Clinical and laboratory characteristics of ocular syphilis and neurosyphilis among individuals with and without HIV infection

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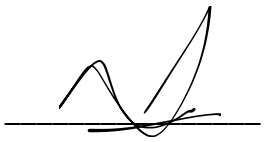
Declaration

I, Dony Mathew, declare that this research report is my own work. It was published in the peer reviewed British Journal of Ophthalmology in 2020. I have not submitted it; in its entirety or in part, in any previous application for a degree or qualification at this or any other university or institute of learning.

This study was approved by the Health, Research and Ethics Committee of Stellenbosch and adhered to the principles of the Declaration of Helsinki.



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1. Summary

BACKGROUND/AIMS: In the era of increasing incidence of syphilis globally, ocular syphilis is re-emerging as an important cause of uveitis. The aim of this study was to determine the clinical and laboratory characteristics of ocular- and neurosyphilis among individuals with and without HIV infection.

METHODS: Retrospective analysis of patients diagnosed with ocular syphilis presenting to Tygerberg Hospital, South Africa, over a 5-year period ending December 2018.

RESULTS: Two-hundred-and-fifteen eyes of 146 patients were included. HIV co-infection was present in 52.1% of the patients, with 23.7% of these patients being newly diagnosed on presentation. The median age was 36.5 $\pm$ 9.8 years. Bilateral involvement occurred in 47.3%; with 68.1% of these patients being HIV positive. The most frequent form of intraocular inflammation was posterior uveitis (40.9%), followed by panuveitis (38.1%); both of which were more predominant in HIV-positive eyes. Seventy-four percent of all eyes had a visual acuity $\leq$ 20/50 and 40% $\leq$ 20/200 at presentation.
A lumbar puncture was performed in 113 patients (77.4%). Sixteen patients had confirmed neurosyphilis and 27 probable neurosyphilis according to the UpToDate algorithms.

CONCLUSION: This study included the largest number of ocular syphilis cases with the largest proportion of HIV infection to date. Forty-three of 146 patients (29.5%) had neurosyphilis. HIV status must be determined in all patients with ocular syphilis since almost ¼ of patients were newly diagnosed with HIV infection by doing so.

Keywords: ocular syphilis, neurosyphilis, uveitis

2. Opsomming

DOELWIT: In die tydperk van verhoogde insidensie van sifilis wêreldwyd, verskyn okulêre sifilis ook as 'n belangrike oorsaak van uveitis. Die doel van hierdie studie is om die kliniese en laboratorium eienskappe van okulêre- en neurosifilis in pasiënte met en sonder MIV infeksie te bepaal.

METODES: 'n Retrospektiewe analise van pasiënte gediagnoseer met okulêre sifilis by Tygerberg Hospitaal, Suid Afrika, in die 5 jaar periode tot en met Desember 2018.

RESULTATE: Twee honderd en vyftien oë van 146 pasiënte is ingesluit. MIV infeksie was teenwoordig in 52.1% van die pasiënte, met 23.7% van hierdie pasiënte wat nuut gediagnoseer was met MIV. Die mediaan ouderdom was 36.5 ± 9.8 jaar. Bilaterale aantasting was teenwoordig in 47.3%; met 68.1% van hierdie pasiënte wat MIV positief was. Die mees algemene vorm van uveitis was posterior uveitis (40.9%), gevolg deur panuveitis (38.1%); waarvan beide meer algemeen was in MIV positiewe pasiënte.Vier en sewentig persent van pasiënte het gesigskerpte van ≤ 20/50 en 40% het ≤ 20/200 gehad met diagnose.
'n Lumbale punksie is gedoen in 113 pasiënte (77.4%). Sestien pasiënte het bevestigde neurosifilis en 27 moontlike neurosifilis gehad volgens die UpToDate algoritmes.

SLOTSOM: Hierdie studie het die grootste getal pasiënte tot dusver met okulêre sifilis en die grootste persentasie wat met MIV besmet is ondersoek. Drie en veertig van die 146 pasiënte (29.5%) het ook neurosifilis gehad. MIV status moet in elke pasiënt met okulêre sifilis bepaal word aangesien byna ¼ van hierdie pasiënte nuut gediagnoseer was met MIV infeksie.

