

Ophthalmological Manifestations in Patients with Syphilitic Uveitis Treated in the ICO "Ramón Pando Ferrer"

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Abstract

Purpose: Describing the ophthalmological manifestations found in patients diagnosed with syphilitic Uveitis in the Uveitis and Eye Inflammation Service of the Pando Ferrer Eye Clinic of Havana, Cuba.

Method: A retrospective longitudinal descriptive study was conducted on 32 eyes (18) patients who came to the specialized consultation office of Uveitis from July 2013 to December 2015. Inclusion criteria were based on patients with clinical and serological diagnoses of Eye Syphilis. Those who refused being included in the study were excluded as well as those who did not cooperate in undergoing the pertinent diagnostic tests. The variables studied were: age, sex, way of manifestation of the eye condition, connection to HIV-AIDS, laterality, visual sharpness, associated complications and loss of visual sharpness.

Results: Male sex was predominant (88,9%), the Age group of 40 years and over displayed a 55,5% of incidence and Caucasians accounted for 66,6% of the sample under study. HIV-AIDS was concomitant in 61,1% of the patients. The 78% of patients with the condition had a bilateral manifestation and in 89% it manifested itself as Pan uveitis. The most frequent clinical manifestation was Vitritis at 77,7% followed by Inner Spotted Retinitis at 66,6% and Neuritis at 61,1%. At the onset of the condition the visual deterioration was marked with 53,1% of patients displaying 50 var and then with significant improvement attained once stabilized thus increasing to more than 80 var 59,4 of the sample. The most frequent complications were: Detachment of the retina (21,8%), cataract (18,7%) and posterior Synechia (15,6%).

Conclusion: Eye Syphilis is frequently concomitant with HIV-AIDS and predominantly affects white male patients over 40 years of age. It turns up bilaterally most of the times, Panuveitis being the most frequent form of manifestation. The most frequent clinical manifestation was Vitritis followed by Inner Spotted Retinitis and Neuritis. The most frequent complications were detachment of the retina, cataract and posterior Synechia. Sight deterioration was very important before treatment mostly when the optic nerve was involved.

Keywords: HIV-AIDS; Syphilis; Uveitis

Introduction

Uveitis is the most common ocular manifestation of acquired syphilis [1-3]. The infection of the eyes can occur at any stage of the disease, and includes interstitial keratitis, anterior, intermediate and posterior uveitis (chorioretinitis, retinitis, retinal vasculitis), of cranial nerves and optic neuropathies [4-6]. Ocular findings may be associated with central nervous system involvement or present as a single manifestation [6-9].

Recent reports show that ocular syphilis begins to increase as a common clinical problem, reflecting an increase in the incidence of syphilis in immunocompetent subjects of all ages and in particular in patients with HIV infection [4,5]. Worldwide there is an estimated 12 million new reported cases of syphilis each year. Of these, more than 90% occur in developing countries [10]. In Europe and the United States, the majority of reported cases have been men, particularly those who have sex with other men [11,12].

Our country is not exempt from this situation, diagnosed each year, a greater number of cases of syphilis, mainly from the decade of the 90s, during which 12 000 new cases were diagnosed, later this trend was maintained, reporting in the 2014, 4046 cases, of them 2591 male, in 2015, 4582 of them 2752 male, and in 2016, 5008 new cases of them 2899 male [13].

The attention has been mainly focused on the co-infection *Treponema Pallidum* and HIV, as they frequently occur, altering its natural course and the typical clinical presentation of the disease, in particular of neurosyphilis [8,9].

Clinical and laboratory diagnosis is frequently uncertain in patients with HIV infection [14]. This is due to the great variety of presentation forms, which is why it is known as the great simulator. When it appears associated with HIV, its natural clinical course varies depending on the stage in which it is found, forming part of the differential diagnosis of any uveitis. In terms of laboratory diagnosis, false negatives can be attributed to the phenomenon of prozone, which is the result of excess antibodies which interfere with the formation of the antibody antigen complex necessary to visualize positive flocculation in the test [15]. This phenomenon is seen in cases of secondary syphilis with disproportionately high antibody titers or in cases with co-infection with HIV [15-17].

