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Case Series

Uveitis Among Children Living with HIV / AIDS in Kinshasa, RD Congo: A Case Series

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ABSTRACT

Purpose: To report the clinical features of a series of children living with HIV / AIDS (CLWHA) with uveitis.

Methods: This was a case series of CLWHA and who had a diagnosis of uveitis examined from November 2010 to April 2011 in five sanitary structures in Kinshasa. For each child, anamnestic elements were collected. Each child underwent an ophthalmological examination including visual acuity measurement, slit lamp examination and fundus examination after dilation.

Results: 15 CLWHA presented with uveitis out of a series of 100 CLWHA examined. Fourteen of the children with uveitis were already on treatment and had normal immune status, the only child who had not yet started treatment had a severe immune deficiency. Retinal vasculitis was the most common disorder in 8 children. It was asymptomatic and mainly concerned the veins on the peripheral retina. Four children presented with chorioretinal scars of unknown etiology. HIV-related microangiopathy was found in 2 children. Unilateral anterior uveitis was the only symptomatic involvement, found in the child who were not on treatment.

Conclusion: Uveitis is common in African CLWHA. Retinal vasculitis of unknown etiology appears to be the most common clinical manifestation in this population. Antiretroviral therapy seems to decrease the frequency of sight-threatening conditions.

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Introduction

Infection by the Human Immunodeficiency Virus (HIV) is a multi-systemic condition that causes a wide range of diseases. Ocular manifestations concern 50 to 80% of people living with HIV / AIDS at some point of the disease [1]. Intraocular inflammation affects more than 50% of people living with HIV / AIDS [2]. Before era of highly active anti-retroviral therapy (HAART), opportunistic infections, neoplasms, and HIV itself were the main etiologies of uveitis in people with HIV infection [2]. Some authors have focused on uveitis in adult patients living with HIV / AIDS, but little data are available on uveitis in children [3-6]. Therefore, the aim of this study was to report clinical features of uveitis among children living with HIV/AIDS (CLWHA).

Patients and Methods

This was a case series of children infected with HIV/AIDS (CLWHA) and who had a diagnosis of uveitis (ocular inflammation) examined from November 2010 to April 2011 in five centers (sanitary structures) in Kinshasa. The clinical stage of HIV / AIDS infection has determined according to the revised classification of the World Health Organization [7]. The immune status of children has been determined according to the WHO classification of immunodeficiency based on CD4 count, (2006) [7]. For each child, the anamnestic elements were collected from parents or legal guardians and in the medical file. Each child received an ophthalmological examination including measure of visual acuity, inspection of the adnexa, a slit lamp examination and fundus

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examination after dilation by indirect ophthalmoscopy and physical examination by a pediatrician.

Description of Cases

A total of 100 CLWHA seen during the study period, 18 eyes of 15 CLWHA with uveitis were enrolled, giving a frequency of 15%. Table 1 presents demographic data including number of eyes, age, clinical stage, immune status and treatment. Retinal vasculitis was the most common disorder seen in eight CLWHA (10 eyes) followed by chorioretinal scars (CLWHA) in four children (5 eyes), isolated cotton wool spots in two children (2 eyes) and unilateral anterior uveitis in one child (1 eye). The distribution of these different manifestations according to age, sex, clinical stage of HIV infection, immune status and treatment are shown in (Table 2).

Retinal vasculitis was diagnosed in 8 CLWHA. Retinal vasculitis was unilateral in six (six eyes) CLWAH and bilateral in two (4 eyes) CLWAH. Among the 8 children who had vasculitis, five had a chronic dry cough. Lesions involved veins in six children, arteries in one and both veins and arteries in one child. They were localized in the peripheral retina in all children and no ocular complains were noted.

Table 1: General characteristics of children with uveitis.

Characteristics	Frequency
• Age (years)	
- 0 - 5	1
- 6 - 10	7
- 11 - 15	7
• Sex	
- Girls	10
- Boys	5
• Clinical stage of HIV infection	
- Stage 1	13
- Stage 2	0
- Stage 3	1
- Stage 4	1
• Immune status	
- Normal	12
- Moderate deficit	2
- Severe deficit	1
• Treatment	
- ARVtherapy+ cotrimoxazole	10
- Cotrimoxazole	4
- No treatment	1

Table 2: Distribution of ocular manifestations according to clinical characteristics.