Sleutelwoorde: okulêre sifilis, neurosifilis, uveitis

3. Acknowledgements

- Associate Professor Derrick Smit for his supervision, guidance, and support with this study.
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4. Publications and presentations

- March 2020: Published in British Journal of Ophthalmology
- June 2020: Oral and poster presentation at the virtual World Ophthalmology Congress hosted by Cape Town, South Africa
- August 2020: Poster presentation at University of Stellenbosch Annual Academic Day
- March 2022: Oral presentation scheduled at the 50th annual congress of the Ophthalmological Society of Southern Africa, Sun City

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ABSTRACT

Background/aims In the era of increasing incidence of syphilis globally, ocular syphilis is re-emerging as an important cause of uveitis. The aim of this study was to determine the clinical and laboratory characteristics of ocular- and neurosyphilis among individuals with and without HIV infection.

Methods Retrospective analysis of patients diagnosed with ocular syphilis presenting to Tygerberg Hospital, South Africa, over a 5-year period ending December 2018.

Results Two-hundred and fifteen eyes of 146 patients were included. HIV coinfection was present in 52.1% of the patients, with 23.7% of these patients being newly diagnosed on presentation. The median age was 36.5±9.8 years. Bilateral involvement occurred in 47.3%, with 68.1% of these patients being HIV positive. The most frequent form of intraocular inflammation was posterior uveitis (40.9%), followed by panuveitis (38.1%), both of which were more predominant in HIV-positive eyes. Seventy-four per cent of all eyes had a visual acuity ≤20/50 and 40% <20/200 at presentation. A lumbar puncture was performed in 113 patients (77.4%). Sixteen patients had confirmed neurosyphilis and 27 probable neurosyphilis according to the UpToDate algorithms.

Conclusion This study included the largest number of ocular syphilis cases with the largest proportion of HIV infection to date. Forty-three of 146 patients (37.0%) had neurosyphilis. HIV status must be determined in all patients with ocular syphilis since almost ¼ of patients were newly diagnosed with HIV infection by doing so.

INTRODUCTION

Syphilis is a systemic infection affecting various organs, including the central nervous system and eyes, and manifests as primary, secondary, latent and tertiary forms. The diagnosis of syphilis is based on suggestive clinical signs in the presence of positive serology. Transmission occurs via sexual contact and transplacental infection. Ocular syphilis refers to the group of inflammatory eye diseases that result from infection of the ocular tissues by the spirochete, *Treponema pallidum*.[1] Uveitis accounts for the majority of cases of ocular syphilis, with various forms of presentation, namely anterior uveitis, intermediate uveitis, posterior uveitis and panuveitis. The Centers for Disease Control and Prevention (CDC) has issued a series of reports over recent years showing the increased incidence of all forms of syphilis in the USA. The lowest recently recorded incidence rate of primary and secondary syphilis was in 2000 and 2001, namely 2.1 cases per 100 000 population per year.[2] There has been a significant increase in the syphilis rate since then, and in 2015–2016, the national syphilis rate increased to 8.7 cases per 100 000 population.[2] The rise has been attributed to factors such as high-risk sexual practices and immune-modulatory impacts of HIV infection and antiretroviral (ARV) therapy.[3]

The estimated overall HIV prevalence is approximately 12.6% among the South African population with the total number of people living with HIV estimated at approximately 7.06 million in 2017. For adults aged 15–49 years, an estimated 18,0% of the population is HIV positive.[4] The increase in the total number of persons in South Africa living with HIV is from an estimated 4.94 million in 2002 to 7.06 million in 2017.[4] With the rising incidence of HIV infection worldwide, there is also a relative increase in the number of reported cases of ocular syphilis in HIV-positive patients compared with HIV-negative cases.[5]

Studies examining the patterns of uveitis in various geographic regions across the world demonstrated distinct differences, and these patterns of uveitis are influenced by combinations of geographical, environmental and genetic factors.[6] Recent studies conducted in North America, Brazil, England and China indicate increased case numbers of ocular syphilis[3 5 7 8]; however, similar data are lacking in sub-Saharan Africa.

