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IL-10 Measurement in Aqueous Humor for Screening Patients with Suspicion of Primary Intraocular Lymphoma

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Abstract

Purpose—To determine the value of IL-10 measurement in aqueous humor (AH) for screening in primary intraocular lymphoma (PIOL).

Methods—One hundred consecutive diagnostic or therapeutic vitrectomies were performed in patients with uveitis. During surgery, 100 µL of both AH and pure vitreous was taken. IL-10 levels were determined with a standard quantitative sandwich enzyme immunoassay technique. Patients were distributed in two groups: 51 patients with proven PIOL, 108 patients with uveitis divided into 74 with uveitis of proven etiology and 34 with idiopathic uveitis. Groups were compared by ANOVA and the Tukey-Kramer test or nonparametric Wilcoxon test. Distributions were compared by using the χ^2 test. Segmentation was derived from the ROC curves by choosing a tradeoff between sensitivity and specificity.

Results—In patients with PIOL, IL-10 mean values were 2205.5 pg/mL (median: 1467 pg/mL) in the vitreous and 543.4 pg/mL (median: 424 pg/mL) in AH. In patients with uveitis (idiopathic and diagnostic uveitis), mean values were 26.6 pg/mL (median: 8 pg/mL) in the vitreous, and 21.9 pg/mL (median: 8 pg/mL) in AH. IL-10 mean values were significantly different between patients with PIOL and patients with uveitis ($P < 10^{-3}$). The areas under the curves were 0.989 and 0.962 for vitreous and AH, respectively. A cutoff of 50 pg/mL in the AH was associated with a sensitivity of 0.89 and a specificity of 0.93. In the vitreous, a cutoff value of 400 pg/mL yielded a specificity of 0.99 and a sensitivity of 0.8.

Conclusions—Diagnosis of PIOL is often made months or years after the initial onset of ocular symptoms. Cytology remains the gold standard for diagnosis. However, measurement of IL-10 in the AH is a good screening test to reduce diagnostic delays.

Primary intraocular lymphoma (PIOL) is a subset of primary central nervous system lymphoma (PCNSL). It is an aggressive, diffuse, large B-cell lymphoma and is generally restricted to the eye and central nervous system (CNS) compartments.¹⁻³ Ocular involvement occurs in 20% to 25% of patients with PCNSL. Of those patients initially affected by PIOL, 56% to 85% later develop a cerebral tumor.^{4,5} PCNSL presents 4% to 6% of all primary cerebral tumors and 1% to 2% of extranodal lymphomas. Within the past two decades, the incidence of PCNSL has approximately tripled in the United States.⁶

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Patients with PIOL typically report blurred vision and floaters. These symptoms are frequently attributed to chronic vitritis or uveitis over the course of several months or even years. The gold standard for diagnosis is cytologic examination of the vitreous after a diagnostic vitrectomy. However, cytologic diagnosis is difficult because of the fragility of lymphoma cells.⁷ False-negative cytology results have been reported in approximately 30% of vitreous biopsy specimens collected from a referral center.⁸

New tools (i.e., cytokine assessment and various other molecular techniques) have recently been developed to improve the diagnostic yield.³

B lymphoma cells are characterized by the production of several cytokines—in particular, IL-10.⁹ An increase of IL-10 levels in the vitreous or an increase in the IL-10/IL-6 ratio to greater than 1 has been reported in the vitreous of patients with PIOL.^{5,10-12} In contrast, in an early study on the subject, Akpek et al.¹³ reported that this ratio may not always be associated with PIOL.

PCNS lymphoma remains a disease of poor prognosis, especially if the eye is involved. Recent data suggest that early diagnosis and treatment result in better disease control and in a longer survival period.¹⁴ In most series, diagnosis is made after a mean period of 12 to 24 months.^{8,13,14}

To reduce this period for diagnosis, we studied the value of IL-10 measurements after an anterior chamber tap, or paracentesis (ACP), as a potential screening test. The samples were collected prospectively. IL-10 measurements were performed in sample lots of 20 every 15 days, and data were then examined once they were all pooled. Clinical data were extracted retrospectively from patients' files at the end of enrollment.

