Ocular manifestations observed in HTLV-I seropositive patients in Rio de Janeiro

Manifestações oculares observadas em indivíduos infectados por HTLV-I no Rio de Janeiro

Rubens Murilo Gibaile Soares [1]
Haroldo Vieira de Moraes Júnior [2]

SUMMARY

Purpose: **To evaluate the frequency of ocular manifestations observed in HTLV-I seropositive patients in Rio de Janeiro.**

Methods: **The study included 17 patients with TSP/HAM (tropical spastic paraparesis/HTLV-I associated myelopathy) and 55 HTLV-I seropositive patients without TSP/HAM or ATLL (adult T-cell leukemia/lymphoma).**

Results: **Regarding the TSP/HAM patient samples, we observed a frequency of 11.8% anterior uveitis, 11.8% retinal vasculitis and 5.9% vitreous opacity. In HTLV-I seropositive patients without TSP/HAM or ATLL, the frequencies of 1.8% retinal vasculitis and 1.8% cotton-wool spot were observed.**

Conclusion: **HTLV-I must be considered as one of the etiological agents to be thought of in those ocular manifestations in endemic areas such as Rio de Janeiro.**

Keywords: HTLV-I; Uveitis; Retinal vasculitis; TSP/HAM.

INTRODUCTION

The human T-lymphotropic virus type I (HTLV-I) was first isolated from humans in 1980 in the United States of America[1]. It is associated with diseases such as leukemia/adult T-cell lymphoma (ATLL) and tropical spastic paraparesis/HTLV-I associated myelopathy (TSP/HAM)[2-4].

Kitagawa et al[5] reported for the first time HTLV-I infection in Brazil in 1986. These authors observed a 10.4% seropositivity among individuals originating from Okinawa and residents of the city of Campo Grande (MS).

In 1989, Andrada-Serpa et al[6] observed a seroprevalence of 0.8% for HTLV-I in an Amazonian community, in the state of Pará, of African origin and relatively isolated for approximately 100 years, and of 3.7% in patients with blood diseases, residents of Rio de Janeiro.

Lee et al[7], also in 1989, found a seroprevalence of 0.4% for HTLV-I among blood donors in the city of Rio de Janeiro.

Association between neuropathies and HTLV-I in Brazil was first reported by Castro et al[8], in São Paulo in 1989. These authors found HTLV-I seropositivity in 37.9% of the patients with chronic myelopathy of unknown etiology and 7.7% of those with a diagnosis of multiple sclerosis.

In Rio de Janeiro, Araújo et al[9, 10] observed in 1993 HTLV-I seropositivity in 56.7% of patients with paraparesis of unknown etiology. They considered sexual transmission as the major risk factor for HTLV-I infection. There was no predominance of sex and the Caucasian patients were the most affected.

From the Master of Medicine thesis, elaborated at the Uveitis/AIDS.
Sector of the Service of Ophthalmology, University Hospital Clementino Fraga Filho, Federal Univesity of Rio de Janeiro.
(1) Master of Medicine, Faculty of Medicine, Federal University of Rio de Janeiro.
(2) Associate Professor, Department of Ophthalmology, Faculty of Medicine of Rio de Janeiro. Coordinator of the Postgraduate Course in Ophthalmology, Faculty of Medicine, Federal University of Rio de Janeiro.

Correspondence: Rubens Murilo Gibaile Soares. R. Cesário Alvim, 55/603 - Rio de Janeiro (RJ). CEP 22261-030.

Also in 1993, Moreira et al[11] found, in Salvador, seroprevalence for HTLV-I in 28.6% of the patients with TSP/HAM, in 22.7% of the patients with AIDS, in 18.8% of those with lymphoma and in 1.8% of the healthy.

Among blood donors, seroprevalence for HTLV-I was 0.2 to 0.4% in São Paulo, 0.4% in Rio de Janeiro, 0.7% in Pernambuco and 0.5% in Minas Gerais and in Belém do Pará[12].

