European Journal of Ophthalmology / Vol. 16 no. 4, 2006 / pp. 588-594

The diagnostic yield of vitrectomy specimen analysis in chronic idiopathic endogenous uveitis

J.G. GARWEG[1,2], D. WANNER[2], G.-M. SARRA[2], M. ALTWEGG[4], H. LOOSLI[3], L. KODJIKIAN[5], M. HALBERSTADT[2]

[1]Swiss Eye Institute, Wabern
[2]Department of Ophthalmology, Inselspital, University of Bern, Bern
[3]Department of Pathology, Inselspital, University of Bern, Bern
[4]Bio-Analytica AG, Luzern - Switzerland
[5]Croix-Rousse Hospital, Department of Ophthalmology, Lyon - France

PURPOSE. *The low diagnostic yield of vitrectomy specimen analysis in chronic idiopathic uveitis (CIU) has been related to the complex nature of the underlying disease and to methodologic and tissue immanent factors in older studies. In an attempt to evaluate the impact of recently acquired analytic methods, the authors assessed the current diagnostic yield in CIU.*
METHODS. *Retrospective analysis of consecutive vitrectomy specimens from patients with chronic endogenous uveitis (n = 56) in whom extensive systemic workup had not revealed a specific diagnosis (idiopathic) and medical treatment had not resulted in a satisfying clinical situation. Patients with acute postoperative endophthalmitis served a basis for methodologic comparison (Group 2; n = 21).*
RESULTS. *In CIU, a specific diagnosis was provided in 17.9% and a specific diagnosis excluded in 21.4%. In 60.7% the laboratory investigations were inconclusive. In postoperative endophthalmitis, microbiological culture established the infectious agent in 47.6%. In six of eight randomly selected cases, eubacterial PCR identified bacterial DNA confirming the culture results in three, remaining negative in two with a positive culture and being positive in three no growth specimens. A double negative result never occurred, suggesting a very high detection rate, when both tests were applied.*
CONCLUSIONS. *The diagnostic yield of vitrectomy specimen analysis has not been improved by currently routinely applied methods in recent years in contrast to the significantly improved sensitivity of combined standardized culture and PCR analysis in endophthalmitis. Consequently, the low diagnostic yield in CIU has to be attributed to insufficient understanding of the underlying pathophysiologic mechanisms. (Eur J Ophthalmol 2006; 16: 588-94)*

KEY WORDS. *Chronic endogenous uveitis, Cytopathology, Diagnostic yield, Eubacterial PCR, Idiopathic uveitis, Microbial growth, Postoperative endophthalmitis, Vitrectomy*

Accepted: February 5, 2006

INTRODUCTION

Establishing a specific diagnosis in chronic endogenous uveitis is often difficult owing to nonspecific ophthalmologic signs and a lack of specific findings in serologic analysis. This has been attributed to the predominantly local nature of the underlying immune mechanisms (1). The literature regarding diagnostic vitrectomy in chronic uveitis is sparse and the diagnostic yield reported to be between 30% and 40% (2, 3). Despite this relatively low rate of yield, diagnostic vitrectomy with clinically directed sample analysis has become an accepted tool in the

1120-6721/588-07$15.00/0

management of cases with atypical clinical course, above all to rule out chronic infectious and neoplastic disease.

To assess the possibility of an underlying infectious etiology in CIU, a prerequisite would be to achieve a sufficient sensitivity of microbiological testing. Surprisingly, the diagnostic sensitivity of standard microbiological means (growth and stains) is only 40% to 70% (4-6). An improved sensitivity might be achieved by the combination of standard microbiological culture and DNA-based tests in the detection of an infectious origin. In order to estimate the sensitivity of this test combination, we also wanted to analyze not pretreated cases of acute postoperative endophthalmitis. Hence, in contrast to CIU, acute postoperative endophthalmitis is a well-defined clinical disease entity in consequence of bacterial infection.

Functional improvement, the therapeutic effect, and complications of vitrectomy onto the inflammatory activity in chronic uveitis have been extensively studied and established as a reason for vitrectomy. They were therefore not addressed in this study although functional outcome was clearly a reason for surgery and beneficial therapeutic effects were desired. In contrast, we focused in this study on the diagnostic yields of clinically guided vitreous specimen workup from idiopathic uveitis cases, where preoperative diagnostic efforts were inconclusive and a clinically guided treatment had not resulted in a satisfying stabilization of inflammatory activity and function.