	Vascularitis	Chorioretinitis	HIV-related microangiopathy	Anterior uveitis	Total
N	8	4	2	1	15
Sex					
- Girls	6	2	2	0	10
- Boys	2	2	0	1	5
Age (years)					
- 0-5	0	0	0	0	0
- 6-10	6	2	0	0	8
- 11-15	2	2	2	1	7
Clinical stage of HIV					
- Stage 1	7	4	2	0	13
- Stage 2	0	0	0	0	0
- Stage 3	1	0	0	0	1
- Stage 4	0	0	0	1	1
Immune deficiency					
- Absent	7	3	2	0	12
- Moderate	1	1	0	0	2
- Advanced	0	0	0	0	0
- Severe	0	0	0	1	1
Treatment					
- Cotrimoxazole	2	0	2	0	4
- Cotrimoxazole	6	4	0	0	10
- + ARV					
- No treatment					
	0	0	0	1	1
Ocular complaints	No	No	No	Yes	
Visual acuity	6/6	6/6	6/6	6/9	

Chorioretinal scars were found in four children; no case of active chorioretinitis was found. Lesions were unilateral in three children and

bilateral in one child. All lesions were located in the peripheral retina. None of these children had any ocular symptoms.

Cotton wool spots as sign of HIV-related microangiopathy was present in two CLWHA. Lesions were unilateral and located in the peripheral retina. These children had no general complaints. One of them had allergic conjunctivitis. The second child had no ocular complaints.

Unilateral anterior uveitis was found in a 12-year-old boy who was in stage 4 of HIV / AIDS infection, with a severe immune deficiency and who has not yet started any treatment. The diagnosis of HIV infection was made twenty days before our examination. He complained of pain in this eye, with visual acuity of 6/9 and a normal posterior segment examination. Contralateral eye was healthy with normal vision. We noted retro-corneal precipitates and a mild Tyndall of aqueous humor.

Discussion

In adult population, intraocular inflammation or uveitis is found in more than 50% of patients living with HIV / AIDS [2]. In our series of 100 HIV-positive children, 15% showed signs of intraocular inflammation. Retinal vasculitis mainly affecting veins in the retinal periphery without any other inflammatory signs and with no visual impact was the most common lesions in our series. This finding is identical to those reported previously in Sub-Saharan Africa [8-12]. Retinal vasculitis is an inflammatory response isolated to the venous, arterial, or capillary retinal vasculature. It can be associated with a number of local or systemic diseases. Retinal vasculitis would be one of the clinical

manifestations of diffuse lymphocytic infiltration syndrome (DILS) which is a clinical syndrome characterized by an increase in circulating CD8 lymphocytes, a reversal of the CD4-CD8 ratio and diffuse lymphocytic tissue infiltration [9].

Clinical manifestations of this syndrome include bilateral parotitis, lymphocytic interstitial pneumonia, splenomegaly, lymphadenopathy, neurological and lacrimal glands involvement. This syndrome is more frequent in patients of African origin and is linked to a genetic predisposition due to the HLA DR5, DR6, DR7 and DR2 genes [13]. Among the 8 children who had vasculitis, five had a chronic dry cough, which could be sign of a lymphocytic interstitial pneumonia (LIP) but none of them showed signs of dyspnea which is the progressive mode of the majority of cases of LIP. No children had clinical signs of involvement of salivary or lacrimal glands. Unfortunately, we have not performed any paraclinical examinations (biopsies of salivary glands) that can confirm the hypothesis of DILS in our series.

Peripheral chorioretinal scars with no visual impact were found in 4% of children in our series. We were unable to determine the etiology of these lesions, which did not have characteristics of ocular toxoplasmosis. Kestelyn in his series found 6 cases of cicatricial chorioretinitis, 2 of them were macular localization suggesting toxoplasmosis, the other 4 being peripheral and their etiologies were difficult to determine [9].

Table 3: Frequencies of uveitis in children living with HIV/AIDS in different studies.