Carvalho et al[13], in 1997, reported a seroprevalence for HTLV-I of 0.4% in Rio de Janeiro, among blood donors and of 10.2% among patients submitted to multiple blood transfusions.

HTLV-I infection may present a series of ocular alterations, such as vascular or noninfectious inflammatory lesions, opportunistic infections and neoplasms[14].

In patients with ATLL, ocular manifestations result in direct infiltration of neoplastic cells, opportunistic infections similar to those found in immunocompromised hosts, due to other forms of leukemia or malignant neoplasia, and uveitis[14-18].

Ocular manifestations in patients with TSP/HAM include retinal vasculitis, retinochoroidal degenerative alterations, uveitis, vitreous opacities and cotton-wool exudates. Such patients are immunocompetent and do not present opportunistic infectious disease[14, 19-26]. Other reported ocular manifestations in patients with TSP/HAM include nystagmus, diplopia, optic atrophy, retrobulbar neuropathy and Behçet's syndrome[9, 27-29].

Several reports correlate uveitis with HTLV-I in patients seropositive for this virus but not with TSP/HAM or ATLL[19, 30-38].

The purpose of this study is to draw the attention of the ophthalmologist to the possibility of an association of ocular alterations with HTLV-I.

PATIENTS AND METHODS

The files of the Uveitis Sector of the Ophthalmology Service of the University Hospital Clementino Fraga Filho of the Federal University of Rio de Janeiro, in Rio de Janeiro, RJ, were retrospectively analyzed.

The study comprised 74 HTLV-I seropositive patients examined in the period from November 8, 1995 to November 19, 1997. Two patients were excluded because they also presented HIV seropositivity, the other 72 patients being seronegative for this virus.

Serologic diagnosis of anti-HTLV-I antibodies was performed by the ELISA method (Organon Teknika, Boxbel, Holland), at the Service of Hematology, Blood Bank sector of the University Hospital Clementino Fraga Filho and confirmed by western blot, performed at the Johns Hopkins Hospital, Baltimore, USA.

All HTLV-I seropositive patients from the following services were submitted to ophthalmologic examination: 17 patients with TSP/HAM from the Service of Neurology or Rheumatology and 55 HTLV-I seropositive patients without TSP/HAM or ATLL, from the Service of Hematology (blood donors) or from the Service of Infectious and Parasitic Diseases of the University Hospital Clementino Fraga Filho.

All patients were examined by the same ophthalmologist. The ophthalmologic examination consisted of anamnesis; visual acuity; anterior segment biomicroscopy; break-up time (BUT), using sodium fluorescein eye drops; direct and indirect ophthalmoscopy with a 20-diopter lens under pupillary dilation using 1% tropicamide eye drops; and applanation tonometry after instillation of 0.5% proxymetacaine hydrochloride eye drops and sodium fluorescein eye drops.

With the purpose of excluding other etiologies for the observed ocular manifestations, the patients were submitted to systemic, clinical and laboratory examinations, including cutaneous and oral and genital mucous membrane ectoscopy; chest X-ray at posteroanterior incidence; tuberculin test, angiotensin converting enzyme; antinuclear factor; and syphilis and toxoplasmosis serology.

RESULTS

Of the 17 patients with TSP/HAM, eight were males (47.1%) and nine females (52.9%). Regarding color, 12 were Afro-Brazilians (70.6%) and five were Caucasians (29.4%).

The age of these patients at the first ophthalmologic examination ranged from 29 to 74 years with an average age of 53 years and ten months.

Concerning origin, 15 patients were from the state of Rio de Janeiro (88.2%) and two from the state of Bahia (11.8%).

No patient reported history of blood transfusion; no analysis was possible regarding sexual and vertical transmission.

Regarding the main ocular complaint reported by the patients with TSP/HAM, nine did not present complaints (52.9%), five complained of visual blurring (29.4%) and three of ocular hyperemia (17.6%) (Table 1).

