

Epidemiology of the Ocular Complications of HIV Infection in Chiang Mai

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Abstract

Objective : To identify the magnitude of ocular complications in HIV infection in Chiang Mai, and determine the signs or symptoms that indicate the risk factors for developing ocular complications in HIV-positive patients

Method : A prospective study was carried out in newly diagnosed HIV-positive patients seen in the Ocular Infectious Disease Clinic of Maharaj Nakorn Chiang Mai Hospital from March 1, 2000 through February 28, 2001. A complete ophthalmic examination was performed on each patient together with a systemic evaluation of present illness and current medications.

Results : Three-hundred and ninety-five HIV-positive patients were seen for ophthalmic evaluation. Of these, 90 were in stage A (asymptomatic), 84 were in stage B (symptomatic), and 221 were in stage C (AIDS). Ocular complications were found in 44.6 per cent of the patients. Cytomegalovirus (CMV) retinitis was the most common ophthalmic complication (33%). Other ocular complications included cotton wool spot (8%), uveitis (4%), optic neuropathy (3%), and keratoconjunctivitis sicca (2%). The clinical presenting symptoms, which were the indicators for ocular complications and CMV retinitis, included chronic cough, oral thrush, chronic diarrhea, weight loss, wasting, and skin disorders. Ocular symptoms, which indicated a high risk of developing CMV retinitis, included flashing, floaters, and scotoma.

Conclusions : Ocular complications are common in HIV-positive patients. CMV retinitis, which is a major vision-threatening problem, represented the most common finding. It is recommended that HIV-positive patients should have their eyes examined regularly, particularly when they have the clinical presenting symptoms previously mentioned. The patients should also notice early symptoms of CMV retinitis, which includes flashing, floaters, and scotoma.

Key word : HIV, Eye Complications, CMV Retinitis

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HIV is still an epidemiologic problem worldwide, including Thailand(1,2). According to the surveillance for HIV infection/AIDS from the Division of Epidemiology, Ministry of Public Health of Thailand, the number of AIDS patients in Thailand from September 1984 to September 2002 were 201,268, in which 70,851 were in the northern part of the country(2).

Ocular manifestations of HIV infection were first described 15 years ago(3). The lifetime cumulative rate of at least one abnormal ocular lesion developing in an HIV-infected patient ranges from 52 per cent to 100 per cent in various studies(4). There was a report that indicated the difference in the manifestations of this disease between industrialized countries and Africa, but the ocular manifestations of HIV infection in Asia have not been well described(5).

Cytomegalovirus (CMV) retinitis is the most common leading cause of vision loss in HIV-infected patients whose CD4+ T-lymphocyte count is below 100 cells/ μ l(6). Due to the high costs of detecting the CD4+ T-lymphocyte count, the predictive parameters of ocular complications, particularly CMV retinitis, would be useful in screening HIV-infected patients, since early diagnosis and prompt treatment may postpone vision loss.

This study was conducted to identify the magnitude of ocular complications in HIV infection in Chiang Mai, and determine the signs or symptoms that indicate the risk factors for developing ocular complications in HIV positive patients.

PATIENTS AND METHOD

The study was carried out over a one-year period at Maharaj Nakorn Chiang Mai Hospital, a tertiary health center and university teaching hospital in northern Thailand.

The recruitment population consisted of newly diagnosed HIV-positive patients, who were seen in the Outpatient Department of the Ocular Infectious Disease and CMV Retinitis Clinic from March 1, 2000 through February 28, 2001.

The clinical presenting symptoms of systemic features, current medications, and visual symptomatology were recorded on a detailed, printed questionnaire. A complete ophthalmic examination was performed, which included best-corrected visual acuity, external eye examination, ocular motility, pupillary reflexes, anterior segment examination by slit-lamp biomicroscopy, dilated fundus examination by indirect

ophthalmoscopy, and intraocular pressure measurement by non-contact tonometry. External, slit-lamp biomicroscope, and fundus photographs were obtained in some cases with positive findings.

Univariable analyses were performed with SPSS for Windows Version 9.01 (SPSS Inc., Chicago, USA). For risk factor analyses, odds ratio and 95 per cent of confidence intervals were computed. Chi-square tests were used to evaluate significant differences in proportion among groups. A p-value < 0.05 was considered statistically significant.