There are two types of serological tests to diagnose syphilis: treponemal and non-treponemal. Treponemal antigen tests such as *Treponema pallidum* haemagglutination test (TPHA), *Treponema pallidum* particle agglutination, fluorescent treponemal antibody absorption test (FTA-ABS) and enzyme immunoassays (EIAs) are specific tests that detect antibodies to treponemal antigens and are expressed qualitatively (reactive or non-reactive).

Non-treponemal tests such as rapid plasma reagin (RPR) and venereal disease research laboratory (VDRL) are non-specific tests that detect antibodies against membrane phospholipids such as cardiolipin and are expressed quantitatively as titres reported in twofold increments (eg, 1:32, 1:64), which correlate with disease severity.[9]

The CDC recommends a treponemal test as an initial screening test for syphilis; this will identify both persons with untreated or partially treated syphilis and persons with previous treatment for syphilis. If positive, this should be followed by a

non-treponemal test such as VDRL or RPR. Specimens with incongruent results (ie, EIA positive and RPR negative) should be submitted for a different treponemal test such as TPHA; if the latter is positive, the diagnosis of syphilis is confirmed.[9]

Reports have suggested that the association between ocular syphilis and neurosyphilis is greater in HIV-positive patients than in immunocompetent patients and that cerebrospinal fluid (CSF) analysis should therefore be performed in all patients with ocular syphilis who are HIV positive.[10]

Neurosyphilis can be divided into two groups: confirmed and probable. According to the CDC, confirmed neurosyphilis is diagnosed when VDRL is positive on CSF; however, a negative result does not exclude neurosyphilis as CSF-VDRL may be negative in 30%–70% of neurosyphilis cases.

The database, UpToDate, proposes separate algorithms for the diagnosis of probable neurosyphilis in patients with and without HIV infection as HIV-positive patients tend to have higher CSF protein levels and lymphocyte counts than HIV-negative patients.

In HIV-negative patients with a non-reactive CSF-VDRL result, a CSF lymphocyte count >5 cells/µL or a protein concentration >45 mg/dL is consistent with the diagnosis of probable neurosyphilis.[11]

In HIV-positive patients, the diagnosis of neurosyphilis can be challenging. In the setting of non-reactive CSF-VDRL, CSF pleocytosis of >20 cells/µL establishes the diagnosis of probable neurosyphilis. The challenge arises with mild CSF pleocytosis (6–20 cells/µL), as HIV itself causes mild CSF pleocytosis and mild elevation of CSF proteins. In this setting, if the CD4 count is <200/µL and the patient is using ARVs *and* HIV RNA <50 copies/mL, then one treats for neurosyphilis.[11] If one or more of these aforementioned criteria are not met, then one would treat for neurosyphilis if the CSF FTA-ABS result is positive.

The early detection of cases of ocular syphilis is essential as prompt initiation of antimicrobial therapy is generally associated with a good visual outcome. Conversely, if misdiagnosis delays appropriate treatment the outcomes may be poor.[3]

AIM

To determine the clinical and laboratory characteristics of ocular syphilis and neurosyphilis in HIV infected and uninfected patients presenting to Tygerberg Hospital during period of January 2014–December 2018.

METHODS

We retrospectively reviewed the clinical and laboratory findings of all patients diagnosed with ocular syphilis in the Ophthalmology Division at Tygerberg Hospital, Cape Town, between January 2014 and December 2018. Tygerberg Hospital is a multidisciplinary tertiary referral hospital that is affiliated with Stellenbosch University.

All positive treponemal antibody (TPAB) and positive non-treponemal serology (RPR) blood tests requested from the ophthalmology clinic and ward were identified from the National Health Laboratory Service (NHLS). The medical records of these patients were reviewed for evidence of ocular inflammation on examination. Clinical data were collected for all patients who presented with inflammatory eye disease that was diagnosed as ocular syphilis on the basis of serological testing. Exclusion criteria were inflammation due to causes other than syphilis and patients who did not fulfil the above serological criteria.

All patients underwent detailed ophthalmic evaluation at the time of presentation, including work-up to rule out other causes of intraocular inflammation as outlined in box 1.[12] HIV testing was offered to all patients, and in HIV-positive patients, CD4+ count and HIV viral load (VL) were requested.