PATIENTS AND METHODS

Clinical and laboratory results were analyzed retrospectively from a consecutive series of patients with idiopathic endogenous uveitis or acute postoperative endophthalmitis who had undergone vitrectomy in a 10-year period from July 1990 to December 2000 at our institution.

The spectrum of laboratory analyses applied to each vitrectomy specimen was directed following clinical suspicion following the recommendations provided by Coté and Rao (7), Fujikawa and Haugen (8), and Verbraeken (9) for chronic endogenous uveitis and the method described by Davis et al (10), Sharma et al (11), and Barza et al (12) for acute endophthalmitis. In selected cases eubacterial PCR was additionally performed according to published protocols (13). PCR amplification of viral (herpes simplex virus, cytomegalovirus, varicella zoster virus) and parasite DNA (Toxoplasma gondii) was performed and total and specific IgG were quantified from aqueous humor and serum samples in cases of suspected viral or toxoplasmic etiology, when indicated (14). None of the tests was performed as a standard in any case.

Chronic endogenous uveitis was diagnosed in accordance with the International Uveitis Study Group recommendations (15). All cases had at least some visual disturbance though visual acuity reached 20/20 in some cases. Disease activity was evident by fresh cellular infiltrates on the corneal backface and the vitreous in all cases, but varied widely between the eyes. None of the cases had acute disease of less than 60 days duration, and disease exacerbation under treatment was in no instance the reason for proceeding to surgery. None of the cases had a focal chorioretinal disease or active chorioretinal lesions compatible with any of the typical underlying infectious etiologies. The clinically tailored work up had therefore always to differentiate between the possibilities of lymphoma, immunologic imbalance, or an infectious etiology. According to clinical judgment, the vitreous analysis included the detection of infectious DNA, antibody and inflammatory cell type analysis, and cytologic definition of inflammatory cell type and activity, evidence for an infectious etiology, i.e. mycobacteria, or malignancy.

Acute postoperative endophthalmitis (Group 2) was defined as severe intraocular inflammation occurring within 14 days after intraocular surgery.

Patients with the following criteria were excluded from the study: 1) eyes with postoperative uveitis due to retained lens fragments or penetrating eye trauma, 2) chronic postoperative endophthalmitis, i.e., of mycotic origin. All patients of Group 1 had gone through extensive serologic testing and clinical rheumatologic work up (Tab. I) prior to surgery.

The primary outcome measure of this study was the overall diagnostic yield of vitrectomy specimen analysis. Descriptive data analysis included mean, standard deviation, as well as minimal and maximal values. Statistical assessment was performed using the two-tailed Student t test for quantitative data comparison (GB-Stat V10, 2003; Dynamic Microsystems, Silver Spring, MD) on a significance level of $p < 0.05$.

RESULTS

From a total of 95 eyes that underwent diagnostic vitrectomy, 56 eyes (58.9%) of 52 patients were assigned to Group 1, 21 (22.1%) eyes of 21 patients to Group 2. Eigh-