RESULTS

Three hundred and ninety-five HIV-positive patients were examined between March 2000 and February 2001. There were 159 men and 236 women. The age of the patients ranged from 8 years to 62 years, with the mean age \pm SD being 33.8 ± 6.8 years

With the use of CDC criteria(7) according to the clinical categories, the patients were classified into 3 stages : A (asymptomatic or acute HIV infection), B (symptomatic), and C (AIDS indicator condition). There were 90, 84, and 221 patients in stage A, B, and C, respectively. Those in stage C had opportunistic infections including cytomegalovirus (59%), pulmonary tuberculosis (29%), *Pneumocystis carinii* pneumonia (20%), central nervous system cryptococcosis (12%), and others. One hundred and seventy-six patients (44.6%) had HIV-related ocular involvement, of whom 8, 21, and 147 were in stage A, B, and C respectively. The relative risk of ocular involvement was 20.3, and 1 in stage C, B, and A, respectively (Table 1).

The clinical presenting symptoms in the patients who had ocular involvement included weight loss, skin disorders, oral thrush, chronic cough, wasting, chronic diarrhea, herpes zoster, and others such as jaundice, sinusitis, headache, and back pain. Most patients had more than one clinical presenting symptom. Statistical significance was found in patients with weight loss, skin disorders, oral thrush, and chronic cough (Table 2).

Current medications received by these patients included antiretroviral drugs, drugs for opportunistic infections (O.I.), and herbal drugs. Ocular complications were seen in 2 of 21, 97 of 172, 6 of 24, 25 of 59, 16 of 35, and 30 of 77 patients who received antiretroviral drugs, drugs for O.I., herbal drugs, antiretroviral drugs and drugs for O.I., drugs for O.I. and herbal drugs, and no drugs, respectively. No ocular

Table 1. Ocular involvement by staging of HIV infection.

HIV Staging	No. of patients	%	No. of patients with ocular involvement	RR*	95% CI**	P***
A	90	23	8	1.0	-	-
B	84	21	21	3.4	1.420-8.221	0.004
C	221	56	147	20.4	9.354-44.323	< 0.001

* RR = Relative risk, the RR of the reference group is 1.0

** CI = Confident interval

*** from χ^2 test

Table 2. Ocular involvement by clinical presenting symptoms.

Presenting symptoms*		No. of patients	No. of patients with ocular involvement	%	Odd ratio	95% CI	P**
Weight loss	Y	123	75	61.0	2.645	1.707-4.099	0.001
	N	272	101	37.1			
Skin disorders	Y	93	60	64.5	2.915	1.797-4.730	< 0.001
	N	302	116	38.4			
Oral thrush	Y	84	55	65.5	2.978	1.799-4931	< 0.001
	N	311	121	38.9			
Chronic cough	Y	70	49	70.0	3.638	2.083-6.354	< 0.001
	N	325	127	39.1			
Wasting	Y	51	30	58.8	1.937	1.066-3.520	0.028
	N	344	146	42.4			
Chronic diarrhea	Y	41	27	65.9	2.653	1.345-5.233	0.004
	N	354	149	42.1			
Herpes zoster	Y	24	14	58.3	1.806	0.782-4.171	0.161
	N	371	162	43.7			
Others	Y	21	8	38.1	0.755	0.303-1.863	0.540
	N	374	168	44.9			

* Some patients had more than one presenting symptom.

** from χ^2 test

Y = Yes, N = No

complications occurred in the patients who received antiretroviral and herbal drugs, or those who had a combination of all three drugs. Statistical significance was found in patients who received antiretroviral drugs, and those who received drugs for O.I. (Table 3).

CMV retinitis was the most common ocular finding, observed in 130 patients (33%). Other findings included cotton wool spots (8%), uveitis (4%), optic neuropathy (3%), keratoconjunctivitis sicca (2%), and others. Many patients had more than one ocular finding (Table 4).

One hundred and ninety-seven eyes of 130 patients developed CMV retinitis. The age of the CMV retinitis patients ranged from 22 to 52 years, with the mean age \pm SD being 33.6 ± 5.8 years. The ratio of men to women was 3 : 4. The visual acuity at initial

presentation was in the 6/6 to 6/18 range in 110 eyes (56%), < 6/18-3/60 range in 24 eyes (12%), < 3/60-PL range in 48 eyes (24%), and NoPL in 15 eyes (8%). The intraocular tension was between 10 and 21 mmHg in 74 eyes (38%), below 10 mmHg in 75 eyes (38%), above 21 mmHg in 7 eyes (3%), and indeterminable in 41 eyes (21%).