An increase of IL-10 levels may indicate to clinicians that an earlier diagnostic vitrectomy may be needed to confirm a diagnosis of PIOL. If PIOL is diagnosed earlier, CNS involvement, a poor prognostic sign, may be prevented.¹⁴

Materials and Methods

Patients

Between 1997 and 2002, 3350 patients were referred to the Department of Ophthalmology, Pitié-Salpêtrière Hospital, Paris, France, for uveitis. A diagnosis was established in roughly 60% of the cases. If the origin of the uveitis remained uncertain after the clinical history was reviewed and an ophthalmic examination was performed, a complete laboratory workup and additional specialized medical consultations were performed. When the etiology remained unknown or if a malignancy or an infectious condition was suspected, an ACP was proposed for IL-10 measurement or polymerase chain reaction (PCR) for viral, *Toxoplasma gondii*, or bacterial DNA amplification. A diagnostic vitrectomy was recommended when the aqueous samples were noncontributory.

If a complication was associated (i.e., retinal detachment, epiretinal membrane, or neovascularization) related to infectious or noninfectious uveitis, vitreoretinal surgery was performed. On the occasion of this surgical procedure, aqueous humor (AH) and vitreous were systematically collected for IL-10 measurements.

One hundred sixty-seven consecutive vitrectomies were performed, during the same period, in patients with uveitis, either related or unrelated to a neoplasm, for diagnostic or therapeutic purposes. Vitreous samples were systematically collected prospectively for cytologic analysis and IL-10 measurement. AH was also collected after an ACP before vitrectomy or during a

surgical procedure. In addition, according to clinical suspicion of PIOL, molecular techniques were applied to the vitreous specimens to screen for clonal IgH rearrangements. PCR was also applied for the diagnosis of ocular toxoplasmosis, viral retinitis, and bacterial infections.

In some patients, the ACP was performed before diagnostic vitrectomy, and a second paracentesis was performed during the diagnostic vitrectomy according to our protocol. In cases of therapeutic vitrectomy, paracentesis was performed during the surgical procedure.

Originally, 167 patients were enrolled in the study. The patients were distributed in two groups. The first comprised 51 patients with PIOL diagnosed by cytologic analysis of the vitreous (47 patients) or by histopathologic analysis of brain or retinal biopsy specimens (three cerebral, one retinal). The second group consisted of 116 patients with diagnosed uveitis and an associated condition ($n = 74$; i.e., sarcoidosis, Behçet disease, HLA B27-related uveitis, ocular toxoplasmosis, or viral retinitis) or with idiopathic uveitis ($n = 42$).

All patients (PIOL, uveitis with diagnosis, idiopathic uveitis) were observed for a mean of 2 years, except 8 patients with idiopathic uveitis lost to follow-up who were excluded from the study, leaving 34 participants with idiopathic disease. All etiologies and associated conditions that composed the nonidiopathic group of patients and type of vitreoretinal surgery (diagnostic or therapeutic vitrectomy) are summarized in Table 2. Patients who underwent vitreoretinal surgery for uveitis-related retinal detachment were referred to emergency at an acute phase of the disease. No corticosteroids were given before surgery, to limit the influence of the treatment on secretion of proinflammatory cytokines.

All patients gave their informed consent after the nature of the study had been fully explained to them. All data were treated confidentially. The study was performed with the approval of the hospital review board. This research conformed to the scientific principles embodied in the World Medical Association Declaration of Helsinki as revised in 1989.