No alterations were observed on biomicroscopy of the anterior segment in six patients with TSP/HAM (35.3%). Five patients presented varying degrees of lens opacification (29.4%), five exhibited seborrheic blepharitis (29.4%), two presented inferiorly distributed pigmented keratic precipitates (11.8%), two presented inferior punctate keratitis (11.8%), one presented diffuse punctate keratitis (5.9%) and one exhibited interstitial keratitis (5.9%) (Table 1).

BUT was decreased in four patients with TSP/HAM (23.5%).

No fundoscopic alterations were observed in 10 patients with TSP/HAM (58.8%). Three patients presented small areas of rarified retinal pigmentary epithelium at the periphery (17.6%), two showed venous sheathing at the retinal periphery (11.8%), one presented fine anterior vitreous opacity (5.9%) and one exhibited a point of hyperplasia of retinal pigmentary epithelium (5.9%) (Table 1).

Intraocular pressure of these patients ranged from 10 mmHg to 16 mmHg with a mean of 11.55 mmHg (Table 1).

Patients with TSP/HAM did not present significant alterations on the performed systemic evaluation.

Table 1. Ophthalmologic examination of patients with TSP/HAM

Patient	Main ocular complaint*	Biomicroscopy of anterior segment**	Break-up time (seconds)	Fundoscopy***	Intraocular pressure (mmHg)****
1	O.H.	N.A.	OU:12	OU: R.R.P.E.	OU: 10
2	A.	OU: L.O.	OU:13	OU: A.V.O.	OU: 10
3	O.H.	OU: D.K.	OU:08	N.A.	-
4	V.B.	OU: L.O.	OU:12	N.A.	OD: 16 OS: 12
5	A.	N.A.	OU:10	N.A.	OU: 13
6	A.	OU: S.B.; I.K.	OU:08	OU: R.E.P.R.	-
7	A.	N.A.	OU:12	N.A.	OU: 10
8	V.B.	OU: L.O.; P.K.P.; S.B. S. B.	OD:04 OS:03	N.A.	OU: 12
9	V.B.	OU: S.B. OD: L.O.	OD:12 OS:10	OD:Ve.S.	OU: 12
10	E.V.	OS: L.O.	OU:15	N.A.	OU: 10
11	A.	OD: P.K.P.	OU:10	N.A.	-
12	A.	OU: S.B.; I.K.	OU:07	N.A.	-
13	A.	N.A.	OU:12	N.A.	OU: 14
14	V.B.	OU: In.K.	OU:10	OU: R.R.P.E.	-
15	A.	N.A.	OU:11	OU: H.R.P.E.	OU: 12
16	O.H.	S.B.	OU:10	N.A.	-
17	A.	N.A.	OU:10	OU: Ve.S.	OU: 10

TSP/HAM: Tropical spastic paraparesis/HTLV-I associated myelopathy
* A.: absent; O.H.: ocular hyperemia; and V.B.: visual blurring.
** OU: both eyes; OD: right eye; OS: left eye; N.A.: no alterations; L.O.: lens opacification; D.K: diffuse punctate keratitis; S.B.: seborrheic blepharitis; I.K.: inferior punctate keratitis; P.K.P.: pigmented keratic precipitates; and In.K.: interstitial keratitis.
*** R.R.P.E.: rarefied retinal pigmentary epithelium; A.V.O.: anterior vitreous opacity; N.A.: no alterations; Ve.S.: venous sheathing; and H.R.P.E.: hyperplasia of the retinal pigmentary epithelium.
****: not performed.

Of the 55 HTLV-I seropositive patients without TSP/HAM or ATLL, 37 were males (67.3%) and 18 females (32.7%). Regarding color, 31 were Caucasians (56.4%) and 24 Afro-Brazilians (43.6%). The patients who presented ocular alterations are listed in Table 2. Age of these patients on the first ophthalmologic examination ranged from 19 to 65 years with a mean of 38 years and nine months.

Concerning origin, 50 patients came from the state of Rio de Janeiro (90.9%), three from Paraná (5.5%), one from Bahia (1.8%) and one from Rio Grande do Sul (1.8%).

