Chapter 7

The aetiology of Uveitis in Suriname

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Abstract

**Background/Aims:** To report on the spectrum of uveitis in the multi-ethnic population of Suriname.

**Methods:** A prospective cohort study of 100 consecutive uveitis cases was performed between July 2014 and January 2015. All patients underwent medical history screening using a specific uveitis screening questionnaire as well as a standard laboratory screening protocol. Subsequently, all patients were classified according to their age, gender, and ethnicity, as well as their anatomical and aetiological diagnosis using the Standardization of Uveitis Nomenclature Working Group (SUN) criteria.

**Results:** Anterior uveitis (AU) was the most common location (64%), followed by panuveitis (panU) in 19%, posterior uveitis (PU) in 15%, and intermediate uveitis (IU) in 2% of patients. Infectious uveitis was diagnosed in 34% of patients, 71% of who had toxoplasmosis. Two of the latter group were also HIV positive. Furthermore, 12% of the patients with infectious uveitis had latent tuberculosis, 9% had ocular syphilis, and 9% herpetic uveitis. Uveitis associated with systemic non-infectious disease was diagnosed or suspected in 7% of patients (rheumatoid arthritis in 3, Crohn’s disease in 1, psoriasis in 1, ankylosing spondylitis in 1, and sarcoidosis in 1 patient, respectively). Fifty-nine percent of the patients remained of undetermined origin.

**Conclusions:** This study is the first to report on the clinical manifestations and causes of uveitis in Suriname, and suggests that infectious uveitis may occur in 34% of uveitis patients in this country. A relatively small number of HIV-positive cases, but no patients with active tuberculosis were identified.

**Introduction**

Uveitis is a multifactorial inflammatory eye disease and represents an important cause of visual impairment (VI) and blindness worldwide.[1,2] The aetiology of uveitis includes infectious causes and associations with diverse non-infectious systemic disorders, and its complications can cause permanent visual loss if not diagnosed and treated early in the course of the disease.

A combination of geographical, environmental, nutritional, socioeconomic, ethnic, and genetic factors influences the causes and prevalence of uveitis throughout the world. [2] The patterns of uveitis observed in South America differ distinctly from the patterns encountered in Europe and the United States of America.[1-2] However, large differences among South American countries are also encountered including differences in prevalence of tuberculosis, toxoplasmosis, onchocerciasis, leprosy, leptospirosis, and other (parasitic) infections.[3-13]

In Suriname, one of the Guiana’s in South America, the prevalence data of different uveitis entities and associated systemic disorders are entirely lacking. Suriname is a relatively small developing country with approximately 573,311 inhabitants and has a tropical climate.[13] Due to trans-continental migration during colonial times, the population of Suriname consists of many ethnic backgrounds. The majority of which includes Creole, Javanese, Maroon, and Hindustani people.[14] A smaller proportion consists of Indigenous, Chinese, and mixed population groups.[14] Primary, secondary, and tertiary eye care in Suriname is mainly concentrated in the Suriname Eye Centre (SEC) at the Academic Hospital Paramaribo (AZP), which is the only tertiary referral centre for uveitis patients in Suriname.

In this prospective study, we determined the specific diagnoses in 100 consecutive patients with active uveitis who visited the SEC.

**Patients and methods**

**Sample and ethical considerations**

Hundred consecutive (not necessarily new) juvenile and adult patients who visited the SEC between the 15th of July 2014 and the 29th of January 2015 for examination and treatment of the ocular inflammation process associated with any type of active uveitis were included in the study. Patients having no signs of inflammatory activity, those who were not able to adhere to the examination protocol, and those with a history of ocular trauma or ocular...
surgery were excluded. The same held true for patients with exogenous endophthalmitis, surgery-related, post-traumatic, and toxic uveitis. The study was approved by the Ethics Committee of the Surinamese Ministry of Health and followed the tenets of the Declaration of Helsinki. All patients signed a written informed consent form.

Anatomical classification
Ophthalmic examination included visual acuity (VA) measurement, slit-lamp biomicroscopy, tonometry, and indirect ophthamoscopy. The presence of anterior chamber reaction or an inflammation process of the vitreous, retina, or choroid defined disease activity. Clinical ocular evaluation and anatomical classification of uveitis were recorded according to the Standardization of Uveitis Nomenclature Working Group (SUN) criteria.[15]