Methods

During or before surgery, 100 μ L of AH was taken from all the patients after an ACP, for IL-10 measurement and microbiologic analysis, depending on clinical suspicion. If the ACP was performed before vitrectomy it was done under topical anesthesia with a 30-gauge needle in the operating theater with a surgical microscope. If it was performed during the surgery or vitrectomy, the patient was under general anesthesia. All vitreous specimens were obtained through a standard three-port pars plana vitrectomy. First, 0.5 mL of AH was obtained after ACP and then 1 mL of pure vitreous was obtained by a syringe attached to the vitrectomy cutter handpiece via a stopcock. The specimen was immediately delivered to the cytopathology laboratory. A minimum of 100 μ L of the undiluted vitreous and 100 μ L of AH were submitted for IL-10 measurement. Specimens were stored at -70°C , and cytokine assays were performed on all specimens, but in lots of 20 freshly thawed samples every 15 days. IL-10 levels were determined by using a standard quantitative sandwich enzyme immunoassay technique (Quantikine; R&D Systems, Abingdon, UK). This procedure has been reported recently.¹⁵ The rest of the undiluted vitreous was prepared for cytologic analysis. The remaining pure vitreous was cytocentrifuged at 600 rpm for 8 minutes, to obtain one or two slides. A core vitrectomy was performed after infusion, and the diluted vitreous was collected in the vitrector cassette and delivered to the laboratory. Cell culture medium (10% fetal calf serum) was added to improve cell viability. The sample was then centrifuged at 1000 rpm for 8 minutes at 4°C . The pellet was resuspended in 2 mL of balanced saline and cytocentrifuged in the same conditions as was used for fresh vitreous. Ten slides were prepared with both undiluted and diluted vitreous. Two slides were stained with May-Grunwald Giemsa. The remaining slides were air dried and fixed by immersion in acetone for 7 minutes. Immunocytochemical staining was performed according to the alkaline phosphatase anti-alkaline phosphatase (APAAP)

method (EnVision System-Alkaline Phosphatase; Dako, Trappes, France), with monoclonal antibodies against pan-T, T-helper, and suppressor/cytotoxic antigens (CD3, CD4, CD8), B-cell antigen CD20, and κ or λ light chain.

Diluted vitreous samples were also prepared for PCR analyses. Detection of clonal Ig and TCR gene rearrangements were performed according to previously published protocols.¹⁶ In ambiguous cases, PCR was performed after microdissection of atypical cells at the National Eye Institute (NEI, Bethesda, MD).¹⁷

Samples of diluted vitreous were also delivered to microbiology laboratories for culture and PCR, to screen for infectious microorganisms according to clinical suspicion.

Statistical Analysis

Groups were compared by ANOVA and the Tukey-Kramer test or nonparametric Wilcoxon (or Kruskal-Wallis) test on ranks. Distributions were compared using X^2 or the Fisher exact test, when appropriate. Correlations between IL-10 levels in the vitreous and in the AH were performed by using Pearson's correlation or nonparametric Spearman correlation (on rank) when necessary. Multifactorial linear models were applied to adjust for covariables. Areas under the ROC (receiver operator characteristic) curves were calculated by nonparametric methods.¹⁸ Segmentation was done from the ROC curves by choosing a tradeoff between sensitivity and specificity and by applying segmentation methods (CART: Classification and Regression Tree). Descriptive statistics and tests were performed with commercial software (JMP software; SAS Institute, Cary, NC), and the ROC curves were studied with another program (Rockit software; University of Chicago).¹⁹ The Youden index (minimum, -1; maximum, +1), defined as (sensitivity) + (specificity) - 1, was used as a simple descriptive synthesis of sensitivity and specificity.²⁰ $P < 0.05$ (two-tailed) were regarded as significant.

Results

Demographic Data

Mean age was 55.5 years in subjects with uveitis, but 25% were older than 70 years. The mean age of patients with PIOL was 69.4 years (median, 72), and 25% of patients were younger than 57 years. There were no significant differences for age and sex between subjects with nonidiopathic uveitis and those with idiopathic uveitis. Patients with PIOL were older ($P < 10^{-3}$) than subjects with uveitis and were more predominantly female ($P = 0.02$; Table 1).

Differences in age distribution were observed among the uveitis group depending on the diagnosis ($P = 0.04$). Patients with bacterial infections were typically older. More women were affected by parasitic (toxoplasmosis or toxocariasis) infections and more men were affected by viral infections.