The clinical presenting symptoms in the CMV retinitis patients, which were statistically significant, included weight loss, skin disorders, oral thrush, chronic cough, wasting, and chronic diarrhea (Table 5).

The medications administered to the CMV retinitis patients, which were statistically significant, included antiretroviral drugs and drugs for O.I. (Table 6).

Table 3. Ocular involvement by current medications.

Current medications		No. of patients	No. of patients with ocular involvement	%	Odd ratio	95% CI	P*
A. Antiretroviral drugs	Y	21	2	9.5	0.121	0.028-0.527	0.001
	N	374	174	46.5			
B. Drugs for OI	Y	172	97	56.4	2.357	1.568-3.544	< 0.001
	N	223	79	35.4			
C. Herbal drugs	Y	24	6	25.0	0.394	0.156-1.015	0.047
	N	371	170	45.8			
D. A + B	Y	59	25	42.4	0.901	0.515-1.576	0.714
	N	336	151	44.9			
E. B + C	Y	35	16	45.7	1.053	0.524-2.113	0.021
	N	360	160	44.4			
F. A + C	Y	2	0	0	NA	-	-
	N	393	176	44.8			
G. A + B + C	Y	5	0	0	NA	-	-
	N	390	176	45.1			
H. None	Y	77	30	39.0	0.752	0.452-1.250	0.271
	N	318	146	45.9			

* from χ^2 test

OI = Opportunistic infection, Y = Yes, N = No, NA = Not applicable

Table 4. Ocular involvement by laterality.

Ocular findings	Unilateral	Bilateral	Total cases*	%	Total eyes
CMVR	63	67	130	32.9	197
CWS	25	7	32	8.1	39
Uveitis	12	5	17	4.3	22
Optic neuropathy	10	3	13	3.3	16
KCS	3	5	8	2.0	13
PORN	4	3	7	1.8	10
Keratitis	1	3	4	1.0	7
Vascular sheathing	2	1	3	0.8	4
Papilledema	1	1	2	0.5	3
Molluscum	1	0	1	0.3	1
CN Palsy	1	0	1	0.3	1
Toxoplasmosis	1	0	1	0.3	1
HZK	1	0	1	0.3	1

* Some patients had more than one ocular finding.

CMVR = Cytomegalovirus retinitis, CWS = Cotton wool spot, KCS = Keratoconjunctivitis Sicca,

PORN = Progressive outer retinal necrosis, CN palsy = Cranial nerve palsy, HZK = Herpes zoster keratitis.

The ocular symptoms in the CMV retinitis patients, which were statistically significant, included blurred vision, floaters, scotoma, flashing, photophobia, and ocular pain (Table 7).

DISCUSSION

Ocular manifestations are common in HIV-infected patients. The present study showed that 45 per cent of the patients had ocular complications. CMV retinitis was the most common finding, affecting 33

per cent of the patients. Other ocular findings were substantially less common than CMV retinitis. They included cotton wool spot (18%), uveitis (14%), optic neuropathy (3%), and keratoconjunctivitis sicca (Table 4). The spectrum of ocular lesions in HIV-positive patients in the present study was different from that seen in other parts of the world, where the cotton wool spot is the most common ocular manifestation (8-10).

This study was carried out at a university teaching hospital, which is a tertiary referral center,

Table 5. CMV retinitis by clinical presenting symptoms.

Presenting symptoms*		No. of patients	No. of patients with CMV retinitis	%	Odd ratio	95% CI	P**
Weight loss	Y	123	61	49.6	2.895	1.852-4.525	< 0.001
	N	272	69	25.4			
Skin disorders	Y	93	48	51.6	2.862	1.772-4.622	< 0.001
	N	302	82	27.2			
Oral thrush	Y	84	45	53.6	3.068	1.868-5.038	< 0.001
	N	311	85	27.3			
Chronic cough	Y	70	41	58.6	3.749	2.197-6.397	< 0.001
	N	325	89	27.4			
Wasting	Y	51	25	49.0	2.189	1.207-3.968	0.009
	N	344	105	30.5			
Chronic diarrhea	Y	41	23	56.1	2.950	1.529-5.691	0.001
	N	354	107	30.2			
Herpes zoster	Y	24	12	50.0	2.144	0.935-4.914	0.066
	N	371	118	31.8			
Others	Y	21	5	38.1	0.623	0.223-1.738	0.362
	N	374	125	33.4			

* Some patients had more than one presenting symptom.