Author	Country Year	Vasculitis	HIV-related microangiopathy	Chorioretinitis	Anterior Uveitis	CMV retinitis
Kestelyn [9]	Rwanda (2000)	38%	0,6%	5%	0%	1,8%
Padhani [10]	Tanzania (2000)	3,2%	3,2%	0%	0%	0%
Ikoona [8]	Ouganda (2003)	31%	0%	0%	0%	4%
M'bongo [11]	Kenya (2008)	13,5%	9,6%	0%	2,9%	0,9%
Nsiangani [7]	DR Congo (2013)	8%	2%	4%	1%	0%

HIV-related microangiopathy is a retinal disorder manifested by cotton-wool spots or hemorrhages that does not progress and have no visual impact [14]. This entity is rare in children with HIV, whereas in adult population it constitutes the most frequent retinal lesion and concerns up to 50% of patients [1]. In our series it concerned 2% of children, in other African pediatric series it was found in frequencies varying from 0 to 9.6% (Table 3). The mechanism of occurrence of this microangiopathy remains imprecise, HIV itself or a host response to infection is thought to be the cause [1]. The cotton-wool spot, which is the most common lesion of HIV retinopathy, results from the accumulation of neurofilaments and dense bodies in the axons of the nerve fibers layer resulting of an ischaemia by occlusion of the retinal capillaries. The mechanism responsible for this occlusion is not certain, several phenomena have been mentioned: direct infection of endothelial cells by HIV, deposition of circulating immune complexes, alterations in hematological factors or secretion of monokines and proteolytic enzymes [15, 16].

We found a case of unilateral acute anterior non-granulomatous uveitis, which was the only symptomatic ocular manifestation. It concerned a child with severe immune deficiency who had not yet started treatment and the diagnosis of its HIV infection had just been made few days before. M'bongo, in Kenya noted 2.9% of cases of anterior uveitis in

children of his series (Table 3) [11]. In adult patients, HIV has been described as a cause of uveitis by several authors and anterior uveitis has been reported to affect 4 % of AIDS patients [2-5]. Rosberger and Kinavisarut described anterior uveitis, which did not respond to steroid therapy and presented an improvement after initiation of ARV therapy [3, 4]. In Rosberger's series, HIV was the only infectious agent found after aqueous humor and vitreous culture in his patients [3]. Kinavisarut found a positive aqueous humor-plasma HIV RNA ratio in its patients, which would suggest the existence of an intraocular replication of HIV, rather than a rupture of the blood-ocular barrier [4, 5].

An identical process of replication of the virus is described at the level of the CNS, which like the eye is a privileged immunological site. Active replication of the virus is believed to be the basis of the intraocular inflammatory response. The supposed sites for this replication are microglia, endothelial cells of retina, choroid, retinal pigment epithelium and iris [4]. The presence of HIV in the eye is associated with a high viral load and not being on ARV therapy [4]. This entity, called "HIV-induced uveitis", represents 11% of cases of uveitis in HIV-positive patients, it must be suspected in HIV-positive patients with a high viral load, who have not yet received antiretroviral therapy or in whom this treatment failed [4, 17]. This uveitis is accompanied by mild to moderate inflammation of the aqueous humor, which can extend to the vitreous,

without associated retinal lesions. The involvement can be unilateral or bilateral, with reduced visual acuity [3, 4]. We can suppose that our case of uveitis could have been due to HIV because the child had no clinical signs of an opportunistic infection and had not yet started antiretroviral therapy. After the start of treatment, signs of ocular inflammation disappeared. Unfortunately, we were unable to perform an anterior chamber for identifying infectious agents in the aqueous humor and confirm the etiology of this uveitis.

No cases of CMV retinitis were noted in our series; this absence of CMV retinitis could be explained by the fact that the majority of our patients were already on treatment and had a normal immune status. Although CMV retinitis is common in adults infected with HIV, in whom it affects around 20% of patients, this condition is rare in the pediatric population with a frequency around 1.2% [18]. This low frequency of CMV retinitis and other opportunistic infections (toxoplasmosis, TBC, cryptococcosis) in children with HIV / AIDS could be explained by the fact that children were not in contact with its organisms, unlike adults who, in the presence of an immunodeficiency, can reactivate these germs to which they have already been in contact beforehand [10].

Unfortunately, the small size of our sample and the fact that we were not able to carry out more paraclinical explorations constitute limits to this work. This study reveals that uveitis is common in African children with HIV / AIDS, retinal vasculitis being the most frequently clinical manifestation found. Etiology of this asymptomatic vasculitis remains to be elucidated. Antiretroviral treatment seems to decrease the frequency of visual threatening manifestations in HIV infected children. A study on a larger series of patients with a more thorough etiological assessment would improve knowledge of main causes of uveitis in this population.

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Conflicts of Interest

None.

Author Contributions

All the authors participated in the planning, research and writing of the final manuscript, as well as reviewing and rewriting of the revised version.

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