td>54 (13.5)</td>
</tr>
<tr>
<td>Studies level</td>
<td>23</td>
<td>77</td>
<td>0.1</td>
<td>100</td>
</tr>
<tr>
<td>Primary or none</td>
<td>49</td>
<td>257</td>
<td></td>
<td>306</td>
</tr>
<tr>
<td>Secondary or universitary</td>
<td>2 (2.7)</td>
<td>8 (2.3)</td>
<td>0.6</td>
<td>10 (2.4)</td>
</tr>
<tr>
<td>HCV Ac positive</td>
<td>4 (5.5)</td>
<td>18 (5.3)</td>
<td>1.0</td>
<td>22 (5.3)</td>
</tr>
<tr>
<td>HBsAg positive</td>
<td>431 (208-595)</td>
<td>428 (254-553)</td>
<td>0.9</td>
<td>429 (251-576)</td>
</tr>
<tr>
<td>CD4 count (cells/μL)</td>
<td>1032 (693-1165)</td>
<td>991 (580-1162)</td>
<td>0.7</td>
<td>999 (604-1162)</td>
</tr>
<tr>
<td>CD8 count (cells/μL)</td>
<td>0.4 (0.2-0.6)</td>
<td>0.5 (0.2-0.6)</td>
<td>0.3</td>
<td>0.5 (0.2-0.6)</td>
</tr>
<tr>
<td>VL (log copies/mL)</td>
<td>4.67 (4.4-5.3)</td>
<td>4.66 (4.2-5.1)</td>
<td>0.9</td>
<td>4.6 (4.2-5.1)</td>
</tr>
<tr>
<td>Seroconversion</td>
<td>31 (43.7)</td>
<td>141 (42.5)</td>
<td>0.9</td>
<td>172 (42.6)</td>
</tr>
<tr>
<td>Initial AIDS</td>
<td>7 (9.7)</td>
<td>31 (9.2)</td>
<td>0.8</td>
<td>38 (9.3)</td>
</tr>
<tr>
<td>Late diagnosis</td>
<td>25 (36.2)</td>
<td>135 (41.2)</td>
<td>0.5</td>
<td>160 (40.3)</td>
</tr>
<tr>
<td>Advanced disease at diagnosis</td>
<td>20 (29.0)</td>
<td>65 (19.8)</td>
<td>0.1</td>
<td>85 (21.4)</td>
</tr>
</tbody>
</table>

Late diagnosis (CD4<350 cells/μL); Advanced disease at diagnosis (AIDS and/or CD4<200 cells/μL).

The continuous variables are expressed as the mean (IQR) and the qualitative variables in n (%).

Abbreviations: VL: Viral Load
the immune response to *Treponema* infection is associated with reductions in the CD4 and CD8 cell counts, even by a mechanism of apoptosis [16]. Anyway, all available data regards the effect of syphilis, and other sexually transmitted infections, on patients with chronic HIV infection [17,18], but there are no reports concerning the effect of syphilis at the time of HIV diagnosis.

In our study the clinical presentation and the immuno-virological data were not affected by infection with *Treponema* when both infections were diagnosed simultaneously. It could be argued that almost half the cases concerned patients with latent syphilis and the degree of systemic involvement was therefore minimum, but the same occurred in the patients who had symptomatic syphilis. On the other hand, nearly half the patients were seroconverters; i.e., with a recent HIV infection, suggesting that in many cases not only was the diagnosis concomitant but also the two infections with HIV and *Treponema*.

In summary, syphilis does not impact on the clinical presentation or on the immuno-virological parameters when the diagnoses of both syphilis and HIV are concomitant. The specific weight that *Treponema pallidum* infection may have in patients with HIV infection not on ART is minimum. However, the risk of transmission is still higher, though not so much due to the increased viral load but rather to the local mucous membrane lesions and mechanisms, as occurs with other sexually transmitted infections [19].

**ACKNOWLEDGMENTS**

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**COMPLIANCE WITH ETHICAL STANDARDS**

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**Ethical approval**

Institutional review board/ethics committee approval was obtained for the study protocol for the analysis of anonymous routine clinical data of patients.

**Informed consent**

Patients were informed about the nature of the study and accepted to be included.

**REFERENCES**