** from χ^2 test

Y = Yes, N = No

Table 6. CMV retinitis by current medications.

Current medications		No. of patients	No. of patients with ocular involvement	%	Odd ratio	95% CI	P*
A. Antiretroviral drugs	Y	21	1	4.5	0.095	0.013-0.716	0.001
	N	374	129	34.5			
B. Drugs for OI	Y	172	76	44.2	2.478	1.613-3.807	< 0.001
	N	223	54	24.2			
C. Herbal drugs	Y	24	5	20.8	0.518	0.189-1.420	0.047
	N	371	125	33.7			
D. A + B	Y	59	16	27.1	0.725	0.391-1.343	0.714
	N	336	114	33.9			
E. B + C	Y	35	11	31.4	0.928	0.440-1.958	0.021
	N	360	119	31.1			
F. A + C	Y	2	0	0	NA	-	-
	N	393	130	33.1			
G. A + B + C	Y	5	0	0	NA	-	-
	N	390	130	33.3			
H. None	Y	77	21	27.3	0.719	0.414-1.249	0.241
	N	318	109	34.3			

* from χ^2 test

OI = Opportunistic infection, Y = Yes, N = No, NA = Not applicable

where a much greater percentage of patients with AIDS (stage C) were referred than those with earlier stages of HIV infection (stage A, and stage B). This partly explains why many CMV retinitis patients were seen in the present study.

In Thailand, patients infected with HIV do not undergo routine ophthalmic evaluation. They are

often referred for ophthalmic examination only if they complain of problems associated with vision. Because isolated cotton wool spots do not cause visual impairment, and in the present study most cases were referred because of complaints of visual impairment, cotton wool spots would probably remain undetected due to this referral bias.

Table 7. CMV retinitis by ocular symptoms.

Ocular symptoms		No. of eyes	No. of eyes with CMV retinitis	%	Odd ratio	95% CI	P*
Blurred vision	Y	205	147	71.7	27.119	17.819-41.273	< 0.001
	N	585	50	8.5			
Floaters	Y	128	101	78.9	22.055	13.694-35.520	< 0.001
	N	662	96	14.5			
Scotoma	Y	43	35	81.4	15.799	7.188-34.725	< 0.001
	N	747	162	21.7			
Flashing	Y	42	38	90.5	35.192	12.376-100.00	< 0.001
	N	748	159	21.3			
FB sensation	Y	38	15	39.5	2.043	1.044-3.998	0.034
	N	752	182	24.2			
Tearing	Y	40	11	27.5	1.150	0.563-2.348	0.701
	N	750	186	24.8			
Photophobia	Y	43	23	53.5	3.787	2.032-7.060	< 0.001
	N	747	174	23.3			
Ocular pain	Y	33	20	60.6	5.041	2.458-10.339	< 0.001
	N	757	177	23.4			

* from χ^2 test

FB sensation = Foreign body sensation

This study attempted to determine whether presenting clinical symptoms were specifically associated with ocular involvement, particularly CMV retinitis. Statistically significant association was found in the clinical symptoms of chronic cough, chronic diarrhea, oral thrush, weight loss, skin disorders and wasting (Table 2 and Table 5). These clinical symptoms are indeed the presenting features of AIDS(9), so it is not surprising that they were associated with ocular involvement in the present study, in which 56 per cent of the patients were in stage C (Table 1). This finding differed from a study of ophthalmic manifestations of AIDS in Kenya(9), which found that there were no statistically significant associations between ocular involvement and any of these clinical symptoms.

From the present study, it is evident that patients who received antiretroviral drugs were at lower risk, but those who received drugs for O.I. had a greater risk of ocular lesions, including CMV retinitis (Table 3 and Table 6). These data must be interpreted cautiously because the patients who received drugs for O.I. usually reflected more severe immunodeficiency than those in the earlier stages of HIV infection, and were, thus, more likely to have ocular complications.

Ocular symptoms were analyzed for the early detection of CMV retinitis (Table 7). Symptoms sig-

nificantly associated included flashing, blurred vision, floaters, and scotoma. Floaters was the ocular symptom previously mentioned in patients with CMV retinitis(11).