Due to the fact that in recent years there has been a greater number of people infected with syphilis in the country, and there has been a growing increase in the incidence of syphilitic uveitis in the Ocular Inflammation and Uveitis Service (SUIO) of the Cuban Institute of Ophthalmology "Ramón Pando Ferrer", as well as the fact that the author did not find sufficient information on the behavior of syphilitic uveitis in the consulted bibliographic reviews of national studies, intends to carry out this research in order to identify the clinical manifestations which occur more frequently in these patients, with the aim of achieving an early diagnosis and thereby treat this entity in a timely manner, preserving as far as possible the vision and life of these patients.

Material and Method

A retrospective longitudinal descriptive study was carried out in a series of 32 eyes (18 patients) attended in the external consultation of the Ocular Inflammation and Uveitis Service of the Cuban Institute of Ophthalmology "Ramón Pando Ferrer" with diagnosis of ocular syphilis in the period of July 2013 to December 2015. Patients with a clinical and serological diagnosis of ocular syphilis were taken into account in the inclusion criteria, and patients who refused to participate in the study or who did not cooperate for the necessary diagnostic tests were excluded. Sociodemographic variables were recorded such as age (40 years and less, and more than 40 years), sex (female and male), race (white, mestizo and black); clinical variables such as clinical manifestations (exudative retinal detachment, focal and multifocal chorioretinitis, necrotizing retinitis, vitritis, internal punctate retinitis, vasculitis and neuritis), laterality (unilateral and bilateral), its presentation according to anatomical classification (anterior, posterior, intermediate and panuveitis) and visual acuity (considering the initial and final best corrected visual acuity (BCVA) taken with the Log Mar chart); results of laboratory tests (VDRL or RPR, TPHA and serology for HIV), associated complications (retinal detachment, cataract, atrophy of the optic nerve, alterations of the RPE (retinal pigment epithelium), choroidal neovascularization, cystic macular edema (CME), posterior synechiae and chorioretinitis). The results are described by patients and by eyes.

The information referring to dynamic refraction or cycloplegic refraction was collected to determine the AVMC by Log Mar chart, biomicroscope of the anterior segment was performed in slit lamp BQ-900 and after that with previous pupillary dilation, biomicroscope of the posterior segment with aerial lenses. (90D and/or 78D) and indirect binocular ophthalmoscopy examination (OBI) with or without scleral indentation for a complete study of the retina and pars plana. Measurements of intraocular pressure were taken with the applanation method.

For the collection of information, the clinical histories of all patients with syphilitic uveitis of the uveitis service were reviewed. The information obtained and recorded in the individual clinical histories of each patient was transcribed into a Microsoft Excel database and the EPIDAT 4.0 and SPSS Version 20 systems were used for the processing and presentation of the results.

Absolute and relative frequency analyzes were performed for each case. To relate the selected variables, the Chi square of association was used, taking as significant those values with $p < 0.05$. The results were expressed in tables and graphs appropriate to the type of variable.

All the patients who participated in the investigation were informed about the objectives of the same and the diagnostic procedures to be carried out in each case, as well as the risk-benefit principles, guaranteeing the confidentiality of the information obtained.

Results

Regarding the distribution according to age groups, the group of patients with 40 and more years prevailed with 55.5% of the cases studied. The male sex represented 88.9% with 16 patients, of them 11 (61.1%) HIV/AIDS and the white race prevailed in 66.6% of the patients studied.

Demographic characteristics		Total		Of them HIV +	
		No	%	No	%*
Sex	Female	2	11.1	0	0
	Male	16	88.9	11	61.1
EDAD	24 to 40 years	8	47.1	7	41.2
	40 and more	10	55.5	4	22.2
RAZA	Blanca	12	66.6	6	33.3
	Black	4	23.5	3	17.6
	Mixed	2	11.8	2	11.8

Source: Clinical History.

Regarding the laterality of the ocular presentation, bilateral presentation predominated in 78.8% of the cases.