Various etiologies or associated conditions were found in the group of patients with nonidiopathic uveitis. Most were affected by infectious uveitis (48 patients). The others were affected by noninfectious uveitis restricted to the eyes (i.e., birdshot, Fuchs' heterochromic cyclitis) or associated with systemic disease (i.e., sarcoidosis, Behçet disease, or HLA B27-related uveitis). Most of the patients in this group underwent vitreoretinal surgery to cure retinal detachment, to treat proliferative retinopathy due to occlusive vasculitis, or to remove vitreous opacities or an epiretinal membrane (Table 2).

Vitrectomy contributed to the diagnosis of PIOL in 47 cases. In four patients, cytology was negative. In one, diagnosis was made after a retinal biopsy. In three patients, diagnosis was made after a stereotaxic brain biopsy. For these four cases, slides were sent for microdissection that was positive in two patients (one Bcl2 translocation, one Ig heavy chain rearrangement).

Results of IL-10 Measurement in AH and in the Vitreous

IL-10 was measured in the vitreous of 49 of 51 patients with PIOL, 69 of 74 patients with nonidiopathic uveitis, and all 34 patients with idiopathic uveitis. IL-10 was measured in the AH of 45 of 51 patients with PIOL, 57 of 74 patients with uveitis, and 31 of 34 patients with idiopathic uveitis.

In some patients, samples were taken only from the AH or the vitreous. For example, 17 patients who agreed only to diagnostic vitrectomy, refused concomitant ACP. In two patients affected by lymphoma both in the eye and in the CNS, we performed only an ACP, because diagnosis had been made by brain biopsy.

In patients with PIOL, mean/median levels of IL-10 were 2205.5/1467 pg/mL in the vitreous and 543.4/424 pg/mL in the AH, but we observed a subgroup (14/51 patients) in whom levels were between 3500 and 8000 pg/mL in the vitreous and 700 and 2000 pg/mL in the AH (Table 3).

In subjects with uveitis (idiopathic or nonidiopathic), mean/median levels of IL-10 were 26.6/8 pg/mL in the vitreous and 21.9/8 pg/mL in the AH.

Detailed analysis of subjects with uveitis showed that the highest levels of IL-10 in the AH were mainly in cases of viral or parasitic uveitis (acute retinal necrosis or ocular toxoplasmosis with severe vitritis). A nonparametric Kruskal-Wallis ANOVA used to compare the different diagnoses of control patients with uveitis indicated a significant global difference ($P < 0.02$) in the AH and a nearly significant test in the vitreous ($P = 0.06$). The difference was mainly caused by the higher concentrations in the infectious uveitis groups (viral, bacterial, or parasitic groups), whereas levels in idiopathic uveitis were in the low range.

Mean IL-10 levels were significantly greater in the 51 patients with PIOL than in the 108 patients with uveitis (nonidiopathic or idiopathic), both in 103 vitreous ($P < 10^{-3}$) and 88 AH ($P < 10^{-3}$; Figs. 1, 2).

Figure 3 shows that the correlation between IL-10 measurements in the vitreous and AH was moderate ($R = 0.56$; non-parametric Spearman rank correlation [$R' = 0.66$], in patients with PIOL; $R = 0.55$ [$R' = 0.47$], in patients with nonidiopathic uveitis; $R = 0.44$ [$R' = 0.43$] in patients with idiopathic uveitis).

Moreover, it should be emphasized that correlation was more or less significant depending on the level of IL-10 ($R = 0.55$ / $R' = 0.66$ [NS]) for higher levels (AH > 50 pg/mL and $R = 0.24$ / $R' = 0.34$) for lower levels (AH < 50 pg/mL).

Figure 4 shows the ROC curves for vitreous (filled circles) and AH (open circles). The areas underneath the curves and confidence intervals are 0.989 (0.97, 0.998) and 0.962 (0.916, 0.985) for vitreous and AH, respectively. These values are not significantly different ($P = 0.06$).