Box 1 Work-up for uveitis

Baseline investigations in all cases
- HIV (and CD4 count if indicated).
- Full blood count.
- Erythrocyte sedimentation rate.
- Rapid plasma reagin and *Treponema pallidum* antibodies.
- Creatinine.
- Serum angiotensin converting enzyme.
- Dipstick urinalysis.
- Chest X-ray.
- Tuberculin skin test.
- Quantiferon-TB Gold.

Other investigations if indicated
- Chest CT (standard or high resolution).
- PET/CT.
- Human leukocyte antigen B27 (HLA-B27).
- Antistreptolysin O titre.

Second-line investigations (if baseline tests negative)
- Anterior chamber tap for:
  - PCR for herpes virus 1–6, rubella and toxoplasma.
  - Goldmann-Witmer coefficient (GWC) for herpes simplex virus (HSV), varicella zoster virus (VZV), cytomegalovirus (CMV) and toxoplasma.
  - Mycobacteria growth indicator tube and IS6110 TB PCR (if ocular TB suspected).

Data collected included patient demographics, Snellen visual acuity of affected eye/s at presentation, laterality of inflammation, HIV status (also CD4 count and HIV VL), serology and CSF results.

At Tygerberg hospital TPAB is the initial screening test, and if the result is negative, the diagnosis of syphilis is ruled out and no further testing is performed. If the result is positive, serum RPR is performed and titres are determined for those with positive results.

Analysis of the CSF also follows this reverse sequence testing algorithm, where the FTA-ABS is performed first, and if this result is positive, a VDRL test is done. All blood tests, serology

Table 1 Demographics of patients presenting with ocular syphilis

	All patients	HIV uninfected	HIV infected	P value
Age (years)				
Median±SD	36.50±9.8	37.83±9.1	33.42±9.4	0.02
Gender, n (%)				
Male	78 (53.4)	32 (41)	46 (59)	
Female	68 (46.6)	38 (55.9)	30 (44.1)	
Total	146	70 (47.9)	76 (52.1)	0.07
Bilateral involvement, n (%)	69 (47.3)	22 (31.9)	47 (68.1)	
RPR titre				
Median	32	12	64	<0.001
Interpercentile range	120	56	112	

RPR, rapid plasma reagin.

Table 2 Anatomical classification of uveitis

Anatomical classification of uveitis, n (%)	All eyes	HIV-negative eyes	HIV-positive eyes
Anterior	28 (13)	16 (57.1)	12 (42.9)
Intermediate	17 (7.9)	15 (88.2)	2 (11.8)
Posterior	88 (40.9)	40 (45.5)	48 (54.5)
Panuveitis	82 (38.1)	21 (25.6)	61 (74.4)
Total eyes	215	92 (42.8)	123 (57.2)

and CSF tests were performed by the NHLS in Tygerberg hospital.

STATISTICAL AND DATA ANALYSIS

Data were entered into Microsoft Excel for initial analysis and development of descriptive statistics. Further statistical analysis was performed using SAS V.9.3 . The significance of syphilis serology findings on serum and CSF was determined using univariate analysis. Serum RPR titre was maintained as a continuous variable, and the Mann-Whitney U test was used to examine the association between HIV status and RPR titre. For categorical variables, the χ^2 test was used. All statistical tests were two sided with $p<0.05$ considered statistically significant.

RESULTS

Demographics

In total, 146 patients presented with inflammatory eye disease diagnosed as ocular syphilis based on serological testing over a 5-year period ending December 2018.

Table 1 shows the demographic data of all patients. HIV-positive patients had a younger median age than HIV-negative patients ($p=0.02$). Seventy-six (52.1%) patients were HIV positive. A male preponderance was noted in both the overall as well as the HIV-positive group. In the HIV-positive group, 58 (76.3%) were previously diagnosed with HIV and on ARV treatment, while 18 (23.7%) were newly diagnosed at presentation. CD4+ counts were available for 63.8% of the patients previously diagnosed with HIV infection, and the median value was 411 cells/µL (range 45–726).

Ocular manifestations

Table 2 shows the anatomical distribution of uveitis in the cases studied. Inflammation was non-granulomatous in 192 eyes (89.4%).