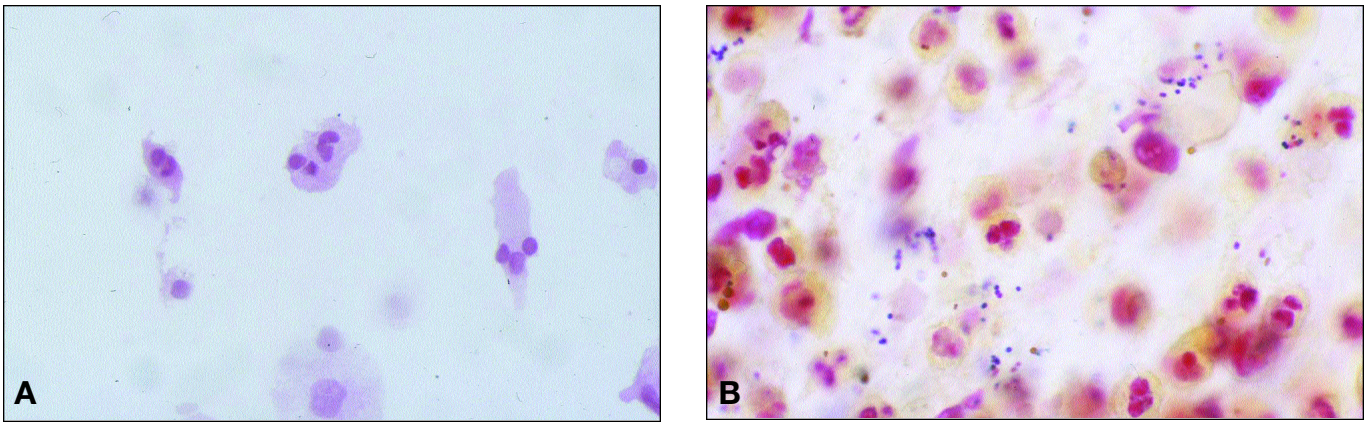

Fig. 1 - (**A**) *Cytopathological smear of a Group 1 vitrectomy sample: a few neutrophils and lymphocytes, two histiocytes, and scattered cell de bris.* (**B**) *Gram stain of a Group 2 vitrectomy sample: gram-positive cocci.*

teen (19%) eyes did not meet the inclusion criteria (drop out). The mean age of Group 1 patients was 50.4 years (range 8–84; SD 20.4 years), that of Group 2 patients 77.5 years (range 61–90; SD 7.0 years; $p < 0.01$). On average, intraocular inflammation had preoperatively been observed for 46.1 months (range 3–372; SD 72.9) in Group 1. The mean follow-up time was 21.2 months (range 1–96; SD 24.5) in Group 1, and 13.9 months (range 1–60; SD 19.2) in Group 2 ($p = 0.22$).

Preoperative serologic workup was normal in 15 patients (28.8%) of Group 1. An autoimmune basis was suspected in 6 patients (11.5%), ocular sarcoidosis in 7 cases (13.5%), either an infectious etiology or lymphoma requiring exclusion prior to the start of immunosuppressive therapy in 25 instances (48.1%). The explicit suspicion of a lymphoma was given in 5 instances (8.9%). The remaining patients showed nonspecific changes. All 21 patients (100%) of Group 2 had an inconspicuous routine serologic workup.

Vitreous sample analyses were guided by the preoperative or intraoperative differential diagnosis (Tab. II).

After interpretation of all performed tests the suspected diagnosis could be confirmed in 10 cases (17.9%) and a presumed diagnosis could be excluded in 12 patients of Group 1 (21.4%). There was presumptive evidence supporting but not confirming the clinical diagnosis in 5 additional cases from Group 1 (8.9%). Finally, there was no diagnostic evidence in 29 of Group 1 (51.8%). Overall, a conclusive result was available in 22 out of 56 (39.3%) eyes in Group 1 (Tab. III).

Neoplastic disease was excluded in nine instances, among them eight suspected intraocular lymphomas. In all these cases, the clinical course was consistent with the cytopathologic diagnosis. In three cases a systemic non-Hodgkin's lymphoma was known at the time of vitrectomy, which was performed to assess ocular involvement. This was confirmed in two instances and denied in one case. An ocular non-Hodgkin's lymphoma was unexpectedly uncovered in two Group 1 cases.

In 15 Group 1 cases aqueous and vitreous samples were submitted for analysis of a possible infectious etiology. Among these, viral or parasite DNA (herpes simplex

TABLE I - WORKUP BASED ON THE PREOPERATIVE EXAMINATION AND CLINICAL HISTORY

Chest x-ray*
Erythrocyte sedimentation rate
C-reactive protein
Blood cell counts and differentiation
T-cell subpopulations*
Total serum IgG, IgA, IgM, and IgE levels
Complement C3 and C4
C1q containing immune complexes
Antinuclear antibodies
Antinuclear cytoplasmic antibodies (c- and p-ANCA)*
Anti SS-A and -B*
Rheuma factor latex screening test
Anticardiolipin antibodies
Antibodies to HSV, VZV, CMV
Anti-Toxoplasma gondii antibodies
Lyme borreliosis serology including immunoblot if positive*
Serum angiotensin converting enzyme activity*
HIV, hepatitis B and C, and lues serology*
HLA-typing*
Intracutan anergy testing (Multitest Merieux) and pathergy test*

*Facultatively performed analyses.

virus 1, cytomegalovirus, and T gondii) could be amplified in three instances. In one of them, intraocular T gondii infection was unexpectedly found, and in three instances, infectious disease was excluded. In another two, evidence for a parasitic, i.e., toxoplasmic etiology was based on a positive antibody ratio (Goldmann Witmer index). In one Group 1 patient, eubacterial PCR identified coagulase-negative Staphylococcus hyicus, most likely a contaminant from the skin flora (Tab. II).