A cutoff of 30 pg/mL IL-10 in the AH is associated with a sensitivity of 0.96 and a specificity of 0.84 (Youden index = 0.8). For a more specific approach and to reduce the number of potentially unnecessary vitrectomies, a cutoff of 50 pg/mL in the AH is associated with a lower sensitivity of 0.89 but a greater specificity: 0.93. (Youden index = 0.82). In the vitreous, a cutoff of 400 pg/mL yields a specificity of 0.99 and a sensitivity of 0.8 (Youden index = 0.79).

Discussion

In this study, we have shown that IL-10 measurement in AH obtained from an anterior chamber aspiration may be a valuable tool for the diagnosis of PIOL.

ACP is a safe procedure that is currently used for diagnosis of infectious diseases in the eye. After an extensive literature survey (National Library of Medicine; search terms: anterior chamber paracentesis, side-effect, corneal abscess, and endophthalmitis), we were able to find only a few case reports of complications after ACP. One patient presented with a corneal abscess, and one patient presented with bacterial endophthalmitis.^{21,22} Van der Lelij and Rothova²³ evaluated the safety of the ACP in 361 patients. None of the patients experienced complications. However, one patient had a traumatic cataract that developed after ACP performed with the slit lamp while the patient was in an upright position. More recently, a study conducted by Cheung et al.²⁴ of 70 patients with uveitis who underwent ACP with a slit lamp for diagnostic purposes did not report any complications due to the procedure. In our study, we also did not observe any complications due to ACP.

In this study, elevated IL-10 levels in the AH were strongly associated with PIOL. Elevated IL-10 in the vitreous was first described by Chan et al.¹⁰ in PIOL in 1995 and was found to be associated with the number of malignant cells. An increase of IL-6 levels in the vitreous, in contrast, was found to be associated with nonmalignant intraocular inflammation.²⁵ Whitcup et al.¹¹ later showed that an IL-10/IL-6 ratio greater than 1 is associated with intraocular lymphoma. The ratio calculation was criticized, because they used diluted vitreous samples to measure cytokine levels.

In our study we measured IL-10 levels only in undiluted ocular fluids. We decided not to calculate IL-10/IL-6 ratios in view of designing a less expensive and simpler test on both the AH and vitreous. High IL-10 levels were found in ocular fluids of most of the patients with PIOL. In AH, 89% of patients with PIOL had levels of IL-10 over the threshold of 50 pg/mL. We also found that, in most of the patients, elevated levels of IL-10 were present in both the AH and vitreous.

Typically, there are no or very few cells in the anterior chamber of patients with PIOL. The presence of IL-10 in the AH is probably due to diffusion from the posterior to the anterior chamber. Such diffusion may vary from one patient to another, thus explaining why the correlation coefficient is not very strong between levels in the two compartments. We cannot explain why in some rare patients,² we found very low levels of IL-10 in the AH while high levels of this cytokine were measured in the vitreous. The latter two patients were phakic with a quiet anterior chamber and a dense vitritis. At this point, we cannot exclude a technical problem during ELISA processing.

Based on the ROC curve (Fig. 4), including IL-10 levels measured in AH of patients with PIOL versus IL-10 levels in both nonidiopathic and idiopathic cases of uveitis we established a threshold in AH for further screening patients. Our statistical analysis showed that for an IL-10 level of 50 pg/mL, sensitivity was 89% and specificity 93%. We considered this level to be the best compromise between sensitivity and specificity.

In six cases (false negative) of proven PIOL, we found IL-10 levels in AH below the measuring threshold of 50 pg/mL. In each case, ocular involvement was limited to minimal vitritis associated with some rare retinal infiltrates. The Department of Neurology referred all patients who were admitted for cerebral lymphoma. For one patient, diagnosis was made immediately after diagnostic vitrectomy. In the other five cases, diagnostic vitrectomy was noncontributory.

Examples of PIOL associated with low levels of IL-10 have been described by Akpek et al.¹³ and Buggage et al.²⁶ However, these cases were difficult to analyze, because diluted vitreous samples from the vitrector cassette had been used to assay the cytokines. Akpek et al.¹³ also mentioned cases of uveitis associated with increased IL-10 levels in the vitreous.