Table 3 shows the affected eyes that presented with a visual acuity of ≤20/50 and ≤20/200 in relation to HIV status. It also suggests that HIV-positive eyes were more likely to present with an acuity of ≤20/200 compared with HIV-negative eyes ($p=0.05$).

Systemic manifestations

A lumbar puncture was performed in 113 patients (77.4%) as part of the diagnostic work-up. Indications for lumbar puncture according to the UpToDate diagnostic algorithms of neurosyphilis included a reactive serum FTA-ABS with a RPR titre ≥1:32 and/or neurological, including ocular, symptoms or signs consistent with neurosyphilis. However, if the patient was known to be HIV positive and had a CD4+ count of <350 cells/µL or in virological failure, a lumbar puncture was also indicated. Table 4 shows the CSF findings in HIV-positive and HIV-negative groups. Among the HIV-negative patients who underwent lumber punctures and had negative CSF VDRL, 11 patients had CSF white cell count (WCC) of >5 cells/mm^3 (figure 1). All 11 patients were also CSF FTA-ABS positive. Only two patients who had CSF WCC ≤5 cells/mm^3 had CSF protein levels >45 mg/dL.

Among the HIV-positive patients who underwent lumbar punctures and had negative CSF VDRL, eight patients had CSF WCC counts >20 cells/mm^3. All eight were also CSF FTA-ABS positive. Six patients had CSF WCC between 6 and 20 cells/mm^3, three of which were newly diagnosed with HIV infection and ARV naive, and the other three having CD4 counts of <200 and in virological failure with HIV viral load >1000 copies/mL. Of the six patients that had CSF WCC between 6 and 20 cells/mm^3, four were CSF FTA-ABS positive.

According to the UpToDate diagnostic algorithms of neurosyphilis in HIV-positive and HIV-negative groups, 16 patients had confirmed neurosyphilis and 27 patients had probable neurosyphilis. Of the 16 patients with confirmed neurosyphilis, 8 were HIV positive and 8 HIV negative. Of the 27 patients assessed to have probable neurosyphilis, 13 were HIV negative and 14 were HIV positive.

Thus, in the HIV-positive patients, 8 patients had confirmed neurosyphilis and 14 patients had probable neurosyphilis. In the HIV-negative patients, 8 patients had confirmed neurosyphilis and 13 patients had probable neurosyphilis.

The mean CSF WCC was higher in CSF FTA-ABS positive samples when compared with CSF FTA-ABS negative samples (33.8 cells/mm^3 vs 4.1 cells/mm^3, $p=0.02$). This was also demonstrated on CSF-VDRL samples (48.6 cell/mm^3 vs 6.5 cells/mm^3, $p=0.01$).

DISCUSSION

HIV coinfection with syphilis has been well described, and what makes this study unique is that it included the largest number of ocular syphilis cases described (146 patients, 215 affected eyes) to date with the largest proportion of patients that have concurrent HIV infection (52.1%), with just under a quarter being newly diagnosed (table 5).

In our study, we observed that the median age of HIV-positive patients was lower than that of HIV-negative individuals. This, together with the male predominance and higher serum RPR titres in patients with HIV coinfection compared with those that were uninfected, was in keeping with other studies.[3 8 13]

Other similarities included a worse mean presenting visual acuity in HIV-positive patients compared with HIV-negative patients (Snellen visual acuity (VA) 20/195 vs 20/66, respectively, $p=0.04$).[3 8 13]

Table 3 Visual acuity at presentation of patients diagnosed with ocular syphilis

Visual acuity, n (%)	All eyes	HIV-negative eyes	HIV-positive eyes	Newly diagnosed HIV-positive eyes	P value
≤20/50	161 (74.9)	71 (44.1)	90 (55.9)	17 (10.6)	0.31
≤20/200	86 (40)	27 (31.4)	59 (68.6)	8 (12.3)	0.05
Total eyes	215	97 (45.1)	118 (54.9)	28	0.15

Table 4 CSF findings in HIV-infected and HIV-uninfected persons

	Total number	Positive CSF-VDRL	Positive CSF FTA-ABS	LP WCC mean (cells/mm^3)	LP protein mean (mg/dL)	LP glucose mean (mmol/L)
HIV uninfected	56	8	20	9.1	0.39	3.5
HIV infected	57	8	24	31.2	0.46	3.0
Total number	113	16 (14.2%)	44 (38.9%)			

CSF, cerebrospinal fluid; FTA-ABS, fluorescent treponemal antibody absorption test; LP, lumbar puncture; VDRL, venereal disease research laboratory; WCC, white cell count.