Bacterial growth was detected in 10 out of 21 Group 2 endophthalmitis samples (47.6%) with the identification of coagulase-negative staphylococci (six times), Staphylococcus aureus (twice), Pseudomonas aeruginosa (once), and viridans streptococcus (once). Eight Group 2 samples, among them five with bacterial growth and three without, were sent out for eubacterial PCR; in six of them bacterial DNA amplification identified a causative agent (75%) consistent with the clinical diagnosis. In one culture-negative sample eubacterial PCR analysis revealed the presence of Abiotrophia defectiva, an organism which has been implicated for ocular infections before (16, 17). A defectiva is difficult to grow and therefore culture results are often false negative. From one sample, a mixture of bacterial DNAs was amplified not allowing further identification. Overall, in Group 2 two out of five culture-confirmed samples were PCR-negative (Tab. IV).

DISCUSSION

The clinically directed analysis of vitrectomy specimens in Group 1 allowed an exclusion or confirmation of a specific diagnosis in 40% of samples. The remaining 60% did not provide diagnostically relevant information. In Group 2, however, the addition of eubacterial PCR increased the diagnostic sensitivity from less than 50% to more than 80%. This provides evidence that the low diagnostic yield in idiopathic uveitis is most likely not related to tissue immanent factors or sample processing methods but most likely related to our insufficient understanding of the disease mechanism.

Obviously, understanding the underlying pathobiology is a prerequisite for a successful diagnostic strategy. Indeed, chronic endogenous uveitis without chorioretinal lesions is the least understood group of intraocular inflammations and has evaded widely all diagnostic efforts. It is thus not surprising that the relevance of vitrectomy sample analysis in endogenous uveitis is controversial (3). This is partially related to immanent confounding factors, i.e., the duration of disease, which is usually long, and a multidrug immunomodulatory pretreatment, both of which may have a substantial impact on the results. Many reports pointed out that preoperative antibacterial or antiviral therapies dramatically lower the sensitivity of diagnostic tests (18-20). The same applies for steroids, which are known to induce apoptosis in lymphoma cells (21). However, the unexpected detection of two intraocular lymphomas in Group 1 underlines the importance of cytopathologic analysis particularly in patients with refractory disease. The exclusion of a specific diagnosis may be achieved in most cases, which is of primary clinical relevance regarding the therapeutic options. And the diagnostic yield in our series is comparable to the more invasive diagnostic chorioretinal biop-

TABLE II - SPECIMEN ANALYISES PERFORMED

Type of analysis	Uveitis, n=56		Endophthalmitis, n=21	
	Total (% of all)	Positive (%)	Total (% of all)	Positive(%)
Cytopathologic	5	219*	4	0
	(92.9)	(36.5)	(19.0)	(0)
Microbiological	9	0	21	10
	(16.1)	(0)	(100)	(47.6)
PCR (viral and Toxoplasma)	15	3	0	0
	(26.8)	(20.0)	(0)	(0)
PCR (eubacterial)	8	1†	8	5
	(14.3)	(12.5)	(38.1)	(62.5)
Quantitative analysis of specific antibodies	6	2	0	0
	(10.7)	(33.3)	(0)	(0)

*Confirming/excluding a suspected diagnosis †Most likely false positive contaminant

sy, which yields a conclusive diagnosis in 54% (22).

The quality of cytopathologic vitrectomy specimen analysis depends widely on the number of intact cells which in turn is related to the cutting rates and suction strength of vitreous cutters (23-25), frequently preventing the application of immunohistochemistry (26). Nevertheless, vitreous cytopathology may be sufficiently sensitive to differentiate acute infectious from chronic inflammatory disease, but fails to provide additional information in most cases (Fig. 1, A and B) (27). However, cytopathology may uncover an underlying fungal, mycobacterial, or lymphomatous etiology (27). The major diagnostic challenge lies in the distinction between inflammatory lymphoid infiltrates and intraocular lymphoma in particular when only very few intact cells are present (28).