In conclusion, CMV retinitis represented the most common ocular finding of the patients in the present study. It is a major vision-threatening problem, which if untreated or treatment is delayed, ultimately leads to blindness(8-11). An important issue in the management of ocular complications, particularly CMV retinitis in HIV-positive patients, is to find practical and cost-effective strategies for early diagnosis and treatment. It is recommended that all HIV-positive patients should have regular ophthalmic examinations, especially those in stage C, or when they present with clinical symptoms such as chronic cough, chronic diarrhea, oral thrush, weight loss, skin disorders, and wasting. Health care providers should advise HIV-positive patients to recognize the ocular symptoms of CMV retinitis before getting blurred vision, which includes flashing, floaters, and scotoma. When they report these symptoms, the patients should be referred promptly to an ophthalmologist for appropriate management.

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ระบบวิทยาของภาวะแทรกซ้อนทางด้านของการติดเชื้อเอชไอวีในเชียงใหม่

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วัตถุประสงค์ : เพื่อสำรวจหาความรุนแรงของภาวะแทรกซ้อนทางด้านผู้ป่วยติดเชื้อเอชไอวี ในจังหวัดเชียงใหม่ และเพื่อหาการหรือการแสลงที่จะเป็นตัวชี้นำของปัจจัยเสี่ยงในการเกิดภาวะแทรกซ้อนทางด้านผู้ป่วยติดเชื้อเอชไอวี

วิธีการศึกษา : ได้ทำการศึกษาในผู้ป่วยใหม่ที่มีเชื้อเอชไอวี ที่มาตรวัดตาที่โรงพยาบาลราชวิถี ตั้งแต่ 1 มีนาคม 2543 ถึง 28 กุมภาพันธ์ 2544 โดยผู้ป่วยได้รับการตรวจตาอย่างละเอียด รวมทั้งประเมินอาการเจ็บป่วยและยาที่ได้รับปัจจุบัน

ผลการศึกษา : มีผู้ป่วยติดเชื้อเอชไอวี ทั้งหมด 395 คน โดยอยู่ในระยะ A (asymptomatic) 90 คน ระยะ B (symptomatic) 84 คน และระยะ C (AIDS) 221 คน พบภาวะแทรกซ้อนทางตาใน 44.6% ของผู้ป่วย โดยพบว่า cyto-megalovirus (CMV) retinitis เป็นภาวะแทรกซ้อนทางตาที่พบบ่อยที่สุด (33%) รองลงมาได้แก่ cotton wool spot (8%) uveitis (4%) optic neuropathy (3%) และ keratoconjunctivitis sicca (2%) อาการแสดงภาวะเจ็บป่วยที่เป็นตัวชี้นำของการเกิดภาวะแทรกซ้อนทางตา และ CMV retinitis ได้แก่ อาการไอเรื้อรัง การมีฝ้าขาวในปาก ห้องเสียเรื้อรัง น้ำหนักลด อ่อนเพลียไม่มีแรง และไข้คิดว่าหัน อาการทางตาที่เป็นเครื่องชี้นำถึงความเสี่ยงต่อการเกิด CMV retinitis ได้แก่ อาการมองเห็นฟ้าແกลบในตา มองเห็นจุดดำล้อมไปด้วยแสง และมองเห็นแสงดับในลานสายตา

สรุป : ภาวะแทรกซ้อนทางตาพบบ่อยในผู้ติดเชื้อเอชไอวี โดย CMV retinitis ซึ่งเป็นโรคที่มีผลต่อสายตามาก เป็นภาวะแทรกซ้อนทางตาที่พบมากที่สุด จึงมีข้อเสนอแนะว่า ผู้ป่วยที่ติดเชื้อเอชไอวี ทุกราย ควรได้รับการตรวจตาเป็นระยะ ๆ โดยเฉพาะอย่างยิ่งเมื่อมีอาการแสดงภาวะเจ็บป่วยเหล่านี้ได้แก่ ไอเรื่องวัง ฝ้าขาวในปาก ห้องเสียรือรัง น้ำหนักลด อ่อนเพลีย ไม่มีแรง และมีโรคผิวหนัง นอกจากนี้ผู้ป่วยควรหมั่นลังเกดอาการทางตาซึ่งเป็นอาการเริมต้นของ CMV retinitis ได้แก่เห็นฟ้าแลบในตา มองเห็นจุดดำลอยไปมา และมองเห็นแสงคำในลานสายตา

คำสำคัญ : เอ็ชไอวี, ภาวะแทรกซ้อนทางตา, จอต้าอักเสบจากไข้โตเมกาโลไวรัส

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