We found the most frequent form of intraocular inflammation was posterior uveitis, followed by panuveitis, both of which were more prominent in HIV-positive eyes. The predominant posterior segment inflammation is in keeping with previous literature review.[3 7] Bilateral ocular involvement was noted in just under 50% of the patients, with the vast majority of these patients being HIV positive (68%). These findings were similar to what Furtado *et al*[3] described (69% of patients with bilateral involvement were HIV positive) and is in keeping with several reports in the literature that have found higher rates of bilateral disease in HIV-positive patients.[3]

Some differences observed in this study compared with other studies was the mean age of affected patients in our study was 36.5 years, which is lower than what is reported in the other literature, where the majority of the patients presented in the fifth decade of life.[3 8 14] We observed that in the eyes documented to have a visual acuity of ≤20/200 (40%), just under 70% were HIV-positive eyes. Furtado *et al* described a similar proportion of patients having an acuity of ≤20/200 (39%), however a significantly less proportion being HIV positive (43%).

Interestingly, we found that positive CSF-VDRL and positive CSF FTA-ABS in patients with confirmed and probable neurosyphilis were found in a similar distribution in HIV-positive and HIV-negative groups (table 4). This is in contrast to the findings described by Lee *et al*[8] where more frequent positive CSF-VDRL or FTA-ABS was found in HIV-positive patients (60% in HIV positive vs 16% in HIV negative); however, these findings were in a small group of 15 patients that underwent lumbar puncture.

Neurosyphilis has been shown to be associated with RPR titres greater than or equal to 1:32 and HIV infection.[11] A total of 43 patients were found to have neurosyphilis, 16 confirmed and 27 probable, and all had RPR titres greater than 32. In HIV-positive patients, we found an elevated lymphocyte cell count to be associated with both a positive CSF-VDRL and CSF FTA-ABS test (p=0.03 and p=0.05, respectively). Also, a positive CSF-VDRL was associated with an elevated total protein (p=0.02). The CSF analysis showed that the HIV-positive group had a higher mean white cell count and protein count compared with that of the HIV-negative group (see table 4).

With the increasing case numbers of ocular syphilis worldwide, the optimum management, indications for lumbar puncture and use of adjunctive corticosteroids has warranted increased scrutiny.[15] A recent study performed in Durban, South Africa, by Reekie *et al*[16] considered the use of lumbar puncture in the management of ocular syphilis and found that out of the 68 patients diagnosed with ocular syphilis, 25.8% of patients had findings suggestive of neurosyphilis. They further concluded that all patients diagnosed with ocular syphilis should undergo a lumbar puncture. However, their study defined probable neurosyphilis as positive CSF FTA-ABS and/or lymphocytic pleocytosis of >20 cells/µL.

The CDC recommends ocular syphilis be managed according to their guidelines for neurosyphilis, which entails that a lumbar puncture with CSF analysis to be performed in all patients with syphilis and inflammatory ocular signs, even in the absence of clinical neurological findings. The recommended regimen is intravenous aqueous crystalline penicillin