Aetiological classification
Relevant patient history and additional patient characteristics were analysed using a standard uveitis screening questionnaire form. Standard laboratory screening for all patients included erythrocyte sedimentation rate (ESR), red and white blood cell counts and differentiation, kidney function, and C-reactive protein (CRP) levels. Serology included testing for antibodies against the human immunodeficiency virus (HIV), Toxoplasma and Treponema pallidum antibody (TPHA), cytomegalovirus (CMV) in HIV-positive patients, and a Venereal Disease Research Laboratory (VDRL) test in TPHA-positive cases. The quantiferon®-TB Goldtest (Cellestis GmbH, Germany) was performed in all participants. This test was used instead of the tuberculin skin test because the results are not influenced by previous vaccination with Bacille-Calmette Guerin (BCG).[16,17]

Immunological screening included evaluation for rheumatoid factor (RF) in patients with a suspected history of rheumatoid arthritis, and assessment of anti-nuclear antibody (ANA) in children. All patients underwent a radiological chest examination. If the chest X-ray showed any abnormal signs, the patients were referred to a pulmonary internal medicine specialist. HLA-B27 typing was not available. However, all patients with uveitis and suspected underlying systemic arthritic disease based on questionnaire results or laboratory screening were evaluated by a rheumatologist to rule out any associated systemic disease.

Definition of diagnosis
Diagnosis of toxoplasma chorioretinitis was based on clinical presentation of focal active chorioretinitis in association with typical hyperpigmented atrophic scars. In all suspected cases Immunoglobulin G (IgG) and Immunoglobulin M (IgM) toxoplasma titres were evaluated to confirm the clinical diagnosis. Tuberculosis-related uveitis was diagnosed in patients with evidence of active systemic tuberculosis (TB) with uveitis of otherwise unknown origin. The diagnosis of herpetic anterior uveitis (AU) was based on clinical presentation in patients with unilateral uveitis, sectorial iris paralysis or atrophy, and elevated intraocular pressure with or without a history of herpes corneal infection in the affected eye. The diagnosis of sarcoidosis was performed using the chest X-ray and systemic examination by a pulmonary specialist. Serum angiotensin-converting enzyme (ACE) analysis was not available. Vogt-Koyanagi-Harada disease and Behçet’s disease were diagnosed using the current guidelines.[18]

Statistical analysis
Statistical analyses were performed using SPSS 21 for Windows. The general, clinical, and laboratory data were recorded, and a P value <0.05 was considered statistically significant. Continuous variables were expressed as means ± SDs (range for age), while categorical data were presented as frequencies. Relationships between categorical variables were assessed using Fisher’s exact test.

Results
Patient characteristics
Table 1 gives the general characteristics of the 100 consecutive patients with uveitis who had been included in the study. There were 41 new cases while the remaining 59 patients
presented with a relapse of active uveitis. The mean age was 42.9 years (range 4-75 years) and the male-to-female ratio was 40/60.

Anatomical classification
Ocular characteristics are presented in Table 1. Anterior uveitis was the most common anatomical type of uveitis (occurring in 64% of cases), followed by panuveitis (panU) in 19%, posterior uveitis (PU) in 15%, and intermediate uveitis (IU) in 2% of patients. Unilateral uveitis (59/100) was more common than bilateral uveitis (41/100, P=0.30).

Results of diagnostic tests
The results of diagnostic tests are shown in Table 2 and classification of patients according to the cause or association with systemic disorders in Table 3.

Infectious uveitis was diagnosed in 34% of patients and association with non-infectious systemic diseases in 7%. Fifty-nine percent of patients remained of undetermined origin.

Positive antibodies for Toxoplasma gondii were found in 48 patients. A positive IgM titre was found in 3 patients. The diagnosis of ocular toxoplasmosis with typical fundus lesions was made in 24 patients including 2 HIV-positive patients. Additionally, 24/48 patients with positive toxoplasma antibodies were diagnosed with only AU; in these cases, the underlying aetiology remained unknown. Of these 24 cases, 7 patients with AU without other identified cause of uveitis had a high IgG titre (>122 IU/mL), possibly associated with active disease. [19] These 7 patients were IgM negative.

Three out of 100 patients were HIV positive; 2 (1 PU, 1 panU) were diagnosed with toxoplasmosis (based on clinical features of focal chorioretinitis, positive serologic results along with a good response to therapy for toxoplasmosis). The remaining HIV-positive patient had an AU and had a positive serum toxoplasmosis serology (IgM positive) without any other features of ocular toxoplasmosis. A positive Quantiferon®-TB Goldtest was found in 7/100 patients, 6 of whom were diagnosed with AU (non-granulomatous, 4 patients with chronic unilateral AU and 2 patients with bilateral AU) and 1 patient with a PU. In the latter patient, the diagnosis of toxoplasmosis was already made based on a typical chorioretinal

Table 1  General characteristics of 100 consecutive patients with uveitis in Suriname