TABLE III - LEVEL OF DIAGNOSTIC EVIDENCE OBTAINED

Level of diagnostic evidence	Uveitis, n=56, n (%)	Endophthalmitis, n=21, n (%)*
Confirmed	10 (17.9)	10 (47.6)
Excluded	12 (21.4)	0
Probable	5 (8.9)	0
None	29 (51.8)	11 (52.4)
Total of conclusive analyses (excluded/confirmed)	22 (39.3)	10 (47.6)

*Only conventional microbiological analysis (culture and stains) included.

In the literature the microbiologic yield (growth and stain) of vitrectomy samples in endophthalmitis varies from 20% to 69% (5, 6, 29) in agreement with our rate of 47.6%. Possibly the yield is largely dependent on tissue processing and the skills of the investigator. The introduction of DNA-based methods has greatly increased the identification rate of a causative organism. The identification of bacteria after amplification of a common bacterial DNA sequence (16S ribosomal RNA) allows for distinction of the major bacterial causes of postoperative endophthalmitis (30, 31). However, all these additional laboratory tests may contribute little if they are not based on clinical grounds. Furthermore, the detection of microorganisms by means of microbiological or molecular techniques does not necessarily confirm their active contribution. Most importantly, it may also be attributable to falsely positive test results due to sample contamination (32). Similar aspects need to be considered for eubacterial PCR. Although it might allow for identification of an organism in case of negative culture testing (33) its clinical relevance in vitreous sample analysis has as yet not been established. The possibility of either pathophysiologically not relevant or contaminating bacterial DNA can never be ruled out and strategies to minimize this risk have been proposed (34-36). However, in this study bacterial DNA was found in only 1/8 (12.5%) Group 1 specimens (Tab. IV). Another source of false-positive results derives from latent host DNA in viral disease. Many herpesviruses, for

TABLE IV - RESULTS OF CULTURE AND EUBACTERIAL PCR IN COMBINED ANALYSIS OF SELECTED CASES

	Sample	Culture	Eubacterial PCR
Group 1	Anterior chamber	Not performed	Negative
	Anterior chamber	Not performed	Negative
	Vitreous	Not performed	Negative
	Anterior chamber	Not performed	Negative
	Vitreous	Not performed	Negative
	Vitreous	Not performed	Negative
	Vitreous	Not performed	*Staphylococcus hyicus*
	Anterior chamber	Not performed	Negative
Group 2	Anterior chamber	Viridans streptococci	*S mitis*
	Vitreous	Coagulase-negative staphylococci	*S haemolyticus*
	Anterior chamber	Coagulase-negative staphylococc	Negative
	Vitreous	Coagulase-negative staphylococci	*S epidermidis*
	Anterior chamber	S aureus	Negative
	Anterior chamber	No growth	*Streptococcus species*
	Anterior chamber	No growth	A defectiva
	Anterior chamber	No growth	Mixture*

*Considered positive (in line with clinical picture.

instance, can become integrated into the host genome; therefore, results of PCR must always be kept in a clinical context (37). Inhibition of PCR by inflammatory or vitreous material (38) was not a major problem in our series as indicated by the fact that 6/8 Group 2 specimens were positive by eubacterial PCR. The fact that all 8 specimens were positive by either or both methods points in the direction that culture and PCR should be performed with specimens from patients with acute postoperative endophthalmitis.

Despite the advances in biotechnology in recent years and an increased reliability to rule out an infectious etiology (39, 40), the diagnostic yield of vitrectomy specimen analysis for chronic endogenous uveitis remains low. Hence an infectious etiology—once considered possibly contributing to the disease—would be detectable with a sufficient high sensitivity; this etiology may be considered rarely underlying this disease.

In conclusion, this study has shown that diagnostic pars plana vitrectomy and clinically directed vitreous fluid analysis can help to establish or exclude a specific diagnosis in a certain, but as yet not satisfying number of chronic endogenous uveitis cases. The benefits of PCR-based assays with a higher sensitivity (41) have not resulted in an improved diagnostic yield and thus generally remain to be evaluated regarding their clinical relevance.

No authors have any proprietary interest.