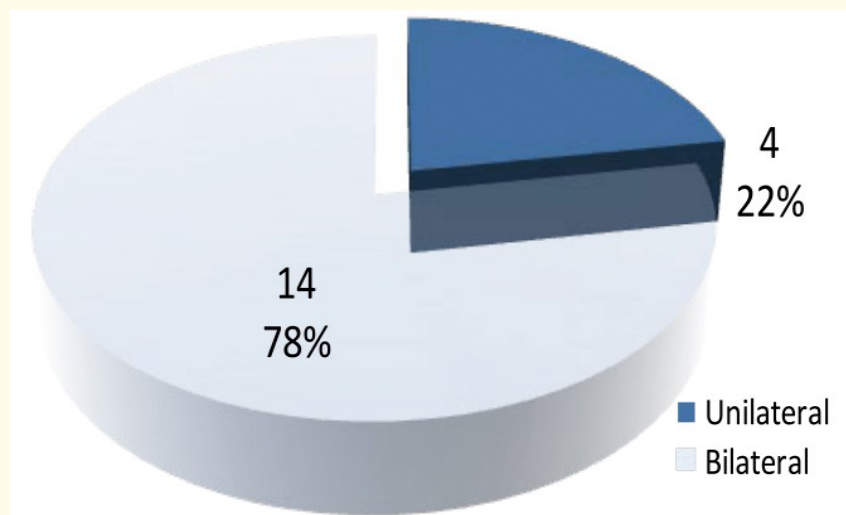


Figure 1

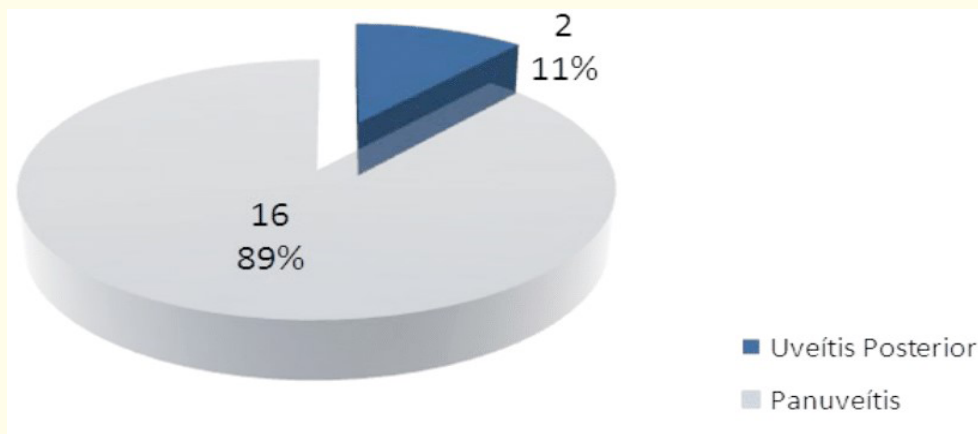


Figure 2

According to anatomical classification, pan uveitis predominated in 89% of the cases.

When analyzing the clinical manifestations, vitritis was the most frequent, being observed in 77.7% of the cases, followed by internal punctate retinitis in 66.6% and thirdly neuritis, in 61.1% of the patients. The fourth place was occupied by vasculitis with 33.3% of cases, followed by exudative retinal detachments with 22.2%, necrotizing retinitis with 11.1%, and focal and multifocal chorioretinitis with 5.5% respectively.

At the onset of the disease more than 50% of the eyes had a MVCA less than 55 var (17 eyes) representing 53.1% of the sample studied, only 15.6% of the diseased eyes had values of MCVA of 80 var. or better (5 eyes) to the debut of his disease.

Regarding the final MCVA, there was a significant variation with respect to the MCVA at the beginning of the disease, obtaining an important visual improvement, since 59.4% [5] of the patients obtained a MCVA of 80 var or better.

In the table it is observed that 14 of the eyes (43.7%) maintained visual acuity without variation compared to their initial value at the onset of the disease, and of these, only 6 maintained a MCVA of less than 55 VAR (35.3%). If 18 eyes were analyzed below the diagonal (56.25%), the CMVA was improved with respect to the initial one, and above the diagonal, no eye worsened the CMVA with respect to the onset of the disease.