We also observed five false-positive cases that had IL-10 levels above the threshold in vitreous or AH. All these patients presented with infectious uveitis. Three patients had an acute retinal necrosis syndrome due to herpes simplex virus in two cases and varicella zoster virus in one case. In all these cases, diagnosis was made clinically according to diagnostic criteria established by the American Uveitis Society and after detection of viral genomes using PCR techniques. The remaining two cases were due to toxoplasmosis (PCR-positive vitreous). In all five cases, vitrectomy was necessary to treat retinal detachment associated with a severe inflammatory reaction in the vitreous. We hypothesized that high levels of IL-10 in such cases were due to massive infiltration of the vitreous by inflammatory cells, especially activated B lymphocytes.

An increase of IL-10 in ocular fluids during acute viral retinal necrosis and ocular toxoplasmosis has been described by Ongkosuwo et al.²⁷ In this study, uveitis of a noninfectious origin was not associated with high IL-10 levels. In another study reported by Lacomba et al.,²⁸ uveitis was not associated with elevated IL-10 levels in the AH. In our study, most of the patients affected with uveitis had IL-10 levels in ocular fluids below the cutoff threshold whether idiopathic or of infectious etiology.

If we consider only the IL-10 level in AH for all the patients, 11 patients (6 PIOL and 5 uveitis) among all the patients screened would be classified incorrectly. ACP accurately classified (PIOL versus non-PIOL) for 91.6% of the patients. IL-10 measurements in AH and/or vitreous may be a useful complement to ophthalmologic clinical examination of suspected PIOL.

After establishing the results of IL-10 measurements in the AH (threshold = 50 pg/mL) and the vitreous (threshold = 400 pg/mL), we recommend performing an ACP to screen patients with clinical suspicion of PIOL. Clinical suspicion of PIOL is based on (1) the knowledge that patients with PIOL are mostly women after the age of 60 years; (2) the fact that chronic posterior bilateral uveitis is unresponsive to corticosteroids; (3) the association that exists between PIOL and cellular vitritis, subretinal and retinal infiltrates, and retinal pigment epithelium alterations; and (4) typical angiographic findings (e.g., hypofluorescent, round lesions and RPE disturbances).²⁹ If IL-10 levels in the AH are more than 50 pg/mL, we propose performing a diagnostic vitrectomy after neurologic work-up if the patient is free of cerebral lesions. IL-10 measurements are associated with cytologic examination of the vitreous body according to the methods fully described by Chan and Wallace.³⁰ Cytologic examination of the vitreous remains mandatory for the definitive diagnosis of PIOL. However, an elevated IL-10 level in undiluted vitreous strengthens a suspicion of PIOL. If cytology fails to demonstrate malignant cells despite all molecular techniques and IL-10 levels in the vitreous over 400 pg/mL, a second vitrectomy possibly combined with a retinal biopsy is justified. Several studies have shown that diagnosis of PIOL in some patients required repeated vitrectomies or retinal biopsy specimens.^{3,5,7,8,30}

Conclusions

PIOL is a disease with a poor prognosis that frequently masquerades as posterior uveitis. Diagnosis of PIOL is often made months or years after the initial onset of ocular symptoms. Recently, Hormigo et al.¹⁴ suggested that early diagnosis and treatment result in longer survival of patients with PIOL. IL-10 measurements in the AH after an ACP is a good screening test and may reduce diagnostic delays.

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FIGURE 1.
Mean $\pm$ SD of IL-10 level in the vitreous by diagnostic group.

FIGURE 2.

Mean $\pm$ SD of IL-10 level in the AH by diagnostic group.

FIGURE 3.
Correlation between IL-10 levels in AH and vitreous (Z, PIOL patients; X, idiopathic uveitis;
■, uveitis).

FIGURE 4.
ROC Curve for IL-10 in the vitreous (●) and AH (○).