No patient reported history of blood transfusion; no analysis was possible regarding sexual and vertical transmission.

Ophthalmologic examination did not present alterations in 34 patients (61.8%).

Regarding the main ocular complaint reported by the HTLV-I seropositive patients without TSP/HAM or ATLL, 50 did not present complaints (90.9%), three complained of ocular hyperemia (5.5%) and two of pruritus (3.6%); these data are listed in Table 2.

No alterations were observed on biomicroscopy of the anterior segment in 38% patients (69.1%). Nine patients presented seborrheic blepharitis (16.4%), four inferior punctate keratitis (7.3%) — with one also presenting pterygium in the left eye (1.8%) — two showed incipient lens opacification (3.6%), one, nummular keratitis and pannus (1.8%), one, diffuse punctate keratitis (1.8%) and one, Ota's nevus; these data are listed in Table 2.

BUT showed to be decreased in 10 HTLV-I seropositive patients without TSP/HAM or ATLL (18.2%) (Table 2).

No fundoscopic alterations were observed in 47 HTLV-I seropositive patients without TSP/HAM or ATLL (85.5%). Five patients presented a focus of inactive chorioretinitis in one or both eyes (9.1%), one showed rarified retinal pigment epithelium areas (1.8%), one presented venous sheathing at the retinal periphery (1.8%) and one exhibited cotton-wool exudate at the inferior nasal quadrant of the right eye (1.8%) without presenting arterial hypertension, diabetes mellitus and collagen diseases; these data are listed in Table 2.

Intraocular pressure of those patients ranged from 10 mmHg to 18 mmHg with a mean of 12.87 mmHg (Table 2).

The HTLV-I seropositive patients without TSP/HAM or ATLL did not present significant alterations on the performed systemic evaluation.

Comparison of ocular alterations in the patients with TSP/HAM and the HTLV-I seropositive patients without TSP/HAM or ATLL is shown in Table 3.

DISCUSSION

HTLV-I has a worldwide distribution, characterized by forming endemic clusters defined by geography or ethnic subgroups. The seroprevalence found in the different studied

Table 2. Ophthalmologic examination of HTLV-I seropositive patients without TSP/HAM or ATLL, with ocular alteration

Patient	Main ocular complaint*	Biomicroscopy of the anterior segment **	Break-up time (seconds)	Fundoscopy***	Intraocular pressure (mmHg)****
1	A.	OU: S.B.	OU:08	N.A.	OU:10
2	A.	OU: N.K. OU: Pa. 360º	OD:11 OS:08	N.A.	OD:12 OS:14
4	O.H.	OU: I.K.	OD:06;OS:09	N.A.	OU:10
13	A.	OU: O.C.	OU:12	N.A.	OU:10
14	A.	O.S.: I.K.; Pt..	OU:08	N.A.	OD:13 OS:16
18	A.	OU: S.B.	OU:10	N.A.	OD:12 OS:11
19	A.	OU: S.B.	OU:08	N.A.	OU:13
20	A.	OS: I.K.	OU:04	N.A.	OU:12
22	A.	N.A.	OU:12	OD: I.C.F.	OU:13
24	A.	OU: O.N.	OU:04	N.A.	OU:10
26	A.	OU: S.B.	OU:10	N.A.	OU:16
32	O.H.	OU: S.B.; I.K.	OU:06	N.A.	-
34	Pr.	OU: S.B.	OU:10	OU: I.C.F.	OU:13
37	A.	OU: D.K.	OU:05	OD: I.C.F.	-
39	O.H.	OU: S.B.	OU:09	OU: I.C.F.	OU:18
41	Pr.	OU: S.B.	OU:11	OS: I.C.F.	OU:16
44	A.	OU: S.B.	OU:12	N.A.	-
50	A.	OU: L.O.	OU:11	N.A.	OU:10
52	A.	N.A.	OU:10	OD: R.R.P.E.	OU:14
54	A.	N.A.	OU:12	OU: Ve.S.	OU:10
55	A.	N.A.	OU:12	OD: C.E.	OU:12