Reprint requests to:
Justus G. Garweg, MD
Swiss Eye Institute
Gossetstr. 43
CH-3084 Wabern, Switzerland
justus.garweg@hotmail.com

REFERENCES

1. Smith JR, Rosenbaum JT. Management of uveitis: a rheumatologic perspective. Arthritis Rheum 2002; 46: 309-18.
2. Priem H, Verbraeken H, de Laey JJ. Diagnostic problems in chronic vitreous inflammation. Graefes Arch Clin Exp Ophthalmol 1993; 231: 453-6.
3. Mruthyunjaya P, Jumper JM, McCallum R, Patel DJ, Cox TA, Jaffe GJ. Diagnostic yield of vitrectomy in eyes with suspected posterior segment infection or malignancy. Ophthalmology 2002; 109: 1123-9.
4. Hanscom TA. Postoperative endophthalmitis. Clin Infect Dis 2004; 38: 542-6.
5. Zell K, Engelmann K, Bialasiewicz AA, Richard G. Endophthalmitis nach Kataraktoperation. Disponierende Faktoren, Erreger und Therapie. Ophthalmologe 2000; 97: 257-63.
6. Han DP, Wisniewski SR, Kelsey SF, Doft BH, Barza M, Pavan PR. Microbiologic yields and complication rates of vitreous needle aspiration versus mechanized vitreous biopsy in the Endophthalmitis Vitrectomy Study. Retina 1999; 19: 98-102.
7. Cote MA, Rao NA. The role of histopathology in the diagnosis and management of uveitis. Int Ophthalmol 1990; 14: 309-16.
8. Fujikawa LS, Haugen JP. Immunopathology of vitreous and retinochoroidal biopsy in posterior uveitis. Ophthalmology 1990; 97: 1644-53.
9. Verbraeken H. Diagnostic vitrectomy and chronic uveitis. Graefes Arch Clin Exp Ophthalmol 1996; 234 Suppl 1: S2-S7.
10. Davis JL, Chan CC, Nussenblatt RB. Diagnostic vitrectomy in intermediate uveitis. Dev Ophthalmol 1992; 23: 120-32.
11. Sharma S, Jalali S, Adiraju MV, Gopinathan U, Das T. Sensitivity and predictability of vitreous cytology, biopsy, and membrane filter culture in endophthalmitis. Retina 1996; 16: 525-9.
12. Barza M, Pavan PR, Doft BH, et al. Evaluation of microbiological diagnostic techniques in postoperative endophthalmitis in the Endophthalmitis Vitrectomy Study. Arch Ophthalmol 1997; 115: 1142-50.
13. Bosshard PP, Kronenberg A, Zbinden R, Ruef C, Bottger EC, Altwegg M. Etiologic diagnosis of infective endocarditis by broad-range polymerase chain reaction: a 3-year experience. Clin Infect Dis 2003; 37: 167-72.
14. Kijlstra A, Luyendijk L, Baarsma GS, et al. Aqueous humor analysis as a diagnostic tool in toxoplasma uveitis. Int Ophthalmol 1989; 13: 383-6.
15. Bloch-Michel E, Nussenblatt RB. International Uveitis Study Group recommendations for the evaluation of intraocular inflammatory disease. Am J Ophthalmol 1987; 103: 234-5.
16. Namdari H, Kintner K, Jackson BA, et al. Abiotrophia