Initial AVMC	AVMC Final			
	More than 80 var No (%)	50-80 var Do not (%)	Less than 50 var No (%)	Total No (%)
More than 80var	5 (100%)	0	0	5 (15.6%)
50-80 var	7 (70%)	3 (30%)	0	10 (31.2%)
Less than 50var	7 (41,2%)	4 (23,5%)	6 (35,3%)	17 (53,1%)
Total	19 (59,4%)	7 (21,8%)	6 (18,8%)	32 (100%)

Source: Clinical History.

$\chi^2 = 13.96$ gl (2) $p < 0.01$.

* AVMC was taken by affected eyes.

Regarding the presentation of ocular complications in patients with syphilitic uveitis, they differ between patients who have coinfection with HIV/AIDS and those who do not have HIV/AIDS, with retinal pigment epithelium atrophy in the latter group (30.8%), second, optic nerve atrophy and chorioretinitis (15.4%), respectively. In the first group where there is coinfection with HIV / AIDS, retinal detachment and cataracts (31.6%) prevailed respectively, and secondly, posterior synechiae (26.3%). Analyzing the total sample, retinal detachment was the most frequent complication (21.8%), secondly cataracts (18.7%), and thirdly, posterior synechiae (15.6%).

Complications ocular	VIH (-) n = 13		VIH (+) n=19		Total n = 32	
	No.	%	No.	%	No.	%
Retinal detachment	1	7.7	6	31.6	7	21.8
Cataract	0	0	6	31.6	6	18.7
Alterations of the EPR	4	30.8	0	0	4	12.5
Optic nerve atrophy	2	15.4	2	15.5	4	12.5
Posterior synechia	0	0	5	26.3	5	15.6
Coriorretinitis	2	15.4	1	5.2	3	9.3
Cystic Macular Edema	1	7.7	0	0	1	3.1
Neovascularización Coroidea	1	7.7	0	0	1	3.1

Ocular complications in eyes with syphilitic uveitis. ICO “Ramón Pando Ferrer” uveitis service 2013-2015.

Discussion and Conclusion

With the increase in the incidence of infection by Syphilis, a re-emergence of ocular syphilis has also been observed, reported in the USA, UK and France [4,5,18]. Thus, Romero., *et al.* (2010), report 10 cases in 13 years in the Clinical Hospital of the University of Chile [19]; Hughes., *et al.* (2010), report 13 cases at Liverpool Hospital and Sidney Eye Hospital. In Sydney, Australia in the period 2006 - 2009 [20]; Restivo L., *et al.* (2013), report 14 cases in the Sapienza University of Rome in the period 2004 - 2010 [21]; Moradi A., *et al.* (2015), report 35 patients in the Johns Hopkins Hospital in the period 1984 - 2014 [22] and Follonosa., *et al.* 50 patients are reported in a retrospective study in eight uveitis reference centers in northern Spain, carried out from 2000 to 2012 [23].

During the period from July 2013 to December 2015, 18 patients (32 eyes) with syphilitic uveitis were diagnosed in the uveitis and eye inflammation service of ICO “Ramón Pando Ferrer”, which made us think that our country was not exempt from the world events, reason is that it motivated us to carry out this study.

Regarding the distribution according to age groups, in the study performed the group of patients with 40 years and more prevailed, with 55.5% of the cases studied and the male sex, the results coincide with some of the literatures reviewed, such as the case of a study conducted by Moradi A., *et al.* at the Johns Hopkins Hospital in the period 1984 - 2014 where the average age was 45 years (24 - 80 years) [22], also coincides with the study conducted by Restivo L., *et al.* (2013), at the Sapienza University of Rome, where the average age was 46.2 years (26 - 60 years) [21] and with the study conducted by Hughes., *et al.* (2010), at Liverpool Hospital and at Sidney Eye Hospital where the average age of the patients was 41.7 years (29 - 69 years) [19]. In all the studies found, the male sex prevailed over the feminine one; as for example, in the study carried out by Hughes., *et al.* In which of the 13 patients that made up the study, 12 belonged to this sex [19].