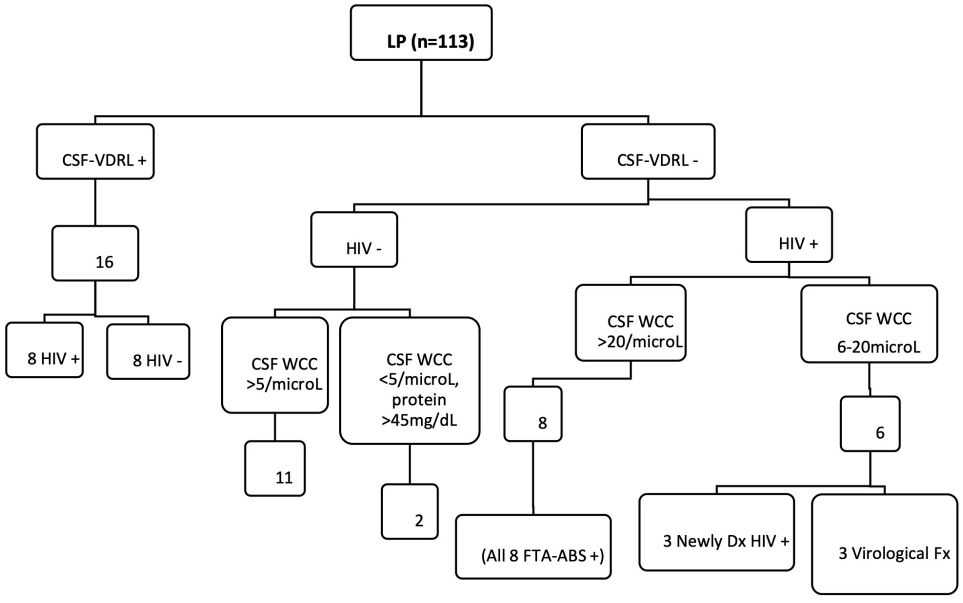

Figure 1 Cerebrospinal fluid (CSF) analysis according to diagnostic algorithms for 'confirmed' and 'probable' neurosyphilis (adapted from reference 11). FTA-ABS, fluorescent treponemal antibody absorption test; LP, lumbar puncture; VRDL, venereal disease research laboratory; WCC, white cell count.

Table 5 Recently reported case series of ocular syphilis

Study	Location	Years	Total number of patients	HIV-positive patients, n (%)
Anshu *et al*	Singapore	1995–2006	22	0
Kunkel *et al*	Berlin, Germany	1998–2006	24	11 (45.8)
Balaskas *et al*	Lausanne, Switzerland	1999–2009	26	2 (7.7)
Yang *et al*	Chongqing, China	2004–2008	19	4 (21.1)
Puech *et al*	Grenoble, France	2005–2007	8	3 (37.5)
Hughes *et al*	Sydney, Australia	2006–2009	13	6 (46.2)
Mathew *et al*	Multicenter, UK	2009–2011	41	13 (31.7)
Bollemer *et al*	Rotterdam, The Netherlands	1984–2013	85	28 (32.9)
Fonollosa *et al*	Multienter, Spain	2000–2013	50	17 (34)
Lee *et al*	California, USA	2008–2014	16	10 (62.5)
Furtado *et al*	Multicentre, Brazil	2013–2015	127	36 (28.3)
(Mathew et al)	Cape Town, South Africa	2014–2018	146	76 (52.1)

Parentheses refers to comparing authors' current study with previously published work.

G for 10–14 days. An alternative regimen is intramuscular procaine penicillin G plus oral probenecid, both for 10–14 days.[17]

Ocular syphilis can present in any stage of the disease; unfortunately, systemic features of syphilis, such as mucosal lesions, rash or lymphadenopathy and the stage of the disease, were not reported in our study. There are mixed reports in the literature of systemic features of syphilis appearing before or in conjunction with the presentation of ocular syphilis, and future studies can compare the onset of systemic signs to the onset of ocular symptoms. Due to the retrospective nature of this study and patients being lost to follow-up, ocular complications and final visual acuity after treatment could not be documented. Furtado *et al* described the sequelae of long-standing ocular inflammation as a result from syphilis and how most patients make an excellent visual recovery, especially when treated in the early stages. Mathew *et al* found that from the 41 patients diagnosed with ocular syphilis, 92% of patients had a final acuity of 20/40 or better, irrespective of the HIV status, and this was corroborated by other studies.[14] However, Yang *et al*[18] found that a worse presenting acuity and HIV coinfection have a negative influence of final acuity.

Ocular syphilis is an important diagnosis to make as serious morbidity can be avoided with prompt treatment. This study underlines the importance of ascertaining HIV status in patients diagnosed with ocular syphilis as more than half of our patients were HIV positive, with just under a quarter of these patients being newly diagnosed with HIV-infection at presentation. This demonstrates that making the diagnosis of ocular syphilis may unmask underlying HIV infection in a significant number of patients.

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