TSP/HAM: Tropical spastic paraparesis/HTLV-I associated myelopathy; ATLL: leukemia/adult T-cell lymphoma.
* A.: absent; O.H.: ocular hyperemia; and Pr.: pruritus.
** OU: both eyes; OD: right eye; OS: left eye; S.B.: seborrheic blepharitis; N.C.: nummular keratitis; Pa.: pannus; I.K.: inferior punctate keratitis; L.O.: lens opacification; Pt.: pterygium; O.N.: Ota's nevus; D.K.: diffuse punctate keratitis; and N.A.: no alterations.
***I.C.F.: inactive chorioretinitis focus; R.R.P.E.: rarefied retinal pigmentary epithelium; Ve.S.: venous sheathing; C.E.: cotton-wool exudate; and N.A.: no alterations.
****: not performed.

groups evidences that HTLV-I is endemic in Rio de Janeiro: 3.7% in patient with malignant diseases, 56.7% in patients with paraparesis of unknown etiology and 0.4% in blood donors[6, 7, 9, 10, 12, 13].

Various ocular manifestations have been related to HTLV-I. The most found have been uveitis and retinal vasculitis[14, 20, 21, 31-38]. Goto et al[38] correlated the incidence of HTLV-I associated uveitis with the incidence of environmental or hereditary factors. The association of HTVL-I with idiopathic uveitis in endemic areas in Japan ranged from 35.4% to 41%[33, 35].

Studies on HTLV-I associated uveitis performed by Mochizuki et al[31-33] revealed "flying flies" and visual blurring of acute or subacute installation as the characteristic symptoms. Nakao and Ohba[35] described the symptoms of persistent "flying flies" and low visual acuity to be present in 12.5% of the patients with HAU. A multicenter study, performed in Japan in 1994, showed that visual blurring or "flying flies", or both, were HAU associated symptoms[37]. In the present study, 29.4% of the patients with TSP/HAM complained of visual blurring, presenting some degree of lens opacification or interstitial keratitis. No HTLV-I seropositive patient without TSP/HAM or ATLL complained of visual blurring. There were no complaints about "flying flies" in none of the patients of this study.

Ohba et al[14] showed the presence of cotton-wool exudates in 23.5%, granulomatous anterior uveitis in 5.9% and vitreous opacity in 5.9% of the patients with TSP/HAM. Sasaki et al[20] reported retinal vasculitis (phlebitis and venous sheathing) in 25% and vitreous opacities in 16.7% of the patients with TSP/HAM. Hayasaka et al[21] also observed retinal vasculitis in a mother and her son with TSP/HAM. Mochizuki et al[31-33], on analyzing patients with HTLV-I associated uveitis, observed 14% uveitis, 66% intermediary uveitis with fine and membranous vitreous opacities, accompanied by iritis and vasculitis, without uveal-scleral lesion; and 19% panuveitis with some uveal-retinal lesions, besides iritis and vitreous opacities[31-33]. Yoshimura et al[34] considered HTLV-I infection as a risk factor for the development of membranous vitreous opacities and retinal vasculitis. Nakao and Ohba[35] observed that in HAU cases, two thirds presented with granulomatous alterations and one third with nongranulomatous alterations; only 2.6% of the patients exhibited mild and transient intraocular pressure increase and no patient developed glaucoma or cataract.