<table>
<thead>
<tr>
<th></th>
<th>Total, N=100</th>
<th>New uveitis patients N=41</th>
<th>Chronic or recurrent uveitis patients N=59</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (range); std</td>
<td>42.9 (4-75); std 15.72</td>
<td>39.2 (4-75); std 16.6</td>
<td>45.4 (12-71); std 14.7</td>
<td>P=0.06</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>40/60</td>
<td>13/28</td>
<td>27/32</td>
<td>P=0.21</td>
</tr>
<tr>
<td>Uni/bilateral ratio</td>
<td>59/41</td>
<td>27/14</td>
<td>32/27</td>
<td>P=0.30</td>
</tr>
<tr>
<td>Ethnic background</td>
<td>Hindustani</td>
<td>44</td>
<td>17</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Creole</td>
<td>24</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Javanese</td>
<td>10</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Maroon</td>
<td>12</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Indigenous</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Chinese</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Mixed</td>
<td>9</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Anterior uveitis N (%)</td>
<td>64 (64%)</td>
<td>24 (24%)</td>
<td>40 (40%)</td>
<td>P=0.34</td>
</tr>
<tr>
<td>Intermediate N (%)</td>
<td>2 (2%)</td>
<td>1 (1%)</td>
<td>1 (3%)</td>
<td>P=0.79</td>
</tr>
<tr>
<td>Posterior uveitis N (%)</td>
<td>15 (15%)</td>
<td>8 (8%)</td>
<td>7 (7%)</td>
<td>P=0.29</td>
</tr>
<tr>
<td>Pan Uveitis N (%)</td>
<td>19 (19%)</td>
<td>8 (8%)</td>
<td>11 (11%)</td>
<td>P=0.91</td>
</tr>
</tbody>
</table>

* this P value represents the distribution of all ethnicities in the two groups (new and chronic uveitis patients)
scar and a good response to cotrimoxazole (Bactrimel®). Five other patients with a positive Quantiferon®-TB Goldtest showed chest X-ray abnormalities of which 2 had an enlarged mediastinum, 1 showed apical cavitation, 1 had reticulonodular densities, and 1 showed interstitial enhancement. These patients were referred to a pulmonologist for further evaluation. Four of these 5 referred patients were diagnosed with latent pulmonary tuberculosis, but none of them fulfilled the guidelines of Gupta et al [20] for the diagnosis of ocular tuberculosis. None of the patients was diagnosed with active pulmonary tuberculosis. One patient with chest X-ray abnormalities was diagnosed with sarcoidosis. The remaining 7/13 patients with X-ray abnormalities were non-specific.

Herpetic anterior uveitis was suspected in 3/100 patients who had unilateral anterior uveitis in combination with elevated intraocular pressure. However, no sectorial iris paralysis or atrophy was seen, and there was no history of herpes keratitis. A total of 3/100 cases had a positive TPHA test together with high VDRL levels and were diagnosed with ocular syphilis. Rheumatoid factor was positive in 4/100 patients, and 3 patients were diagnosed with sclerouveitis associated with rheumatoid arthritis. The remaining patient with positive rheumatoid factor was diagnosed with Crohn’s disease. All these patients were referred to a rheumatologist for confirmation of the diagnosis and for further evaluation and treatment.

Children
In children aged younger than 18 years (N=9), PU was the most common anatomical location (5/9, 56%). All PU cases in children were caused by toxoplasmosis. The cause of AU (2/9) and panU (2/9) remained undetermined.

Discussion
This study on uveitis in Suriname is the first to present data on the aetiology of this ocular

Table 2  Anatomical classification of uveitis and results of screening in 100 consecutive patients with uveitis

<table>
<thead>
<tr>
<th>Examination</th>
<th>Total</th>
<th>Anterior Uveitis</th>
<th>Intermediate Uveitis</th>
<th>Posterior Uveitis</th>
<th>Pan Uveitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid factor positive</td>
<td>4/100</td>
<td>4/4</td>
<td>0/4</td>
<td>0/4</td>
<td>0/4</td>
</tr>
<tr>
<td>HIV positive</td>
<td>3/100</td>
<td>1/3</td>
<td>0/3</td>
<td>1/3</td>
<td>1/3</td>
</tr>
<tr>
<td>VDRL positive</td>
<td>3/100</td>
<td>0/3</td>
<td>0/3</td>
<td>1/3</td>
<td>2/3</td>
</tr>
<tr>
<td>Toxoplasma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG positive*</td>
<td>48/100</td>
<td>24/48</td>
<td>1/48</td>
<td>10/48</td>
<td>13/48</td>
</tr>
<tr>
<td>IgM positive**</td>
<td>3/100</td>
<td>2/3</td>
<td>0/3</td>
<td>0/3</td>
<td>1/3</td>
</tr>
<tr>
<td>Quantiferon Test***</td>
<td>7/100</td>
<td>6/7</td>
<td>0/7</td>
<td>1/7</td>
<td>0/7</td>
</tr>
<tr>
<td>Chest X-ray abnormalities</td>
<td>13/100</td>
<td>10/13</td>
<td>0/13</td>
<td>2/13</td>
<td>1/13</td>
</tr>
</tbody>
</table>

* P < 0.05  
** IgM positive cases were also IgG positive  
*** in 14 patients we were not able to perform a Quantiferon test.