species as a cause of endophthalmitis following cataract extraction. J Clin Microbiol 1999; 37: 1564-6.
17. Ormerod LD, Ruoff KL, Meisler DM, et al. Infectious crystalline keratopathy. Role of nutritionally variant streptococci and other bacterial factors. Ophthalmology 1991; 98: 159-69.
18. Chee SP, Jap A. Endogenous endophthalmitis. Curr Opin Ophthalmol 2001; 12: 464-70.
19. Okada AA, Johnson RP, Liles WC, D'Amico DJ, Baker AS. Endogenous bacterial endophthalmitis. Report of a ten-year retrospective study. Ophthalmology 1994; 101: 832-8.
20. Nogueira ML, Siqueira RC, Freitas N, et al. Detection of herpesvirus DNA by the polymerase chain reaction (PCR) in vitreous samples from patients with necrotising retinitis. J Clin Pathol 2001; 54: 103-6.
21. Chan CC, Buggage RR, Nussenblatt RB. Intraocular lymphoma. Curr Opin Ophthalmol 2002; 13: 411-8.
22. Johnston RL, Tufail A, Lightman S, et al. Retinal and choroidal biopsies are helpful in unclear uveitis of suspected infectious or malignant origin. Ophthalmology 2004; 111: 522-8.
23. Uy HS, Foster CS. Diagnostic vitrectomy and Uveitis. Int Ophthalmol Clin 1999; 39: 223-35.
24. Huang JS, Russack V, Flores-Aguilar M, Gharib M, Freeman WR. Evaluation of cytologic specimens obtained during experimental vitreous biopsy. Retina 1993; 13: 160-5.
25. Sebag J. Anomalous posterior vitreous detachment: a unifying concept in vitreo-retinal disease. Graefes Arch Clin Exp Ophthalmol 2004; 242: 690-8.
26. Davis JL, Solomon D, Nussenblatt RB, Palestine AG, Chan CC. Immunocytochemical staining of vitreous cells. Indications, techniques, and results. Ophthalmology 1992; 99: 250-6.
27. Liu K, Klintworth GK, Dodd LG. Cytologic findings in vitreous fluids. Analysis of 74 specimens. Acta Cytol 1999; 43: 201-6.
28. Karikehalli S, Nazeer T, Lee CY. Intraocular large B-cell lymphoma. A case report. Acta Cytol 2004; 48: 207-10.
29. Palexas GN, Green WR, Goldberg MF, Ding Y. Diagnostic pars plana vitrectomy report of a 21-year retrospective study. Trans Am Ophthalmol Soc 1995; 93: 281-308.
30. Knox CM, Cevallos V, Margolis TP, Dean D. Identification of bacterial pathogens in patients with endophthalmitis by 16S ribosomal DNA typing. Am J Ophthalmol 1999; 128: 511-2.
31. Okhravi N, Adamson P, Matheson MM, Towler HM, Lightman S. PCR-RFLP-mediated detection and speciation of bacterial species causing endophthalmitis. Invest Ophthalmol Vis Sci 2000; 41: 1438-47.
32. Mames RN, Friedman SM, Stinson WG, Margo CE. Positive vitreous cultures from eyes without signs of infectious endophthalmitis. Ophthalmic Surg Lasers 1997; 28: 365-9.
33. Kerkhoff FT, van der ZA, Bergmans AM, Rothova A. Polymerase chain reaction detection of Neisseria meningitidis in the intraocular fluid of a patient with endogenous endophthalmitis but without associated meningitis. Ophthalmology 2003; 110: 2134-6.
34. Frelich VS, Murray DL, Goei S, Nussbaum J, Butler H. Neisseria meningitidis endophthalmitis: use of polymerase chain reaction to support an etiologic diagnosis. Pediatr Infect Dis J 2003; 22: 288-90.
35. Sharma S, Das D, Anand R, Das T, Kannabiran C. Reliability of nested polymerase chain reaction in the diagnosis of bacterial endophthalmitis. Am J Ophthalmol 2002; 133: 142-4.
36. Buggage RR, Callanan DG, Shen DF, Chan CC. Propionibacterium acnes endophthalmitis diagnosed by microdissection and PCR. Br J Ophthalmol 2003; 87: 1190-1.
37. Van Gelder RN. Applications of the polymerase chain reaction to diagnosis of ophthalmic disease. Surv Ophthalmol 2001; 46: 248-58.
38. Wiedbrauk DL, Werner JC, Drevon AM. Inhibition of PCR by aqueous and vitreous fluids. J Clin Microbiol 1995; 33: 2643-6.
39. Lohmann CP, Heeb M, Linde HJ, Gabel VP, Reischl U. Diagnosis of infectious endophthalmitis after cataract surgery by polymerase chain reaction. J Cataract Refract Surg 1998; 24: 821-6.
40. Knox CM, Chandler D, Short GA, Margolis T. Polymerase chain reaction-based assays of vitreous samples for the diagnosis of viral retinitis. Use in diagnostic dilemmas. Ophthalmology 1998; 105: 37-44.
41. Therese KL, Anand AR, Madhavan HN. Polymerase chain reaction in the diagnosis of bacterial endophthalmitis. Br J Ophthalmol 1998; 82: 1078-82.