TABLE 1

Demographic Data

Diagnosis	Subjects (n)	Men/Women	Age (Median and Range)	Age (Mean $\pm$ SD)
PIOL patients	51	14/37	72 (37-89)	69.4 (13)
Uveitis patients	108	51/57	56 (6-84)	55.5 (18.6)
Uveitis (with diagnosis) patients	74	36/38	56 (6-84)	55.1 (19.5)
Mycosis	5	4/1	38 (30-65)	44.2 (15.5)
Viral	13	11/2	50 (30-75)	51.6 (13.5)
Bacterial	19	6/13	70 (34-84)	67.6 (12.2)
Parasitic	11	2/9	38 (16-78)	46.8 (23.7)
Noninfectious	26	13/13	55 (6-84)	53.3 (21.8)
Idiopathic uveitis patients	34	15/19	57 (8-78)	56.3 (16.6)

TABLE 2

Breakdown of the Different Etiologies and Associated Conditions of the Three Patient Groups and the Purpose of Vitreoretinal Surgery

Uveitis	Patients (n)	Etiologies or Associated Conditions	Vitreoretinal Surgery	Lymphoma Cells
Viral	13	ARN syndrome 10 CMV retinitis 3	Therapeutic (RD) Therapeutic (RD)	Neg Neg
Parasitic	11	Toxoplasmosis 6 Toxocariasis 5	Therapeutic (RD) Therapeutic (RD)	Neg Neg
Fungal	5	Candida 4	Therapeutic and diagnostic	Neg
Bacterial	19	Aspergillosis 1 Delay-onset endoph 6 Bartonella 3 Whipple 1 Syphilis 3 TB (Immune-mediated uveitis) 6	Therapeutic and diagnostic Diagnostic Therapeutic (PR) Therapeutic (PR, RD, ERM)	Neg Neg
Noninfectious	25	Fuchs 1 Pars planitis 1 Behçet 4 JIA 2 B27 1 Sarcoidosis 12 SO 1 Birdshot 1 Miscellaneous 2	Optic Optic, ERM, RD Therapeutic (hypotonia Macular hole) RD, intravitreal hemorrhage ERM	 Neg Positive 47 Neg. 4 Neg
PIOL	51		Diagnostic	
Idiopathic	34		Diagnostic	

TB, tuberculosis; JIA, juvenile idiopathic arthritis; B27, uveitis related to HLA B27; SO, sympathetic ophthalmia; RD, retinal detachment; PR, proliferative retinopathy; ERM, epiretinal membrane.

TABLE 3

Distribution of IL-10 in Vitreous and Aqueous Humor

Diagnosis	Vitreous (Subjects, <i>n</i>)	Vitreous Median (Range)	Vitreous (Mean $\pm$ SD)	Aqueous Humor (Subjects, <i>n</i>)	Aqueous Humor Median (Range)	Aqueous Humor (Mean $\pm$ SD)
PIOL patients	49	1467 (22-7950)	2205.5 (2003.9)	45	424 (8-1500)	543.4 (469)
Uveitis subjects	103	8 (0.5-450)	26.6 (61.5)	88	8 (0-375)	21.9 (48.4)
Uveitis with diagnosis	69	9.5 (0.5-450)	30.5 (73.9)	57	8 (0.5-375)	28.2 (58.7)
Fungal	5	12 (3-49)	18.6 (18.4)	3	8 (3-18)	9.7 (7.6)
Viral	10	24.8 (6-450)	107.6 (169.6)	12	17.5 (5-375)	68.7 (110.7)
Bacterial	19	8 (0.5-23)	10.7 (6.4)	16	8 (0.5-161)	23.4 (39.6)
Parasitic	10	11.5 (8-170)	41.3 (58.1)	6	24 (4-76)	34 (32.3)
Noninfectious	25	8 (2-56)	12.9 (12.5)	20	7.9 (1-28)	8.9 (7.2)
Idiopathic uveitis	34	8 (8-76)	18.7 (18.1)	31	8 (0-45)	10.2 (11.6)

Data are expressed in picograms per milliliter.