In the study conducted, the male sex represented 88.9% with 16 patients, of them 11 (61.1%) HIV/AIDS, and the white race prevailed in 66.6% of the cases studied. This also coincides with the studies reviewed, as in the study conducted by Moradi A., *et al.* at Jonhs Hop-

kins Hospital where 54% of cases concomitantly with HIV and 94.8% of HIV patients were men [22]. Restivo L., *et al.* found that 42.8% of patients con committed with HIV [21]. Romero., *et al.*, At the Clinical Hospital of the University of Chile also observed a syphilis/HIV co-infection of 30% [18].

In all patients with ocular syphilis, the presence of HIV infection must be ruled out, both diseases share the same risk factors, both of which may be present [1,24,25]. Ocular syphilis can be more serious in HIV-infected patients who are not receiving anti-retroviral therapy [4,11].

Regarding the laterality of the ocular presentation, in this study bilateral presentation predominated in 78.8% of the cases. Other studies such as the one carried out by Restivo L., *et al.* found bilateral presentation in 50% of cases [21] and in the one by Moradi A., *et al.* At the Johns Hopkins Hospital, the presentation was bilateral in the $\frac{3}{4}$ of the patients [22].

In this study according to anatomical classification, panuveitis prevailed in 89% of the cases, coinciding with Hughes., *et al.* [19], Moradi A., *et al* [22] and with Restivo L., *et al* [21] who also found panuveitis in their studies as the predominant presentation form.

Regarding clinical manifestations, in this study, vitritis was the most frequent, being observed in 77.7% of cases, followed by internal punctate retinitis in 66.6% and thirdly neuritis, in 61.1% of patients. Romero., *et al.* In the Clinical Hospital of the University of Chile [18] and Follonosa., *et al.* [23] also refer to optic neuritis as one of the most frequent clinical manifestations in their study. Hughes., *et al.* [19] mention peripheral retinitis as the most common form of presentation. In a study conducted by Wickremasinghe S., *et al.* at the Ocular Immunology Clinic at the Royal Victorian Eye and Ear Hospital, Melbourne [26]; in a period of 8 months, he observed that the group of patients studied had marked anterior uveitis and vitritis, associated with marked arteriolitis and internal punctate retinitis. However, most of the studies reviewed do not mention the forms of presentation according to clinical manifestations, although we appreciate that in the study conducted there are similarities with the bibliography found.

In the studied patients, the final CMVA improved significantly with respect to the CMVA at the beginning of the disease, since 59.4% (19) of the patients had a BCVA of 80 var or better. Moradi A., *et al.* [24] at the Johns Hopkins Hospital found that one third of the patients improved visual acuity in at least 2 lines of the Snellen chart and more than half of the eyes maintained stable visual acuity. Wickremasinghe S., *et al.* [25] report the improvement of vision in all the patients of their study after receiving the specific treatment. Hughes., *et al.* [19] reported in their study that the final visual acuity was good in all patients where 17 of 19 eyes (89%) reached 6/9 or more and all eyes reached 6/12 or more. Follonosa., *et al.* report that the mean initial visual acuity and in the last consultation in 93 affected eyes was 20/50 (20/20 - 20/2000) and 20/22 (20/20 - 20/2000), respectively. The studies consulted coincide with the results found in this study.

Analyzing the total sample, retinal detachment was the most frequent complication (21.8%), secondly cataracts (18.7%), and thirdly, posterior synechiae (15.6%). Moradi A., *et al.* [22] at the Johns Hopkins Hospital found cataracts, chorioretinitis and posterior synechiae as the most frequent complications. Restivo L., *et al.* [21] the cystoid macular edema, the epirretinal membranes and the retinal detachment. Follonosa., *et al.* [23] reported cataracts, followed by papilla pallor and chorioretinal scars as the most frequent complications. Showing coincidence with some of the results in the study carried out.

We can conclude that our study shows results similar to others performed in other latitudes and with it we have contributed to the better knowledge of the behavior of this disease in our country.

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