Table 3  Specific diagnoses of 100 patients with uveitis in Suriname

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious cause, total</td>
<td>34</td>
</tr>
<tr>
<td>Toxoplasma chorioretinitis</td>
<td>24</td>
</tr>
<tr>
<td>Syphilis</td>
<td>3</td>
</tr>
<tr>
<td>Miscellaneous*</td>
<td>7</td>
</tr>
<tr>
<td>Associated with non-infectious systemic disease**</td>
<td>7</td>
</tr>
<tr>
<td>Unknown***</td>
<td>59</td>
</tr>
</tbody>
</table>

* includes 3 patients with herpetic uveitis, 4 with latent tuberculosis  
** includes 3 patients with rheumatoid arthritis, 1 with Crohn’s disease, 1 with psoriasis and arthralgia’s, 1 with ankylosing spondylitis and 1 with sarcoidosis.  
*** includes 7 patients with anterior uveitis of undetermined cause but with high IgG serum toxoplasma titres (> 122 IU/mL)
disease in the country. The results show that 64% of uveitis patients in Suriname had an AU, which is within the range reported by large surveys on uveitis in other parts of the world. [21] Toxoplasma chorioretinitis was the most common cause of uveitis, but no underlying cause was identified in the majority of cases (59%).

These findings are consistent with those of most studies conducted in Western countries where AU was also found to be the most common location of uveitis with frequencies ranging from 25% to 91% of cases.[8] In Brazil, AU was diagnosed in 70.1% of patients followed by PU and panU, whereas IU was rare. [3] In contrast, AU is less prevalent in other developing countries, especially in areas with a high number of HIV-positive patients. This is probably due to the fact that HIV causes an increase in opportunistic infections which are more frequently associated with AU.

Most cases of AU were idiopathic which is consistent with studies from neighbouring countries.[3,6] Similarly to the current study, the most frequent diagnosis in PU and panU patients throughout South America was toxoplasma chorioretinitis (24%, 24/100 patients). Similar results were found in North America, Europe, and Africa.[1,22] Remarkably, 7 patients with AU of undetermined origin had high IgG anti-toxoplasma titres (but negative IgM titres), which could be associated with active systemic infection.[19] Temporary AU has been reported in many systemic infections and an association between systemic toxoplasmosis and AU has previously been noted.[23]

The underlying cause of uveitis in the three HIV-positive patients in the current study was toxoplasmosis. Results in other developing countries demonstrated a high burden of infectious CMV retinitis in HIV-positive patients which was not encountered in the present series.[24] The low prevalence of HIV among patients with uveitis also reflects the relatively low estimates reported by the National AIDS Programme (NAP) in Suriname, which indicates that the prevalence of HIV infection in the Surinamese population is 1.1% (0.9%-1.3%).[25]

Other infectious cases found in the current study were latent tuberculosis (4%) and syphilis (3%). Since it was not possible to perform all diagnostic tests for the identification of infectious causes such as the aqueous assessment, the real number of patients with infectious uveitis might have been even higher than the 34% found in this study.

Several other aetiologies of uveitis observed in industrialized countries – including presumed ocular histoplasmosis, birdshot chorioretinopathy, Fuchs’ uveitis, Posner-Schlossman syndrome, Eales disease, serpiginous chorioretinopathy, and other less common entities - were not observed in the current series. In addition, low numbers of patients with uveitis and associated non-infectious diseases were diagnosed. This may, in part, be due to the relatively low number of patients enrolled in the current study, the limited availability of diagnostic tools, and a presumably low prevalence of these entities of uveitis in Suriname.

In conclusion, the current study is, to our knowledge, the first to assess the spectrum of uveitis in the Surinamese population and suggests that at least 34% of uveitis cases are of infectious origins with toxoplasmosis being the most common cause. Furthermore, both tuberculosis- and HIV-associated uveitis seems uncommon. Despite the relatively small sample size and lack of diagnostic tools, the findings of this study can be used for the development of a targeted screening programme for uveitis patients in Suriname, which is essential for optimal management of affected patients.
References


