Neurosyphilis in people living with HIV: current incidence and diagnostic approach

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INTRODUCTION

The diagnosis of neurosyphilis in people living with HIV (PWH) remains controversial.

Different approaches coexist regarding the need of cerebrospinal fluid (CSF) analysis in this population.

Two diagnostic approaches are predominantly used:

- **Based on neurological signs/symptoms or treatment failure** (CDC, 2021).
- **Based on CD4+ counts ≤ 350 cells/µL or RPR titers ≥ 1:32** (Marra CM, et al. Sex Transm Dis. 2018 Sep;45:S10-S12).

OBJECTIVE

To assess the incidence and characteristics of neurosyphilis in people living with HIV using the current diagnostic approach based on neurological signs/symptoms or treatment failure.

METHODS

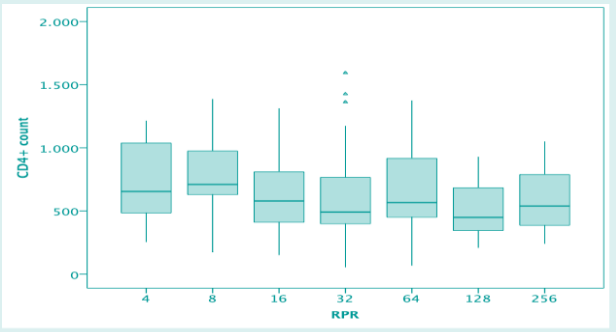
- Prospective longitudinal study of PLW with syphilis serological testing (RPR, EIA, HAI) every 6 months.
- A lumbar puncture was performed to individuals with neurological signs at presentation or treatment failure at 12-month follow-up.
- Treatment failure was defined as failure of non-treponemal test titers to decrease fourfold (2 dilutions) within 12 months after therapy for primary or secondary syphilis, excluding reinfections (RPR increase or new compatible lesions).

RESULTS

Table 1. Baseline characteristics of the population (n=205)

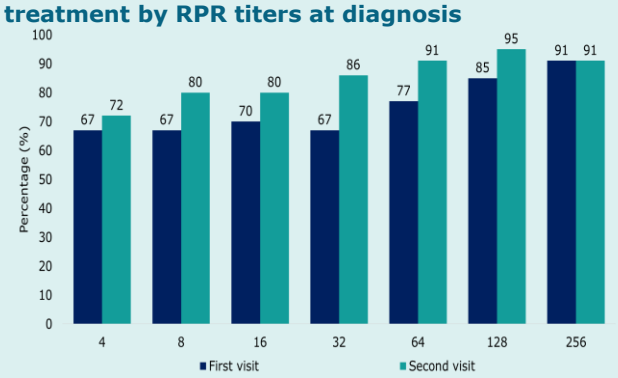
Age, median (IQR)	43 (36-52)
Male gender, n (%)	205 (100)
MSM, n (%)	199 (97)
Time of HIV diagnosis, median (IQR) **Syphilis at HIV diagnosis, n (%)**	81 (22-143) 15 (7)
CD4+ nadir, median (IQR), cells/µL	302 (166-420)
CD4+ current, median (IQR), cells/µL CD4+ < 350 cels/mcL, n (%)	581 (423-856) 33 (16)
Syphilis stage, n (%) Primary Secondary Early latent Late latent or of unknown duration	 30 (15) 40 (20) 60 (29) 75 (36)
RPR titers, median (IQR) RPR titers ≥ 1/32 at diagnosis, n (%)	1/32 (1/16-1/64) 146 (71)
Neurological symptoms, n (%) Posterior uveitis, n (%) Cochleitis, n (%)	4 (2) 2 (1) 2 (1)

Figure 1. Distribution of RPR titers according to CD4+ counts



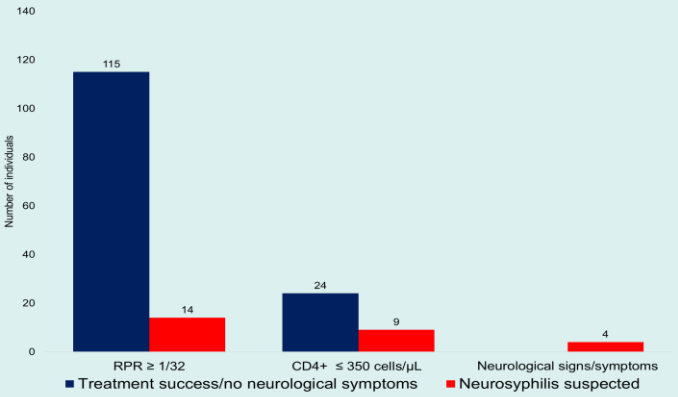
- There was an inverse correlation between CD4 count at diagnosis and RPR titers (rho=-0.172, p=0.02).

Figure 2. Percentage of serological response after treatment by RPR titers at diagnosis



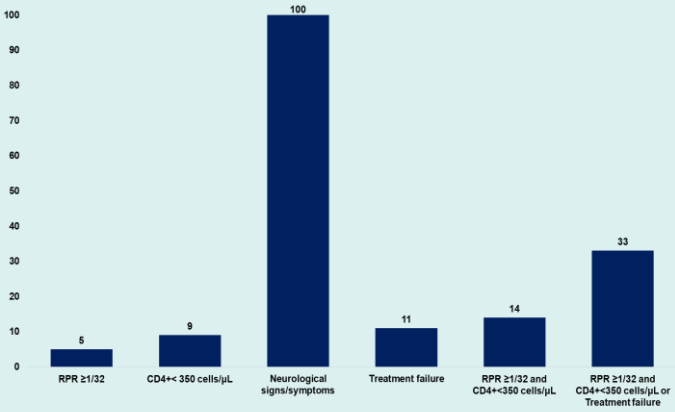
- After a median time of 147 (IQR 109-214) days (first visit), 156 (76%) PLWH had a serological response, increasing to 177 (87%) after 366 (IQR 288-467) days (second visit).
- RPR titers ≥1:32 were associated with serologic response (89% vs 76% if RPR <1:32; p=0.06), whereas CD4 counts ≤350 cells/µL were associated with treatment failure (27% vs 11% if CD4 >350 cells/µL, p=0.021).

Figure 3. Number of individuals with suspected neurosyphilis according to baseline presentation



- After excluding reinfection, 19 (9%) PWH with neurological signs/symptoms or treatment failure underwent a lumbar puncture, with cerebrospinal fluid (CSF) pleocytosis (≥6 white blood cells/µL) in 8 (42%) individuals, increased protein concentration in 3 (16%), and positive VDRL in 2 (11%).
- A final diagnosis of neurosyphilis was made in 7 individuals
  - 3% of the initial population
  - 37% of those with CSF testing indication according to the current diagnostic approach.
- If the traditional diagnostic approach had been used (based on RPR ≥ 1/32, CD4+ ≤ 350 cells/µL, or both), lumbar puncture with CSF testing would have been suspected in twice as many individuals (18%).

Figure 4. Percentage of individuals with final diagnosis of neurosyphilis according to baseline presentation.



- Individuals with confirmed neurosyphilis (n=7) had RPR ≥ 1/32 but they only represented 5% of the cases with that RPR values. Likewise, only 3 of the 7 individuals had the criteria of RPR ≥1/32, CD4+<350 cells/µL and serological failure at one year.
- All cases of neurological symptoms had a final diagnosis of CNS involvement.

CONCLUSION

Neurosyphilis was unusual in our population. The current diagnosis approach enabled the selection of individuals at high risk of neurosyphilis, avoiding the use of invasive tests and saving resources.

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