Table 3. Ocular alterations in patients with TSP/HAM and in HTLV-I seropositive patients without TSP/HAM or ATLL

Ocular Alterations	Patients with TSP/HAM	HTLV-I seropositive patients without TSP/HAM or ATLL
Lens opacification	29.4%	3.6%
Seborrheic blepharitis	29.4%	16.4%
Pigmented keratic precipitates	11.8%	–
Inferior punctate keratitis	11.8%	7.3%
Diffuse punctate keratitis	5.9%	1.8%
Interstitial keratitis	5.9%	–
Pterygium	–	1.8%
Nummular keratitis and pannus	–	1.8%
Ota's nevus	–	1.8%
Rarefied RPE	17.6%	1.8%
Venous sheathing	11.8%	1.8%
Anterior vitreous opacity	5.9%	–
Hyperplasia of RPE	5.9%	–
Inactive chorioretinitis	–	9.1%
Cotton-wool exudate	–	1.8%
Break-up time	23.5%	18.2%

TSP/HAM: Tropical spastic paraparesis/HTLV-I associated myelopathy; ATLL: Leukemia/adult T-cell lymphoma; RPE: Retinal pigmentary epithelium.

The multicenter study performed in Japan in 1994, indicated that HAU occurred in an acute form in middle aged adults of both sexes, being characterized by a granulomatous or non-granulomatous reaction, accompanied by vitreous opacities and retinal vasculitis with rare exudative retinochoroidal alterations in one or both eyes, and occurring as an isolated entity and, sometimes, associated with TSP/HAM. Pinheiro et al[25] reported a case of bilateral nongranulomatous anterior uveitis and Sjögren's syndrome in a patient with TSP/HAM and migratory arthritis. The present study revealed pigmented keratic precipitates in 11.8% of the patients with TSP/HAM and in none of the HTLV-I seropositive patients without TSP/HAM or ATLL; venous sheathing was observed in 11.8% of the patients with TSP/HAM and in 1.8% of those HTLV-I seropositive without TSP/HAM or ATLL; anterior vitreous opacity was observed in 5.9% of the patients with TSP/HAM and in none of those HTLV-I seropositive without TSP/HAM or ATLL. Cotton-wool exudate was not observed in the patients with TSP/HAM but was observed in 1.8% of those HTLV-I seropositive without TSP/HAM or ATLL. No patient showed increased intraocular pressure.

Nakao et al[23] and Ohba et al[24] observed, retrospectively, retinochoroidal degenerations in 9% of TSP/HAM cases, including cases of pigmentary retinosis and degenerative alterations in the retina and choroid. The results of the present study indicated rarefied retinal pigmentary epithelium in 17.6% of the patients with TSP/HAM and only in 1.8% of the HTLV-I seropositive patients without TSP/HAM or ATLL; hyperplasia of retinal pigmentary epithelium was found in 5.9% of the patients with TSP/HAM and in none of the HTLV-I seropositive patients without TSP/HAM or ATLL.

At present, a study in progress includes the use of 1% rose bengal, Schirmer's test and conjunctiva biopsy for a better analysis of lacrimal alterations in HTLV-I seropositive patients in Brazil.

HTLV-I should be considered a possible etiologic agent in uveitis, vitreous opacity, retinal vasculitis and cotton-wool exudate cases, formerly considered to be idiopathic, in Rio de Janeiro.

RESUMO

Objetivo: *Avaliar a freqüência de manifestações oculares observadas em pacientes soropositivos para HTLV-I no Rio de Janeiro.*

Métodos: *O estudo abrangeu 17 pacientes portadores de TSP/HAM (paraparesia tropical espástica/mielopatia associada ao HTLV-I) e 55 pacientes soropositivos para HTLV-I não-portadores de TSP/HAM ou ATLL (leucemia/linfoma de células T do adulto).*

Resultados: *Nos pacientes portadores de TSP/HAM foi observada a freqüência de 11,8% de uveíte anterior, 11,8% de vasculite retiniana e 5,9% de opacidade vítrea. No grupo de pacientes soropositivos para HTLV-I não-portadores de TSP/HAM ou ATLL, observou-se a freqüência de 1,8% de vasculite retiniana e 1,8% de exsudato algodonoso.*

Conclusão: *Concluiu-se que, em tais manifestações oculares, o HTLV-I deve ser considerado como um dos agentes etiológicos a serem pesquisados em áreas endêmicas como o Rio de Janeiro.*

Palavras-chave: *HTLV-I; Uveíte; Vasculite retiniana; TSP.*

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